

## Strain Bull's Eye Plot Derived from 3D Speckle Tracking Imaging in Children with Dilated Cardiomyopathy

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### ABSTRACT

**Background:** Cardiomyopathies (CMPs) are a group of myocardial diseases with adverse outcomes.

**Aim of the study:** Was to evaluate the global and segmental 3-dimensional strain using speckle tracking echocardiography in children with dilated cardiomyopathy and correlate this parameter with other echocardiographic findings especially 2-dimensional strain (2DS bull's eye).

**Patients and Methods:** 100 subjects were categorized into 2 groups: Group 1; 50 patients with dilated cardiomyopathy. Group 2; 50 healthy controls matched with the patient group. Echocardiographic studies were performed by the following: Routine echocardiographic examination, tissue Doppler examination (TDE): [systolic and diastolic mitral annulus velocities - LV myocardial performance Index (MPI)], speckling tracking technique [2D LV longitudinal strain (2DS bull's eye) - Auto EF for LV systolic function - sphericity index] and transthoracic 3DE examination (3DRTE) [3D longitudinal strain (3DS bull's eye)].

**Results:** There was a significant reduction in left ventricular ejection fraction (LVEF), sphericity index (SI), mitral annulus systolic velocity (S), early diastolic mitral annulus tissue velocity and late diastolic mitral annulus tissue velocity (E/A) and LV GLS (global longitudinal strain) in patients when compared with controls but there was a significant increase in myocardial performance index (MPI) and 2 dimensional (2DS) than 3 dimensional (3DS) in patients when compared with controls. There was significant positive correlation between 2DS and 3DS GLS among patients also, there was good agreement between all items in 2DS and 3DS in patients group. **Conclusion:** The bull's eye plot offers an intuitive visual overview of LV myocardial function status in cardiomyopathies.

**Keywords:** Strain Bull's Eye Plot, 3D Speckle Tracking imaging, Dilated Cardiomyopathy.

### INTRODUCTION

Cardiomyopathy (CMP) is defined as a disease of the myocardium linked to cardiac dysfunction. Understanding of CMP is very important, because it is related to heart failure in children and is the most common indicator for heart transplantation in children over one year old <sup>(1)</sup>.

Dilated Cardiomyopathy (DCM) is a myocardial disorder characterized by a dilated left ventricular (LV) chamber and systolic dysfunction which usually leads to congestive heart failure (CHF). In some patients, right ventricular dysfunction (RVD) is also noted and observed and may increase the severity of the clinical disease <sup>(2)</sup>.

The newly developed 3D speckle tracking in real time 3D echocardiographic (RT3DE) datasets has the potential to circumvent these limitations because: (i) it does not depend on 2D views that can be foreshortened, and (ii) it tracks motion of speckles within the scan volume, irrespective of its direction. Three-dimensional (3D) STE has been shown to enable analysis of deformities in myocardium in its longitudinal, circumferential and radial direction in a single 3D volume set <sup>(3)</sup>. Three-dimensional strain-relay on sequences provides both quantitative and qualitative information regarding tissue motion and deformation <sup>(4)</sup>.

### AIM OF THE STUDY

It was to evaluate the global and segmental 3-dimensional strain using speckle tracking echocardiography in children with dilated cardiomyopathy and correlate this parameter with other echocardiographic findings especially 2-dimensional strain (2DS bull's eye).

### PATIENTS AND METHODS

This observational case-control study was carried out during the period from April 2018 to January 2019 at Pediatric Cardiology Unit, Tanta University Hospital. It included 100 subjects who were classified into 2 groups. **Group 1:** 50 patients with primary dilated cardiomyopathy aged from 6 months up to 8 years, those patients attended the Cardiology Unit Pediatric department, Tanta University Hospital. **Group 2:** 50 healthy children matched for age and sex.

**Inclusion criteria:** Children less than 15 years with primary dilated cardiomyopathy.

**Exclusion criteria:** Children with congenital or acquired heart diseases other than dilated cardiomyopathy. Also; children with dilated cardiomyopathy secondary to systemic diseases were excluded. Written informed consent was obtained from

the parents or guardians of the child.

**The study was approved by the Ethics Committee of Faculty of Medicine, Tanta University.**

**Collection of data:** All infants and children were subjected to:

1. **Complete History Taking:** Including personal, birth, developmental, feeding, and family history.
2. **Thorough Clinical Examination:** Including general, regional and systemic examination as body weight, height and vital signs; heart rate, blood pressure. Cardiac examination for detection of cardiomegaly and evidence of murmur was performed.
3. **Investigations:**
  - Echocardiographic Examination.
    - 1- Machine: Echocardiographic studies were performed using a commercially available ultrasound transducer and equipment (Vivid 7 or Vivid 9, GE Healthcare, Horten, Norway).
    - 2- Transducers: Data acquisition was performed with a 3.5-MHz transducer, S7, and V3 matrix real-time 3 dimensional probes.
    - 3- Workstation: Digital loops were stored on the hard disk of the echocardiography machine, and transferred to a workstation (Echo PAC PC, 112 and 113; GE, and Horten, Norway) for offline analysis.
  - Echocardiographic technique:
    - 1- Routine conventional echocardiographic

examination:

- 2- Tissue Doppler Examination (TDE):
  - (A) Systolic and diastolic mitral annulus velocities<sup>(5)</sup>.
  - (B) LV Myocardial Performance Index (MPI)<sup>(6)</sup>.
- 3- Speckling Tracking Technique:
  - (A) 2D LV Longitudinal Strain<sup>(7)</sup> and Longitudinal strain bull's eye plot acquisition<sup>(8)</sup>.
  - (B) Auto EF for LV systolic function<sup>(9)</sup>.
  - (C) Sphericity Index<sup>(9)</sup>.
- 4- Transthoracic 3DE Examination (3DRTE): 3D Longitudinal Strain (3DS bull's eye)<sup>(10)</sup>.

**Statistical analysis**

In addition to the descriptive data, statistical analysis was done using IBM SPSS STATISTIC VERSION 23 PROGRAM. Data were expressed as mean ± SD and analyzed using the standard student "t test", test of significance of the difference between two means. The calculated "t" was compared with tabulated one at different levels of significance at the degree of freedom (df). P <0.05 was accepted as significant. Coefficient (r) of two variables was also done by using Pearson correlation coefficient (r) with p-value Calculation.

**RESULTS**

Laboratory assessments of the measured parameters are presented in the following tables and figures:

**Table (1): Comparison between patients and controls regarding age**

Groups	Age (years)		T-test	
	Range	Mean±SD	T	P-value
Patients	0.5 - 8	4.466 ± 1.814	1.679	0.090
Controls	0.75 - 8	3.633 2.024		

Table (1) showed that there was no statistically significant difference was found between studied groups regarding age.

**Table (2): Sex distribution in the studied groups**

Sex		Groups		
		Patients	Controls	Total
Male	N	30	30	60
	%	60	60	60.00
Female	N	20	20	40
	%	40	40	40.00
Total	N	50	50	100
	%	100.00	100.00	100.00
Chi-Square	X <sup>2</sup>	0.016		
	P-value	0.901		

Table (2) showed that there was no statistically significant difference was found between studied groups regarding sex.

**Table (3): Comparison between patients and control as regards ejection fraction (EF) measured by auto EF**

Groups	LVEF(%)		T-test	
	Range	Mean $\pm$ SD	T	P-value
Patients	13 - 60	43.360 $\pm$ 11.760	2.137	<0.001*
Controls	60 - 70	65.234 $\pm$ 7.589		

Table (3) showed that the LVEF in Patients ranged from 13.0 – 60.0 with mean 43.360  $\pm$  11.760. The LVEF in control ranged from 60.0 – 70.0 with mean 65.234  $\pm$  7.589. There was a statistically significant reduction in LVEF in patients when compared with controls. There was a significant reduction of EF in patients when compared with controls.

**Table (4): Comparison between patients and control as regards sphericity index (SI) measured by 3DE**

Groups	LV SI		T-test	
	Range	Mean $\pm$ SD	T	P-value
Patients	0.11 - 1.63	1.197 $\pm$ 0.345	4.599	<0.001*
Controls	1.2 - 2.15	1.566 $\pm$ 0.272		

P-value <0.05 = Significant

Table (4) showed that the SI in patient ranged from 0.11 to 1.63 with mean 1.197  $\pm$  0.345, the SI in control group ranged from 1.2 to 2.15 with mean 1.566  $\pm$  0.272, there was a statistically significant reduction in SI in patients when compared with controls.

**Table (5): Comparison between patients and control as regards (Mitral Annulus systolic velocity) measured by Tissue Doppler examination (TDI)**

Group	S(cm/second)		T-test	
	Range	Mean $\pm$ SD	T	P-value
Patients	2 - 6	3.667 $\pm$ 1.061	13.554	<0.001*
Control	6 - 8	6.933 $\pm$ 0.785		

S: Mitral Annulus systolic velocity.

Table (5) showed that the S in studied group ranged from 2 to 6 cm/sec with mean 3.667 $\pm$  1.061, The S in control group ranged from 6 to 8 cm/sec. with mean 6.933 $\pm$  0.785. There was a significant reduction of mitral annulus systolic velocity in patients when compared with controls.

**Table (6): Comparison between patients and control as regards (E'/A' ratio) measured by Tissue Doppler Imaging (TDI).**

Group	E'/A'		T-test	
	Range	Mean $\pm$ SD	T	P-value
Patients	0.6 - 1.8	1.147 $\pm$ 0.401	4.584	<0.001*
Controls	1.1 - 1.9	1.540 $\pm$ 0.246		

E'=Early diastolic mitral annulus tissue velocity and A'= Late diastolic mitral annulus tissue velocity.

Table (6): Shows comparison of mean value of E'/A' in relation to studied group:

- The E'/A' in studied group ranged from 0.6 to 1.8 with mean 1.147  $\pm$  0.401,
- The E'/A' in control group ranged from 1.1 to 1.9 with mean 1.540 $\pm$  0.246,
- There was a significant reduction of (E'/A' ratio) in patients when compared with controls.

**Table (7): Comparison between patients and control as regards LV Myocardial Performance Index (MPI) measured by Tissue Doppler Imaging (TDI).**

Groups	MPI		T-test	
	Range	Mean ±SD	T	P-value
Patients	1.57 - 2.64	1.876 ±0.233	32.793	<0.001*
Control	0.3 - 0.5	0.407 ± 0.078		

MPI: myocardial performance index.

Table (7) shows comparison of mean value of MPI in relation to studied group:

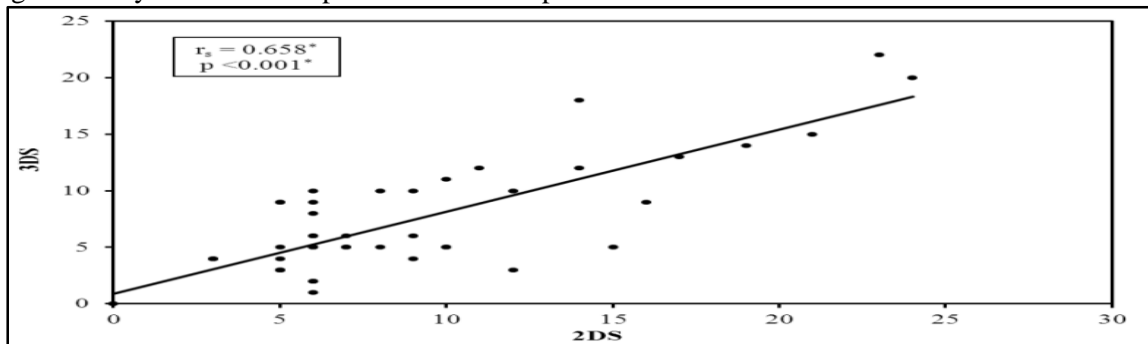
- The MPI of the studied group ranged from 1.57 to 2.64 with mean 1.876± 0.233
- The MPI of the control group ranged from 0.3 to 0.5 with mean 0.407± 0.078
- There was a significant increase in LV Myocardial Performance Index in patients when compared with controls.

**Table (8): Comparison between patients and control as regard LV GLS (LV Global Longitudinal strain) measured by 2 D STE**

Groups	LV GLS (%)		T-test	
	Range	Mean ±SD	T	P-value
Patients	(-5) – (-23)	-12.667 ± 4.943	12.361	<0.001*
Controls	(-22) - (-27)	-24.400 ± 1.610		

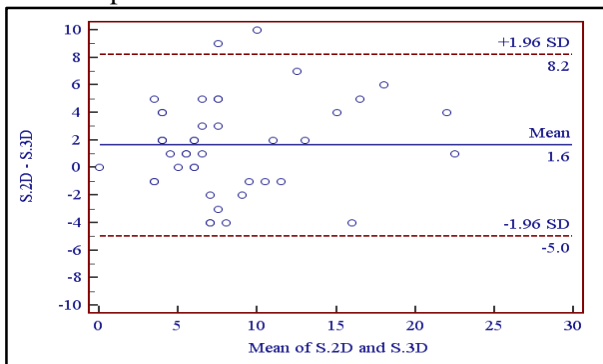
LV GLSS: left ventricular global longitudinal strain.

Table (8) showed that the LV GLS of the studied group ranged from -5 to -23 with mean -12.667± 4.943, The GLSS of the control group ranged from -22 to -27 with mean -24.400 ±1.610, There was significant reduction of LV global longitudinal systolic strain in patients when compared with controls.

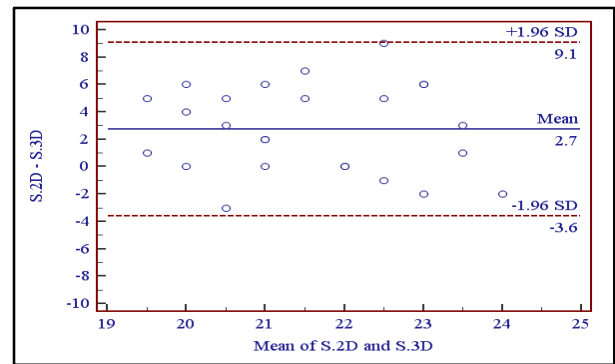


**Figure (1): Correlation between 2DS and 3DS in patients group.**

Figure (1) showed that there was statistically significant positive correlation between 2DS and 3DS among cases with p value = <0.001.



**Figure (2): Agreement between 2DS and 3DS in patients group. p = 0.003\* (Fixed Bias)**



**Figure (3): Agreement between 2DS and 3DS in patients group. p < 0.001\* (Fixed Bias)**

Figure (2, 3) showed that there was an agreement between 2DS and 3DS in patients group.

**Table (9): Comparison between 2D and 3D GLS in each group**

	2DS GLS	3DS GLS	Mean difference	t(p)	r (p)
<b>Patients</b>					
<b>Min. – Max.</b>	(-5.0) – (-23.0)	(-0.30) – (-22.0)	1.63 ± 3.37	3.164* (<0.003*)	0.796* (<0.001*)
<b>Mean ± SD</b>	-12.66 ± 4.94	-7.51 ± 4.99			
<b>Median</b>	-7.50	-6.0			
<b>Control</b>					
<b>Min. – Max.</b>	(-22) – (-27)	-17.0 – 25.0	2.72 ± 3.23	4.205* (<0.001*)	-0.186 (0.374)
<b>Mean ± SD</b>	-24.92 ± 2.0	-20.20 ± 2.20			
<b>Median</b>	-22.0	-20.0			

t: Paired t-test for comparing between the two techniques (if significant there is a difference), r: Pearson coefficient, \*: Statistically significant at  $p \leq 0.05$  GLS=Global Longitudinal Strain

Table (9) showed the following:

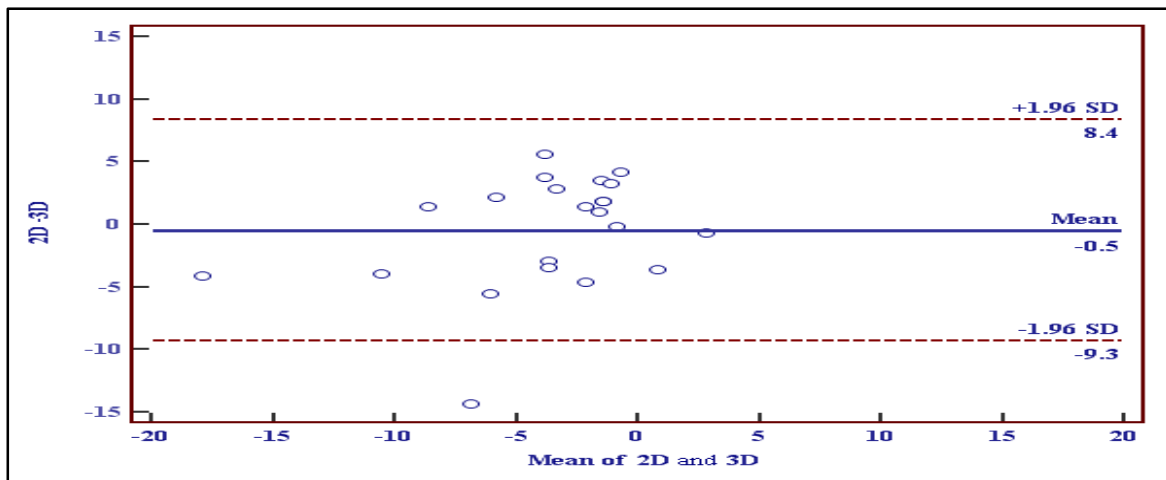
- The 2DS in Patients ranged from -5.0 to -23 with mean  $-12.66 \pm 4.94$ , 3DS in Patients ranged from -0.30 to -22 with mean  $-7.51 \pm 4.99$  There was a statistically significant increase in 2DS than 3DS among cases.
- The 2DS in control group ranged from -22 to -27 with mean  $-24.92 \pm 2.0$ . The 3DS in control group ranged from -17 to -25 with mean  $20.20 \pm 2.20$ , There was a statistically significant increase in 2DS than 3DS among cases among control.

**Table (10): Correlation coefficients of segmental 2D and 3D LS**

2D vs 3D SLSo	r	p	ICC (95% CI)
Basal Ant	0.101	0.681	0.097(-0.352 – 0.515)
Basal anti post.	-0.042	0.887	-0.041(-0.608 – 0.504)
Basal infro. Post.	0.263	0.324	0.216(-0.325 – 0.638)
Basal infer.	0.295	0.220	0.300(-0.178 – 0.659)
Basal Info lat.	0.378	0.100	0.302(-0.078 – 0.631)
Basal ant. Lat.	0.009	0.970	0.009(-0.394 – 0.433)
Mid ant.	-0.008	0.971	-0.009(-0.448 – 0.417)
Mid. Ant. 6 SEBT.	0.186	0.432	0.180(-0.298 – 0.576)
Med inf. Sep.	0.701*	0.001*	0.704(0.395 – 0.871)
Med inf.	0.327	0.254	0.318(-0.214 – 0.712)
Med inf. Lat.	0.331	0.179	0.294(-0.213 – 0.666)
Med ant. Lat.	0.045	0.854	0.046(-0.428 – 0.488)
Apical ant.	0.029	0.907	0.018(-0.292 – 0.394)
Apical sept.	-0.176	0.432	-0.091(-0.387 – 0.279)
Apical in.	0.499*	0.025*	0.371(-0.086 – 0.695)
Apical lat.	-0.178	0.493	-0.124(-0.531 – 0.351)
Apex	-0.141	0.577	-0.044(-0.429 – 0.393)

r: Pearson coefficient \*: Statistically significant at  $p \leq 0.05$  ICC: Interclass Correlation CI: Confidence interval SLS=Segmental Longitudinal Strain.

Table (10) showed that the ICCs were classified using a system suggested by McGraw and Wong 11 as follows: (1) less than 0.75 Z poor agreement; 0.75 to less than 0.90 Z moderate agreement; (3) 0.90 or greater Z high agreement. P value less than 0.05 was considered statistically significant.



**Figure (4): Agreement between 2DS and 3D GLS in patients group(global longitudinal strain)**

Figure (4) showed that there was good agreement between all items between 2DS and 3DS (global longitudinal strain)

## DISCUSSION

Assessing the size and functions of the heart is an integral part of evaluation of cardiac status. For assessing the cardiac functions, M-mode, 2D imaging and Doppler methods can be used to assess the functions of ventricles<sup>(11)</sup>.

A complete 3D echocardiographic study includes assessment of ventricular function, morphology of valves, and hemodynamic status. Unlike 2D echocardiography, where standard views are described depending on the plane through which they pass, 3D echocardiography is inherently volumetric. As such, it allows both an external view of the heart and multiple internal perspectives (through cropping)<sup>(12)</sup>.

The hallmark of the disease is LV dilatation and/or dysfunction. Dilatation may precede dysfunction in many patients and therefore attention to accurate chamber dimensions, indexed according to the surface area of the body is important. This is of particular relevance in the long-term follow-up of DCM patients, in order to evaluate disease progression or response to treatments<sup>(13)</sup>.

The work was conducted on 100 children (50 patients who suffered from primary dilated cardiomyopathy and 50 healthy children as a control group). The age of patients ranged from 6 months up to 8 years, with mean  $4.466 \pm 1.814$  years. There was no significant difference between patients and controls as regard to age and sex. The male distribution was more among dilated cardiomyopathy 27 (54%). The present study is in agreement with **Hershberger et al.**<sup>(14)</sup>, it agrees also with **Towbin et al.**<sup>(15)</sup> and **Cox et al.**<sup>(16)</sup> who explained that boys have a higher DCM incidence than girls, related to X-linked genetic causes.

In the current study SI in patients was measured using speckling tracking technique and was ranged

from 0.11 to 1.63 with mean  $1.197 \pm 0.345$ , The SI in control group was ranged from 1.2 to 2.15 with mean  $1.5666 \pm 0.272$ , There was a statistically significant reduction in SI in patients when compared with controls.

The sphericity index (SI) is the ratio between the short diameter (mid-cavity level in the short axis view) and the long diameter (length between the mitral annulus to apex in the apical view) and this ratio predicts the remodeling of LV and functional capacity in patients with LV dysfunction<sup>(17)</sup>.

**Van Dalen et al.**<sup>(18)</sup> found that, that LV sphericity index was the strongest independent predictor of basal and apical LV peak systolic rotation ( $Rot_{max}$ ) and instantaneous LV peak systolic twist ( $Twist_{max}$ ). LV apical rotation and twist are significantly influenced by LV configuration.

The current study showed that, the mitral annulus systolic velocity (S) assisted by tissue Doppler in patients was ranged from 2 to 6 cm/s with mean  $3.667 \pm 1.061$ , the S in control group was ranged from 6 to 8 cm/s with mean  $6.933 \pm 0.785$ . There was a statistically significant reduction in S in patients when compared with controls. This agrees with previous studies **Abduch et al.**<sup>(19)</sup> who found (S) was significantly lower in the DCM group compared to controls group.

The present study was supported by previous data as **Abduch et al.**<sup>(19)</sup>, **Yu et al.**<sup>(20)</sup>, **McMahon et al.**<sup>(21)</sup>, **Zamorano and Lennie**<sup>(22)</sup>, and **Mohammed and Friedberg**<sup>(23)</sup> who confirmed usefulness for measuring the S' as a tool for assessment of systolic function.

The current study showed that, The E'/A' ratio assisted by tissue Doppler in patients was ranged from. 0.6 to 1.8 with mean  $1.147 \pm 0.401$ , The E'/A' in control

group ranged from 1.1 to 1.9 with mean  $1.540 \pm 0.246$ . There was a statistically significant reduction in E'/A' in patients when compared with controls. These data confirm the diastolic dysfunction in dilated cardiomyopathy patients with impaired LV filling. Similar findings were reported by **Mark et al.**<sup>(24)</sup>. The current study is in contrast with **Abduch et al.**<sup>(19)</sup> who found that, E'/A' ratio was higher in the DCM group compared with controls. The explanation of this discrepancy that the patients of that study may be advanced patients and suffering from restrictive filling during diastole.

The present study showed that the Myocardial Performance Index (MPI) assisted by tissue Doppler in patients was ranged from 1.57 to 2.64 with mean  $1.876 \pm 0.233$ . The MPI in control was ranged from 0.3 to 0.5 with mean  $0.407 \pm 0.078$ , there was a statistically significant increase in MPI in patients when compared with controls. The current study agrees with previous reports as **Abduch et al.**<sup>(19)</sup> and **McMahon et al.**<sup>(21)</sup>. This could be explained due to LV systolic and diastolic dysfunction that reported in our patients, as the MPI reflects both systolic and diastolic function of the ventricles.

The present study showed that the Left ventricular ejection fraction (LVEF) assisted by speckling tracking (auto EF) in patients was ranged from 13 – 60% with mean  $43.360 \pm 11.760$ , the LVEF in control ranged from 60 – 70 % with mean  $65.234 \pm 7.589$ , there was a statistically significant reduction in LVEF in patients when compared with controls. This agrees with **Elkilary et al.**<sup>(2)</sup>, **Abduch et al.**<sup>(19)</sup>, **Koestenberger et al.**<sup>(25)</sup>, **Bergenzaun**<sup>(26)</sup> and **Taşolar et al.**<sup>(27)</sup> who found that LVEF was lower in the DCM group compared to controls group.

This study showed that, the 2DS in patients was ranged from -5 to -23 % with mean  $-12.66 \pm 4.94$ . 3DS in patients was ranged from -3 to -22 with mean  $-7.51 \pm 4.99$ , the 2DS in control group was ranged from -22 to -27 with mean  $-24.92 \pm 2.0$ , the 3DS in control group ranged from -17 to -25 with mean  $-20.20 \pm 2.20$ .

There was significant reduction of LV global longitudinal systolic strain in patients when compared with controls as regard to both 2DS and 3DS. There was a statistically significant increase in 2DS than 3DS among patients. However, there was statistically significant positive correlation between 2DS and 3DS among patients. There was also a good agreement between 2DS and 3D segmental and global longitudinal strain.

This agrees with **Trache et al.**<sup>(28)</sup> who found that, there was statistically significant positive correlation between 2DS and 3DS. They also made comparison of 3D and 2D speckle tracking performed

on standard 2D and triplane 2D datasets of normal and pathological left ventricular (LV) wall-motion patterns with a focus on the effect that 3D volume rate (3DVR), image quality and tracking artifacts have on the agreement between 2D and 3D speckle tracking. 37 patients with normal LV function and 18 patients with ischemic wall-motion abnormalities underwent 2D and 3D echo-cardiography, followed by offline speckle tracking measurements. The values of 3D global, regional and segmental strain were compared with the standard 2D strain values.

The comparative analysis of 2D and 3D GLS values showed very good correlation coefficients between standard/triplane 2D and 3D GLS. Nevertheless, a systematic bias was observed between the 2D and 3D measurements, which was also documented by **Reant et al.**<sup>(29)</sup> that the 3D GLS values were systematically lower than the 2D GLS values, with differences reaching statistical significance. This effect was explained as an effect of out-of-plane speckle patterns, as well as technical differences between the two methods.

## CONCLUSION

The bull's eye plot offers an intuitive visual overview of the global and regional LV myocardial function status in cardiomyopathies. Although the bull's eye plot could provide additional important information in patients with cardiomyopathies with LVH, a comprehensive cardiac workup remains essential to confirm the diagnosis of cardiomyopathies, including the evaluation of family and clinical history, non-cardiac involvements assessment, laboratory and eventually genetic tests, ECG, and multi-modality cardiac imaging (echocardiography, CMRI).

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