Speckle tracking evaluation of right ventricular functions in children with sickle cell disease

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ABSTRACT

Background : **Cardiac dysfunction is a risk factor for death in patients with sickle cell disease (SCD).**

Aim of the Work : **Aim of the work is to evaluate the right ventricular systolic and diastolic functions by tissue Doppler and speckling tracking imaging in children with SCD.**

Subjects and Methods : **Thirty children with SCD and thirty controls were subjected to clinical, laboratory evaluations, and echocardiographic study using GE Vivid 7 (GE Medical System, Horten, Norway with a 3.5-MHz multifrequency transducer) including; Two-dimensional and tissue Doppler echocardiographic study (lateral tricuspid valve annulus peak E′ velocity, lateral tricuspid valve annulus peak A′ velocity, E′/A′ ratio, isovolumetric relaxation time, lateral tricuspid valve annulus S′ and septal S′ waves and peak longitudinal systolic strain [PLSS] and time to PLSS) were done in six right ventricular segments.**

Results : **There was a significant decrease in right ventricular systolic and diastolic function in patients group when compared to controls.**

Conclusions : **Children with SCD have impaired right ventricular systolic and diastolic functions when compared to healthy children with early evaluation of the systolic dysfunction by speckle tracking imaging technique.**

Keywords : Right ventricular functions, sickle cell disease, speckling tracking, tissue Doppler

INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive genetic blood disorder.[1] Under low oxygen conditions, sickle hemoglobin (Hb) distort the shape of red blood cells into a sickle shape, decreasing their elasticity and causing structural damage of in red cell membrane. This leads to impairment of blood flow to microvasculature leading to hemolysis and vaso-occlusive episodes.[2] The process of hemolysis initiates a global attack on the arginine-nitric oxide pathway.[3]

Cardiac abnormalities in SCD are thought to be secondary to volume overload caused by anemia. Persistent anemia results in need for increased cardiac output which is achieved by dilation of all cardiac chambers. However, other factors such as transfusion therapy with iron toxicity and cardiopulmonary injury attributed to vaso-occlusive effect of sickle Hb on the circulation are involved in the pathogenesis of cardiac injuries in sickle patients.[4] Diastolic dysfunction and pulmonary hypertension have been shown to have poor prognosis in patients with SCD.[5] Diastolic and systolic dysfunction

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can be evaluated by tissue Doppler echocardiography and speckle tracking imaging. Speckle tracking is considered an angle-independent technique in the evaluation of myocardial performance.[6]

The aim of the work is to evaluate the right ventricular systolic and diastolic functionby tissue Doppler echocardiography and speckle tracking imaging in children with SCD.

SUBJECTS AND METHODS

After ethics committee approval and informed written consent obtained from all participants in this research; this prospective, randomized, controlled study was conducted on sixty children who were divided into Group (A): thirty children with SCD under follow-up at Hematology and Oncology Unit of Pediatric Department, Tanta University Hospital. Group (B): thirty healthy children as control group matched in age and sex distribution. The inclusion criteria were SCD with age ranged between 6 months to 18 years. The exclusion criteria were other chronic hemolytic anemia, patients with congenital or rheumatic heart diseases.

Methods

All children participating in the study were subjected to the following careful history taking and full clinical examination including full cardiac examination. Echocardiography was performed in Cardiology Unit, Pediatric Department, Tanta University Hospital using GE Vivid 7 (GE Medical System, Horten, Norway with a 3.5 - MHz multifrequency transducer). The echocardiography imaging included the following: Two-dimensional and tissue Doppler echocardiographic study including lateral tricuspid valve annulus peak E' velocity, lateral tricuspid valve annulus peak A' velocity, E'/A' ratio, isovolumetric relaxation time (IVRT), lateral tricuspid valve annulus S' and septal S' waves. Peak longitudinal systolic strain (PLSS) and time to PLSS in 6 RV segments (the basal, mid, and apical segments of the RV free wall and septum) by tracking speckles inside the myocardium using grayscale images. Global PLSS and time to PLSS was based on the average of the six regional values.

Echocardiographic imaging took place in the left lateral decubitus position. Besides the standard parasternal (long and short axis) and apical (2- and 4-chamber) images, additional apical (4-chamber) images were obtained that included the interventricular septum, the apex and the RV free wall up to tricuspid annulus. Images were digitally stored in the cine-loop format for offline analysis. Longitudinal strain was assessed offline, on the 4-chamber cine-loop that included the RV free wall, using speckle-tracking analysis. The speckle-tracking software (Echo PAC Version 112, GE Medical Systems, Horten, Norway) uses natural acoustic markers, or speckles, to determine frame-to-frame movement of myocardium. Images were subdivided into blocks of approximately 20-40 pixels that contain stable patterns of speckles which were followed through the cardiac cycle.[7] In these blocks, the location of speckles was tracked with a dedicated algorithm that uses the sum of absolute differences and specific correlation criteria. After local tissue velocity vectors were derived from the spatial and temporal data of each speckle, strain could be assessed from temporal differences in the mutual distance of neighboring speckles. For longitudinal strain assessment, the software calculated the length of a predefined segment as a percentage of the original length; shortening of a segment was represented as negative strain and lengthening of a segment was represented as positive strain.

Right ventricular longitudinal peak systolic strain was calculated in a user interface by delineating the endocardial border from the basal septum to the apex, along the RV free wall to the tricuspid valve annulus. After a region of interest was set covering the complete width of the myocardium, the software automatically distinguished three predefined septal segments and three RV free wall segments in which longitudinal peak systolic strain was calculated. From these segments, GLPSS was obtained, which is a factory specified weighted average of all six segments.[8] Furthermore, RV LPSS FW was calculated as the average of the three free wall segments. The minimum frame rate used to calculate longitudinal strain was 40 frames/s.

Statistical analysis

Statistical analysis was performed with Statistical Package for Social Science (SPSS version 17).[9] For quantitative data, the mean and the standard deviation were calculated, comparison between the studied groups was performed with Student's *t*-test, with $P < 0.05$ was considered statistically significant. Correlation between variables was evaluated using Pearson's correlation coefficient.

RESULTS

The mean age of patients with SCD was 6–24 months with a mean value 30.6 ± 7.3 months. Hemolytic attacks and vasooclusive crises were the most common presentations (66.7% and 53.3%, respectively). Table 1 summarized laoratory data of the studied patients and controls,there were statistically significant decrease in hemoglobin percent and increase in LDH and serum ferritin in patients when compared to controls. With regard to systolic pulmonary artery pressure estimated by tricuspid regurgitation jet (mmHg), there was no significant difference between patients (30 ± 5) and controls (27 ± 5). There was no significant difference between patients and controls with reagard to right atrial size and right ventricular size. With regard to tissue Doppler echocardiographic parameters in the studied

groups, there was a significant decrease in E', E'/A', IVRT in patient group when compared to controls with a significant increase in A', but a nonsignificant difference was noted as regard to in S' [Table 2]. Trans-tricuspid pulsed wave Doppler and tissue Doppler (E/E') revealed significant increase in patients' E/E' ratio (3.05 ± 0.88) when compared to controls (1.89 ± 0.33). With regard to PLSS and time to PLSS, patients had significantly lower PLSS when compared with controls. No significant difference was noted between patients and controls regarding time to PLSS [Table 3]. There was a significant correlation between PLSS and E', S', and time to PLSS, but no significant correlation was found between PLSS and age, Hb% or ferritin [Tables 4 and 5].

DISCUSSION

Left ventricular dysfunction in patients with SCD has been reported in several studies.[10] The evaluation of right ventricular function is more challenging compared to the left ventricle. The speckle tracking method is more superior over ordinary tissue Doppler techniques because it is angle independent.[11] And also, it depends on deformation measurement which is better than velocity estimation because the latter method may be affected by tethering and translation of healthy myocardium.[12]

In our study, we aimed to use speckle tracking imaging for evaluation of the right ventricular function.

In this study of assessment of Right ventricular function in patients with SCD, we found they had significantly lower E'/A' ratio, lower IVRT, lower peak E' velocity, and higher peak A' velocity in comparison to controls. However, no significant difference was noted between studied groups regarding peak S' wave velocity. There was no significant correlation between E'/A' ratio and age, Hb % and ferritin. Eddine *et al.*, 2012,[13] in their assessment of diastolic function in 55 children with SCD, noted that there is higher E'/A' ratio, and the RV function appears to be well preserved in SCD children. The decrease in IVRT can be explained by the finding of significant increase in E/E' which indicates higher RA mean pressure so that RV-RA pressure cross-over has occured early.

Impairment of diastolic parameters of RV function may be due to the higher susceptibility of the RV. Hyperkinetic circulation and vaso-occlusive effects may have also more effect on the RV, which has substantially a smaller mass than the LV, resulting in faster functional derangement.[4] Furthermore, in agreement with Hankins *et al.*, 2010[14] who studied thirty children with sickle cell anemia, noted that ventricular diastolic dysfunction is common but not associated with myocardial iron deposition. Hence, diastolic dysfunction likely results from disease pathophysiology and severity rather than iron overload.

Table 1: Laboratory investigations of the studied groups

Parameter	Patients (*n*=30)	Controls (*n*=30)	*t*-test	*P*
HB (g/dl)				
Range	7-10.2	11.2-13.5	3.265	0.019*
Mean±SD	7.14±0.76	11.25±2.69		
LDH (u/L)				
Range	265-630	155-225	4.623	0.009*
Mean±SD	352.6±124.40	196.3±48.1		
Serum ferritin (ng\ml)				
Range	1670-5288	100-155	4.611	0.031*
Mean±SD	2152.7±521.5	120.2±5.3		

*P>0.05 considede non significant. HB: Hemoglobin, LDH: Lactate dehydrogenase, SD: Standard deviation

Table 2: Some echocardiographic parameters of the studied groups

Parameter	Patients (*n*=30)	Controls (*n*=30)	*t*	*P*
E' (m/s)				
Range	0.11-0.16	0.12-0.20	1.869	0.047*
Mean±SD	0.128±0.036	0.149±0.024		
A' (m/s)				
Range	0.01-0.06	0.02-0.05	3.326	0.022*
Mean±SD	0.046±0.01	0.032±0.02		
E'/A'				
Range	1.1-2.61	1.22-2.98	5.325	0.001*
Mean±SD	1.47±0.43	2.85±0.62		
S' (m/s)				
Range	0.06-0.08	0.05-0.08	0.635	0.741
Mean±SD	0.06±0.005	0.07±0.006		
IVRT (ms)				
Range	29-58	43-63	2.531	0.017*
Mean±SD	45.6±9.65	52.8±5.30		

*P<0.05 considede significant. E': Early diastolic velocity of TV annulus, A': Late diastolic velocity of TV annulus, S': Tricuspid annular systolic myocardial velocity, IVRT: Isovolumetric relaxation time of RV

Table 3: Peak longitudinal systolic strain and time to peak longitudinal systolic strain of the studied groups

Parameter	Patients (*n*=30)	Controls (*n*=30)	*t*	*P*
PLSS (%)				
Range	−9-−22	−16-−23	2.817	0.009*
Mean±SD	−14.66±4.25	−18.08±1.99		
Time to PLSS (ms)				
Range	312-512	329-538	1.209	0.237
Mean±SD	401.2±53.44	427.4±64.95		

*Significant. PLSS: Peak longitudinal systolic strain, SD: Standard deviation

Table 4: Correlation of peak longitudinal systolic strain to other echocardiographic findings

Parameter	PLSS (%)	
	R	*P*
E' (m/s)	−0.475	0.008*
A' (m/s)	0.173	0.360
E'/A' (ratio)	−0.115	0.682
S' (m/s)	0.555	0.001*
IVRT (ms)	−0.163	0.389
Time to PLSS (ms)	0.336	0.024*

*P<0.01 considede highly significant. E': Early diastolic velocity of TV annulus, A': Late diastolic velocity of TV annulus, S': tricuspid annular systolic myocardial velocity, IVRT: Isovolumetric relaxation time of RV, PLSS: Peak longitudinal systolic strain of right ventricle

Table 5: Correlation of peak longitudinal systolic strain to some demographic and laboratory data

Parameter	PLSS	
	R	*P*
Age	0.301	0.275
Hemoglobin	−0.371	0.173
Ferritin (ng/ml)	−0.060	0.833

PLSS: Peak longitudinal systolic strain

Our comparison of PLSS and time to PLSS in patients versus controls found that patients with SCD had significantly lower PLSS when compared with controls. No significant differences were noted between patients and controls regarding time to PLSS. This result may denote RV systolic dysfunction in children with SCD.

This result was in agreement with Di Maria MV *et al.*, 2015,[15] who performed a study to assess segmental myocardial deformation in East African children with SCD. Their study was performed on 193 children with SCD using speckle tracking technique. The conclusion of their study was that despite normal fractional shortening in all patients; there is a disturbance of cardiac deformation related to SCD.

Blanc *et al.*, 2012,[16] reported significant alteration in global RV longitudinal systolic strain in children with SCD.

The drawback of our study was the small number of studied patients, and we think that further large scale studies are needed to detect the beneficial value of speckle tracking in early detection of right ventricular dysfunction in children suffering from SCD.

CONCLUSION

Children with SCD have impaired right ventricular systolic and diastolic function indices when compared to healthy children, even at an early age. An early detection of systolic dysfunction by speckling tracking imaging technique is feasible.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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