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Value of Speckle Tracking Echocardiography for Detection of Clinically Silent Left and Right Ventricular Dysfunction in Patients with β-Thalassemia Major

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Abstract
Background: Since beta-thalassemia is a genetic condition with a variety of clinical manifestations, there has been an increase in interest in biomarkers that could aid in the early identification, staging, and prognosis of cardiac disease in beta-thalassemia patients. Recent advances in quantitative ultrasound technology have made speckle tracking echocardiography a viable option for precisely assessing cardiac function.
Aim of the work: Determine the efficacy of Speckle Tracking Echocardiography (STE) in the early diagnosis of myocardial affection in B- Thalassemia patients utilizing various echocardiographic modalities.
Methodology: 100 patients between the ages of 5 and 25 were enrolled in a cross-sectional study, 50 of them had known beta thalassemia. From March 2022 to January 2023, pediatric Cardiology and Hematology units at Banha University Hospital, Faculty of Medicine, used various echocardiographic modalities on a major patient from a hematology outpatient clinic and 50 control, seemingly healthy patients.
Results: The gender split was 50% male and 50% female, with a mean age of 18.03 4.08. There was no EF affliction, all of which were within normal ranges. By using the 2D speckle tracking technique, the beta thalassemia group's global longitudinal strain (GLS) mean was -16.72 4.14 and the group of controls' GLS mean was -20.80 2.69. This difference was highly significant, with a p value of 0.001 indicating the early detection of myocardial systolic and diastolic affection despite normal EF values.
Conclusion: speckle tracking echocardiography is valuable in assessment of cardiac function in patient with beta thalassemia and silent cardiac dysfunction.

Keywords: β-Thalassemia, speckle tracking, left ventricular dysfunction

1. Introduction

β-Thalassemia is considered as one of the most common inherited hemoglobin disorders caused by the declined synthesis of β-globin chains, resulting in ineffective erythropoiesis, subsequent chronic hemolytic anemia and iron overload.[1]

The phenotypic spectrum varies considerably as we face both asymptomatic thalassemia carrier and the clinically severe thalassemia major.[2]

β-Thalassemia major represents with severe anemia through the first year of life and depends on life-long transfusion therapy [3]. In spite of advances in therapeutic management of thalassemia, iron-mediated cardiomyopathy is the leading cause of death and morbidity.[4]

Besides iron overload, chronic anemia, the presence of hemoglobin F with increased oxygen affinity and production of free oxygen radicals induced by toxic free irons, all are contributors of cardiomyopathy in these patients.**[5]**

It is postulated that the development of dilated cardiomyopathy in β-thalassemia is multifactorial including immunoinflammatory and inherited components.[6]

Many thalassemia patients may develop no symptom until becoming decompensated. But with development of overt heart failure, only 50% of patients will survive.[7]

Global ventricular function and exercise capacity may remain within normal value until late stage of disease process.

2. Patients and methods

The current study was done on β-thalassemia patients at Benha University Hospital for echocardiographic assessment. The study was conducted from March 2022 to January 2023 through 9 months. The study was done in a single centre (Cardiology Department, Benha University, Egypt). After receiving their written informed consent and receiving the ethics committee of Benha University Hospitals' approval, patients were enrolled in the study.

Subjects were divided into two groups:

Group (1) representing patients with β-thalassemia major (50 patients, 25 males and 25 females) selected from those seen in Benha Hospital.

Group (2) represents the control group (50 patients, matched for age and sex, without any systemic or heart disease).

Inclusion Criteria:

All patients with beta-thalassemia major.

Patient were receiving long-term blood transfusions and undergoing iron chelation therapy

Patients aged more than 4 years old.

Patient with good systolic function (EF >50%)

Exclusion Criteria:

The following conditions prohibited patients from participating:

Patients aged less than 4 years old.

LV dysfunction defined as ejection fraction <50%

Patients with sustained atrial or ventricular arrhythmias.

Patients with congenital heart diseases.

Patient with history of ischemic heart disease or prior cardiomyopathy.

Methods

All the studied groups were subjected for:

- **History taking including:**

Age, gender, first blood transfusion age, monthly transfusion totals, chelation therapy start date, chelation therapy compliance, and type of chelation, Additionally, it includes questions about splenectomy, consanguinity, and thalassemia in the family.

- **General clinical examination:**

Clinical examination focusing on thalassaemic characteristics (big head, frontal and parietal posing, depressed nasal bridge, protruded maxilla), leg ulcers, presence of hepatomegaly, splenomegaly, and lymphadenopathy.

- **Full cardiac examination:**

By inspection, palpation, percussion, and auscultation, it was done to evaluate the symptoms of heart failure, such as gallop rhythm, cardiomegaly, congested hepatomegaly, and arrhythmia.

Investigations:

Routine investigations:

Laboratory: CBC and serum ferritin.

ECG: to detect arrhythmia or conduction disorders.

Conventional echocardiography: the patients were checked in the cardiology department at Benha faculty of medicine hospital.

Speckle tracking echocardiography.

All Study participants underwent:

Conventional Echocardiography with Doppler studies

All patients will undergo standard echocardiographic examinations in the supine left lateral decubitus position using a Philips epic 7c ultrasound system.

Left Ventricle:

- **Assessment of LV dimensions:**

The Simpson's technique measurements required the LV to be fully shown and echo loops with at least three consecutive cardiac cycles. In the PLAX view and the A4C view, the LV volume calculated by Simpson's technique was measured either directly or offline later by tracing the endocardial border on each chosen image.

3. Results and discussion

In the present study, the mean age was 18 ±5 years, 25 patients (50%) were male and 25 patients (25%) were female. 45 patients (90%) had positive family history about beta thalassemia.

By using demographic data and by doing comparison to detect the significant difference between the studied groups as regard age and sex, there was non-statistically significant difference between the group of beta thalassemia major and the control group. This came in agreement with the study of Seham et al.2015,[8] who evaluated left ventricular function in 25 patients with beta-thalassemia major and 20 healthy control to investigate non-overt cardiac dysfunctions in thalassemia group using pulsed wave Tissue Doppler Imaging (TD I) and its relation to iron overload and brain natriuretic peptide and found that no significant difference regarding age and sex. Also, Garadah et al., 2010 who studied 38 patients with beta-thalassemia major and 38 healthy controls using pulse and tissue Doppler echocardiogram to assess systolic and diastolic functions of left ventricle (LV) in beta thalassemia major group compared with age- and sex-matched controls [9].Compared with controls, there was no significant difference between 2 groups regarding age and sex.

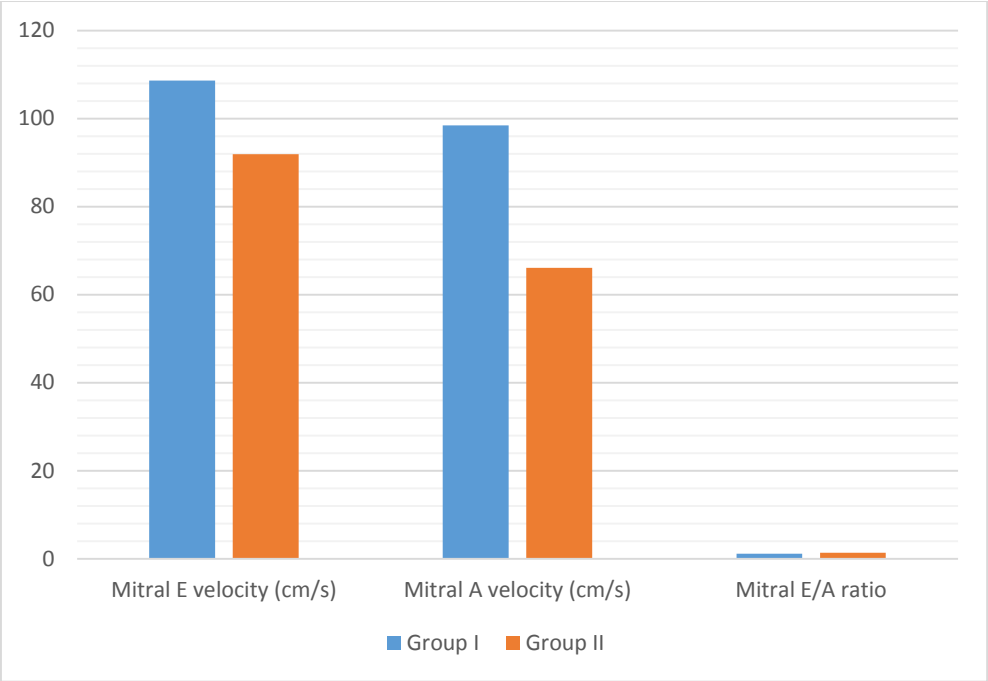
Table (1) Study groups regarding demographic characteristics

Characteristics		Group I (n=50)		Group II (n=50)		Test of sig.	p-value
Age (mean ± SD)		18.03	4.08	18.37	4.12	0.4	0.7
Sex No. (%)	Female	25	50.0%	20	40.0%	1.3	0.3
	Male	25	50.0%	30	60.0%		
Positive family history No. (%)		45	90.0%	0	0.0%	98.2	<0.001*
Risk factors No. (%)	DM	5	10.0%	4	6.7%	0.1	0.7
	HTN	5	10.0%	6	10.0%	---	---

Table (2) Study groups regarding clinical features

Characteristics	**Group I (n=50)**		**Group II (n=50)**		**Test of sig.**	**p-value**
SBP (mean ± SD)	120.00	11.24	115.33	11.93	0.8	0.4
DBP (mean ± SD)	70.50	6.78	70.23	7.47	0.9	0.4
HR (mean ± SD)	85.37	12.90	75.80	6.66	5.1	<0.001*
Pallor No. (%)	44	80.8%	0	0.0%	83.7	<0.001*
Jaundice No. (%)	36	73.3%	0	0.0%	69.5	<0.001*
Hepatomegaly No. (%)	33	66.7%	0	0.0%	60	<0.001*
Thalassemia features No. (%)	41	83.3%	0	0.0%	85.7	<0.001*
Splenectomy No. (%)	23	46.7%	0	0.0%	36.5	<0.001*

Fig. (1) Study groups regarding mitral conventional Echo



Clinically, all patients had pallor and jaundice, but controls were free. 33 patients had hepatomegaly and splenectomy was done for 23 patients. 38 patients are compliant for chelation therapy.

Upon assessment of LV systolic function by conventional echocardiography, although echo parameters were in normal range in both groups, it was found that, the group of thalassaemic patients is significantly higher than the control ($P < 0.05$) as LVEDV. Also, there is a statistically highly significant difference between patients and controls regarding LVESV, Mitral E velocity , Mitral A velocity which were higher in thalassaemic group and LV EF and Mitral E/A ratio which were higher in control group (p value < 0.001).

This was confirmed by Ebru et al. 2010 who evaluate left ventricular function in 33 patients with beta-thalassemia major and 20 healthy control using echocardiography and found that LVESV and LVEDV were significantly increased compared to healthy controls. The study also found that LVEF was significantly lower in patients with beta-thalassemia major compared to healthy controls.[10]

beta-thalassemia major and showed no significant difference of EF, LVESV and LVEDV between two groups. This was in concordance with the result from Fadime et al., 2022 who studied 41 patients with beta-thalassemia major and 25 healthy control evaluate electrocardiography, echocardiography according cardiac T2* and ferritin findings of patients followed-up for β-thalassemia major, and to investigate the importance of these findings for early detection of cardiac complications and found that no significant difference regarding to EF, LVESV and LVESDV between 2 groups.[11]

Compared with controls, the diastolic indices of LV in beta thalassemia major patients showed significantly higher E wave velocity which confirmed by Ragab et al., 2015 who studied 25 patients with beta-thalassemia major and 20 healthy controls to investigate non-overt cardiac dysfunctions in beta thalassemia major patients using pulsed wave Tissue Doppler Imaging (TD I) and its relation to iron overload and brain natriuretic peptide and found that significant increase of E wave velocity in additional to non-significant difference of A wave velocity and E/A ratio in beta thalassemia major patient comparing with health control group [12]. Similar results to these findings were recorded by Chanpura et al., 2019 this study included 35 patients with beta-thalassemia major and 35 healthy to document echocardiographic changes of cardiac iron overload in patients of thalassemia major even before appearance of symptoms and found that E wave velocity was significantly high in beta thalassemia major patient comparing with health control group [13] .The study also found that A wave velocity and E/A ratio were significantly high in beta thalassemia major patient comparing with health control group. This was further confirmed by Ebru et al., 2010.[10]

Another diastolic index of LV is A wave which is significantly high in in beta thalassemia major patient comparing with health control group. This finding was consistent with Khattab et al., 2020 who studied 50 patients with beta-thalassemia major and 25 healthy controls To assess left ventricular (LV) functions in patients with beta-thalassemia major on regular blood transfusion (without cardiac manifestations) by speckle tracking echocardiography[14].

In our study, there was a significant reduction in LV GLS. It can be described as although iron overload still has a central role in development of LV dysfunction in thalassemia. The results of the present study have demonstrated the presence of subclinical myocardial systolic and diastolic dysfunction in thalassemic patients with no cardiac manifestations.

Despite a normal LVEF with 2D Echocardiography, β-thalassemia patients showed impairment of LV global longitudinal strain. This was in concordance with Khattab et al., 2020 who proved in his study that the global LV longitudinal strain rates were reduced in the thalassemia group in comparison with the control groups denoting that the results of both studies demonstrated the presence of subclinical myocardial systolic and diastolic dysfunction in thalassemia patients, with no cardiac manifestations, and was asymptomatic[14].

4. Conclusion

From the present study the following were concluded:

Even if they do not have overt heart failure, patients with -thalassemia show early regional systolic dysfunction in the LV walls.

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