

# Echocardiographic evaluation of systolic and diastolic heart function in patients suffering from beta-thalassemia major aged 5-10 years at the Zahedan Research Center for Children and Adolescent Health

*Zahedan Çocuk ve Genç Sağlığı Araştırma Merkezindeki 5-10 yaşlarındaki beta-talasemi majörü olan hastalarda sistolik ve diyastolik kalp fonksiyonunun ekokardiyografik değerlendirmesi*

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## ABSTRACT

**Objective:** Cardiac complications are the major cause of morbidity and mortality in beta-thalassemia major. The aim of the study was to evaluate right (RV) and left (LV) ventricular systolic and diastolic functions using myocardial performance index in young, asymptomatic children suffering from thalassemia major, for early detection of cardiac function impairment, preventing further cardiac damage by modifying disease progression and treatment.

**Methods:** A case-controlled, cross-sectional study involving 80 patients suffering from beta-thalassemia major and 80 children adjusted in terms of age and sex served as a control group were studied in Research Center for Children and Adolescent Health Zahedan. The relevant echocardiographic parameters were measured in both subject groups: myocardial performance index (MPI), isovolumic relaxation time (IRT), isovolumic contraction time (ICT), pre-ejection period (PEP), ejection time (ET), PEP/ET ratio, deceleration time (DT) and acceleration time (AT). Data were analyzed by unpaired Student t test.

**Results:** The left ventricular mean IRT in the patient group was 114±21 and in the control group 94±10 msec (p<0.05). The mean MPI (LV) in the patient group was 0.58±0.18 and in the control group 0.41±0.08 (p<0.05). The mean ET (LV) in the patient group was 237±36 msec and in the control group 266±25 msec (p<0.05). The mean ET (RV) in the patient group was 237±39 msec and in the control group 261±36 msec (p<0.05).

**Conclusion:** There is an early systolic and diastolic dysfunction in children younger than 10 years with beta-thalassemia major. Even in young asymptomatic children with beta-thalassemia major, serial echocardiography seems warranted in order to adjust cardioprotective therapy. (*Anadolu Kardiyol Derg 2010; 10: 150-3*)

**Key words:** Beta-thalassemia major, systolic function, diastolic function, echocardiography, children

## ÖZET

**Amaç:** Çalışmanın amacı, kalp fonksiyon bozukluğunu erkenden teşhis ederek, daha sonraki kalp hasarını önlemek için hastalığın seyrinde ve tedavisinde gerekli değişiklikleri yapmada talasemi majörlü genç ve asemptomatik çocuklarda miyokart indeksini kullanarak sağ ve sol ventrikülün sistolik ve diyastolik fonksiyonlarını değerlendirmektir.

**Yöntemler:** Zahedan Çocuk ve Genç Sağlığı Araştırma Merkezinde yaş ve cinsine göre uyumlu, 80 sağlıklı çocuk ve beta-talasemi majörlü 80 hastanın dahil olduğu olgu-kontrollü, enine-kesitsel bir çalışma yapıldı.

Her iki grupta da ilgili ekokardiyografik parametreler ölçüldü: Miyokart performans indeksi (MPI), izovolümik relaksasyon zamanı (IRT), izovolümik kasılma zamanı (ICT), pre-ejeksiyon dönemi, PEP/ET oranı, deselerasyon zamanı (DT) ve akselerasyon zamanı (AT). Veriler eşleştirilmemiş Student t testi ile analiz edildi.

**Bulgular:** Sol ventrikül ortalama IRT hasta grubunda 114±21 ve kontrol grubunda 94±10 msn (p<0.05) idi. Hasta grubunda ortalama MPI (LV) 0.58±0.18 ve kontrol grubunda 0.41±0.08 (p<0.05) oldu. Hasta grubunda ortalama ET (LV) 237±36'ydı ve kontrol grubunda 266±25 msn oldu (p<0.05). Hasta grubunda ortalama ET (RV) 237±39'du ve kontrol grubunda 261±36 msn oldu (p<0.05).

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**Accepted/Kabul Tarihi:** 09.02.2010

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doi:10.5152/akd.2010.041

**Sonuç:** Beta-talasemi majörlü 10 yaşın altındaki çocuklarda, erken sistolik ve diyastolik disfonksiyon vardı. Beta-talasemili genç asemptomatik çocuklarda bile, kalp koruyucu tedaviyi düzenlemek için seri ekokardiyografi gerekli görünüyor. (*Anadolu Kardiyol Derg 2010; 10: 150-3*)

**Anahtar kelimeler:** Beta-talasemi, sistolik fonksiyon, diyastolik fonksiyon, ekokardiyografi, çocuklar

## Introduction

Cardiac complications are still the most common cause of death in patients with major thalassemia. Iron overload causes severe and permanent cardiac damage even more than untreated anemia. Cardiac complications due to iron overload are recurrent pericarditis, recurrent forms of heart block, ectopic ventricular beats, ventricular tachycardia, ventricular fibrillation, cardiomegaly, left ventricular (LV) dysfunction and finally heart failure resistant to any therapeutic measures (1).

In thalassemic patients with normal systolic function and iron overload, the first sign of diastolic dysfunction is abnormality in LV relaxation time manifested as prolonged isovolumic relaxation time (IRT) (2, 3).

Left ventricular volumes and shapes, mass index, mass/volume ratio, systolic and diastolic function, stroke volume and cardiac index have been investigated by two-dimensional and M-mode echocardiography in thalassemic patients (4, 5).

Left ventricular systolic and diastolic function in patients with major thalassemia with varying degrees of cardiac involvement has recently been investigated by Doppler echocardiography (6).

Myocardial performance index (MPI) or Tei index is a Doppler derived index of ventricular function that is free of geometric constraints. It involves simultaneous (or near simultaneous at equivalent heart rates) measurement of atrioventricular inflow and ipsilateral semilunar outflow Doppler velocities. It allows to assess global function and because it incorporates both systolic and diastolic components of the cardiac cycle, it is also global from a temporal perspective as well (7).

Myocardial performance index is correlated to invasive methods of measurements of ventricular systolic and diastolic function (8, 9).

There are few studies discussing echocardiographic index parameters in thalassemic patients younger than 10 years. Pre-ejection period to ejection time (PEP/ET) ratio and deceleration time (DT) are other indices of systolic and diastolic function that have been investigated (10, 11) and correlated to radionuclide examination and cardiac catheterization (12).

There have been new studies on thalassemic patients comparing echocardiographic parameters of MPI by pulsed tissue Doppler imaging and parameters derived from conventional echocardiography but none of these studies have been performed on asymptomatic children below ten years old (13).

The aim of the study was to evaluate right and left ventricular systolic and diastolic function using MPI in young, asymptomatic children suffering from thalassemia major, for early detection of cardiac function impairment, preventing further cardiac damage by modifying disease progression and treatment.

## Methods

This study was designed as a case-controlled, cross-sectional study on thalassemic patients at age range of 5-10 years

and was performed from January 2005 to April 2006. Asymptomatic thalassemia patients with a normal physical examination and normal electrocardiogram and thoracic X-ray were included. Exclusion criteria were mitral valve insufficiency, severe anemia, hypertension, cardiac structural disorders, heart failure, and hemoglobin below ten and cardiac drug usage. Finally, 80 patients were included into the study. All echocardiography examinations were performed after a blood transfusion and by the same examiner. A control group of 80 children with normal hearts matched for age and sex was selected. Informed consent was taken from parents of all the children.

### Echocardiographic assessment

Echocardiography was performed with a Challenge 7000 echocardiography machine ( Esaote Biomedica, Florence, Italy) with a 3.5/5 and 2.5/3.5 MHZ transducer. Patient's recordings were taken while patients were in supine position without breath holding. M-mode, 2D and Doppler echocardiographic parameters were averaged over 3 cardiac cycles and all echocardiographic measurements were performed according to the guidelines for performance of a pediatric echocardiogram by American Society of Echocardiography (14).

M-mode views were obtained from a parasternal position at mitral and tricuspid valves level. Systolic and diastolic interventricular septum diameter, LV end-diastolic diameter, LV end-systolic diameter, LV posterior wall thickness in diastole and systole, and ejection fraction were calculated by M-mode echocardiography. Pulsed Doppler method was used for blood flow measurements from cardiac valves (mitral, aortic, tricuspid and pulmonary): flow velocity during early filling (E), flow velocity during atrial contraction (A) and ejection time (ET), pre-ejection period (PEP) were measured and then E/A and PEP/ET ratios were calculated. Isovolumic relaxation time was obtained from the apical five-chamber view and MPI was measured according to the formula:

$MPI = (IRT + ICT/ET)$ . Doppler and M-mode views were recorded at 50 mm/s velocity (2, 15).

### Statistical analysis

All statistical analyses were performed using SPSS for Windows version 14 software (SPSS Inc. Chicago, Illinois, USA). Descriptive statistics are shown as mean $\pm$ SD. Data were analyzed by unpaired Student t test and p value <0.05 was considered as significant.

## Results

In this study 80 patients with major thalassemia at age of 5-10 years were assessed by 2D, M-mode and Doppler echocardiography and were compared with 80 healthy children of the same age and sex. Mean age in the patients group was 7.33 $\pm$ 1.95 years and in

the control group 7.53±1.88 years (p>0.05). The control group consisted of 40 boys and 40 girls and the patients group included 38 girls and 42 boys. Heart rate in the patients group was 98±15 beats/min and in the control group - 80±10 beats/min (p<0.05).

As can be seen from Tables 1 and 2 patients had significantly higher LV and right ventricular (RV) MPI than controls (p<0.05 for both).

The LV ejection fraction was significantly lower in patients than the controls (p<0.05).

The LV PEP/EP ratio was an index that varied significantly in patients and control group (p<0.05).

The IRT was significantly higher in the left ventricle of the patients group in comparison to the control one (p<0.05).

E/A ratio were significantly lower in the RV of the patients in comparison to the controls (p<0.05).

### Discussion

We studied cardiac systolic and diastolic function in thalassemic patients at age 5-10 years. Myocardial performance index of right and left myocardium in patients group was significantly increased in comparison to the control group. Isovolumic relaxation time and ICT were significantly increased, while there was no difference in ET between patients and control group. This finally describes the increase in MPI in case group in comparison to control group.

Cardiac function has been studied in patients at puberty or adulthood and there are few studies at childhood especially in patients younger than 10 years. Mean age of our patients was 7.33±1.95 years that was lower than in other studies with ages from 15.5±3.6 to 26±6 years (3, 4). The heart rate was significantly increased in case group in comparison to control group that was the same as other studies (5, 6).

Low capacity for oxygen transportation leads to increased cardiac output in patients that result in increased venous return and increased heart rate due to Frank- Starling mechanism.

Ocal et al. (7) studied on determination of MPI of left heart in patients that received Doxorubicin. Myocardial performance index was increased in case group and was due to increased IRT and decreased ET, but ICT was not different (7). Increased MPI in this study shows both systolic and diastolic dysfunction in every ventricle in thalassemic patients. On the other hand, increase in MPI shows decrease in cardiac function that was similar to other studies (2, 8, 9).

Increase in IRT, one of the diastolic function indices, has been previously reported in thalassemic patients in several studies and reflects the decrease in ventricular relaxation due to iron overload and restrictive cardiomyopathy (3, 5, 10).

In this study, PEP/ET in left ventricle is increased that is similar to Ghafours et al. study (4). In this study PEP/ET was increased in almost two third of the patients (4). Increase in PEP/ET shows early diastolic ventricular dysfunction. According to Hahalis et al. (11) diastolic function in thalassemic patients abnormally changes, but the left ventricular filling is equal to

**Table 1. Echocardiographic parameters of left ventricle in patient's and control groups**

Variables	Patients	Controls	p*
Age, years	7.33±1.95	7.53±1.88	>0.05
ICT, msec	26.3±23.5	15.8±16.3	<0.05
MPI	0.59±0.38	0.41±0.08	<0.05
PEP, msec	96±20	91±91	>0.05
ET, msec	237±36	266±25	<0.05
PEP/ET ratio	0.440±0.295	0.342±0.317	<0.05
IRT, msec	114±21	94±10	<0.05
AT, msec	60±10	56±15	<0.05
DT, msec	102±15	120±18	<0.05
E, cm/sec	98.05±19.51	116.7±11.64	>0.05
A, cm/sec	58.765±13.787	61.19±15.194	>0.05
E/A ratio	1.734±0.484	1.945±1.746	>0.05
LVEDD, mm	42.5±3.4	40.20±3.60	<0.05
LVESD, mm	29.1±2.3	26.8±3.2	<0.05
EF, %	60±6	63±6	<0.05

Data are presented as mean ±SD

\*. unpaired Student's t test

A - flow velocity during atrial contraction, AT- acceleration time, DT - deceleration time  
E - flow velocity during rapid ventricular filling, EF - ejection fraction, ET - ejection time,  
ICT - isovolumic contraction time, IRT - isovolumic relaxation time, LV - left ventricle,  
LVEDD - left ventricular end-diastolic dimension, LVESD - left ventricular end-systolic dimension, MPI - myocardial performance index, PEP - pre- ejection period

**Table 2. Echocardiographic parameters of right ventricle in patient's and control groups**

Variables	Patients	Controls	p*
MPI	0.66±0.29	0.49±0.11	<0.05
PEP, msec	92±19	77± 6	<0.05
ET, msec	237±39	260±36	<0.05
PEP/ET ratio	0.449±0.439	0.335±0.385	>0.05
IRT, msec	129±31	107±96	>0.05
DT, msec	103±17	124±19	>0.05
E, cm/sec	62.33±20.13	61.27±15.29	>0.05
A, cm/sec	48.83±14.77	43.57±10.12	<0.05
E/A ratio	1.329±0.398	1.450±0.291	<0.05

Data are presented as mean ±SD

\*. unpaired Student's t test

A - flow velocity during atrial contraction, DT - deceleration time, E - flow velocity during rapid ventricular filling, EF - ejection fraction, ET - ejection time, IRT - isovolumic relaxation time, MPI - myocardial performance index, PEP - pre- ejection period

increase in preload. In another study Hahalis et al. (12) showed that LV function in asymptomatic thalassemic patients was within normal range, but they demonstrated increase in RV IRT and decrease in RV DT to be the signs of early RV dysfunction and have prognostic significance.

In our study, E/A ratio does not show any significant difference between patients and control groups. In contrary, in other studies (5, 6) E/A ratio was increased significantly in thalassemic patients (5). However, Gharzuddine et al (10) reported that E/A ratio did not differ in 50 thalassemic patients and 29 healthy control subjects. Similar results were published by Iarussi et al. (3).

In our study, there was no significant difference in E/A ratio in two groups, due to exclusion of patients with heart failure symptoms and low mean age range of patients. Although, change in E/A ratio does not seem to be a sign of diastolic dysfunction.

In this study, ejection fraction in patients group was less than in control group, which is in agreement with previous studies (5, 6) that did not include the children with the age below 10 years.

In this study, LV end-diastolic diameter and LV end-systolic diameter were significantly increased in patients with beta-thalassemia major. Akar et al. (16) and Aessopos et al. (17) reported similar to our study results.

According to increased LV diameter in systole and diastole that is observed in major thalassemia, LV morphology is changed in early stages because of iron overload, but its function is spared yet. Finally, since cardiomyopathy is the main cause of mortality and morbidity in thalassemic patients, early diagnosis may be useful for control of disease progression, transfusion planning, time to start and dosage of desferal, and how to prescribe it for control of cardiac dysfunction.

#### Study limitations

There are studies comparing the echocardiographic data of systolic and diastolic function of the thalassemic patients comparing them with invasive data such as catheterization (12). Our study was based on echocardiographic data and in future we can compare data of catheterization with echocardiographic parameters.

#### Conclusion

Diastolic function of right and left heart in thalassemic patients under 10 years old is affected by multiple transfusions and final iron overload. Myocardial performance index of right and left heart is increased in these patients that show cardiac systolic and diastolic dysfunction. Even in young asymptomatic children with beta-thalassemia major, serial echocardiography seems warranted in order to adjust cardioprotective therapy.

**Conflict of interest:** None declared

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