Evaluation of cardiovascular complications with $^{99m}$Tc tetrofosmin gated myocardial perfusion scintigraphy in patients with thalassemia major

G.K. GÜDAČ, M. ÇAĞLAR, S. ÜNAL and F. GÜMBÜK


Objective. Iron overload limits the life expectancy of thalassaemic patients by causing cardiac toxicity. Iron also plays a catalytic role in the pathogenesis of atherosclerosis. The aim of this study was to evaluate the role of $^{99m}$Tc Tetrofosmin gated myocardial perfusion scintigraphy (GPMSS) in the detection of cardiac dysfunction in patients with thalassemia major.

Materials and methods. Forty two patients with homozygous beta-thalassemia were enrolled in the study. Myocardial perfusion and wall motion were analysed in all patients (mean age 17 ± 5.28) and 34 age-matched controls using GPMSS. Clinical data, liver function tests, hemoglobin, ferritin, low density lipoprotein (LDL) and cholesterol levels, and the total number and frequency of transfusions were collected from patient records.

Results. 97.6 % and 78.5 % of patients had normal myocardial perfusion and wall motion respectively. Nine out of 42 thalassaemic patients had abnormal left ventricular wall motion; half of these had septal hypokinesia. No significant correlation was found between the total number of transfusions, serum ferritin levels and left ventricular ejection fraction ($p = 0.442$ and $p = 1.00$, respectively). Echocardiography revealed systolic dysfunction in 5 out of 9 patients with wall motion abnormality. LDL was normal in 38 out of 42 patients and cholesterol levels were normal in 37 out of 42 patients.

Conclusions. Regional wall motion abnormalities can be seen in patients with thalassemia major. This early damage is frequently located in the septum and can be detected by GPMSS. Serum ferritin levels and the number of blood transfusions are inadequate as predictors of myocardial dysfunction.

KEY WORDS: thalassemia major, cardiac toxicity, atherosclerosis, $^{99m}$Tc tetrofosmin, scintigraphy.

Resumen.—Objetivo. La sobrecarga de hierro limita la esperanza de vida de los pacientes talásicos debido a su toxicidad cardíaca. El hierro también tiene un papel catalítico en la patogenia de la aterosclerosis. El objetivo de este estudio era evaluar el papel de la gammagrafía de perfusión miocárdica con $^{99m}$Tc tetrofosmina (GPM) en la detección de disfunción cardíaca en pacientes con talasemia mayor.

Materiales y métodos. Se incluyeron 42 pacientes con beta talasemia homocigota. Se analizó la perfusión miocárdica y el movimiento de la pared cardiaca mediante GPM en todos los pacientes (edad media 17 ± 5.28 años) y 34 controles de edad comparable. Se registraron los datos clínicos, las pruebas de función hepática, los niveles de hemoglobina, ferritina, lipoproteína de baja densidad (LDL) y colesterol, y el número total y la frecuencia de transfusiones a partir de los informes de los pacientes.

Resultados. El 97.6 % y el 78.5 % de los pacientes mostraron normalidad en la perfusión miocárdica y el movimiento de la pared cardiaca, respectivamente. En 9 de 42 pacientes talásicos se observó un movimiento anómalo de la pared ventricular izquierda, y la mitad de ellos mostraron hipoinesia septal. No se observó una correlación significativa entre el número total de transfusiones, los niveles de ferritina sérica y la fracción de eyeción del ventrículo izquierdo ($p = 0.442$ y $p = 1.00$, respectivamente). La ecocardiografía reveló una disfunción sistólica en 5 de los 9 pacientes con movimiento anómalo de la pared cardiaca. El nivel de LDL fue normal en 38 de 42 pacientes, y el nivel de colesterol fue normal en 37 de 42 pacientes.

Conclusiones. En pacientes con talasemia mayor se pueden observar alteraciones regionales del movimiento de la pared cardiaca. Esta alteración precisa suele localizarse en el tabique interventricular y puede detectarse mediante GPM. Los niveles de ferritina sérica y el número de transfusiones de sangre no son adecuados como factores de pronóstico de disfunción miocárdica.

PALABRAS CLAVE: talasemia mayor, toxicidad cardíaca, aterosclerosis, $^{99m}$Tc tetrofosmina, gammagrafía.
INTRODUCTION

Beta thalassemia is a hereditary chronic hemolytic anemia caused by impaired synthesis of the beta (β) chain of hemoglobin. Although near-normal growth and development can be achieved by blood transfusions and iron chelation with desferrioxamine, most patients develop iron overload and multiorgan failure. Cardiac dysfunction is the most common cause of death.

There is increasing evidence showing a relationship between elevated iron levels and development of cardiovascular complications. Iron, which is the essential component of various enzymes, becomes highly cytotoxic when excess quantities in the tissue are deposited in patients with thalassemia major secondary to repeated blood transfusions.

Iron induced myocardial dysfunction present as regional wall motion abnormalities, arrhythmias and congestive heart failure. In addition, excess iron may accelerate lipid peroxidation by virtue of its pro-oxidant properties and thus promote early atherogenesis.

Once clinical findings of cardiac dysfunction become apparent, the prognosis is poor. Most patients die of cardiac disorders related either to congestive heart failure or to sudden death presumably caused by cardiac arrhythmias. In an attempt to identify early cardiac dysfunction, investigators have used non-invasive techniques such as echocardiography to demonstrate reduced myocardial function. These studies performed while the patients were at rest indicated that patients may manifest abnormal ventricular performance before cardiac disease becomes apparent clinically. Some authors who have applied radionuclide ventriculography during stress found that functional abnormalities can often be detected during exercise before they become apparent at rest. These studies functional reserve was described by identifying the preclinical phase of cardiac dysfunction. Recently, there has been some other studies which reported the role of magnetic resonance imaging in assessing cardiac iron overload. Another valuable diagnostic test is gated myocardial perfusion scintigraphy (GMPS) which enables to determine left ventricular function and myocardial perfusion. The goal of this study is to evaluate the potential role of GMPS for the assessment of myocardial perfusion and function during stress and rest in patients with beta thalassemia major.

MATERIAL AND METHODS

Study population

Between October 2003 and November 2004, 42 thalassemia major patients were prospectively enrolled in the study (22 females, 20 males, age range 10-30 years, mean age 17.0 ± 5.3 years). Cardiac functions of thalassemic patients were compared with 34 control patients (age range 9-25 years, mean 13.9 ± 2.9 years). These control patients were followed for 1 year without any evidence of coronary artery disease.

Patients with thalassemia major were on a blood transfusion therapy program with 3 week intervals in order to keep hemoglobin level above 10 g/dL. None had any clinical signs of heart failure and all of them were on chelation therapy (they were receiving desferrioxamine 30-40 mg/kg s.c). All patients were imaged 48 hours after the last blood transfusion.

Informed consent was obtained from all the patients who were above 18 years and from the parents of those who were below 18. The study protocol was approved by the local ethics committee (number: LUT 03/28-10).

Blood measurements

Laboratory data included measurement of liver function tests, hemoglobin (Hb), serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), low density lipoprotein (LDL), cholesterol and ferritin levels. Ferritin levels were measured with electrophoresis immunoassay method by using a commercial kit (Elecys, Roche, Mannheim, Germany). ALT and AST levels were measured with a commercial kit (IFCC without pyridoxal activation, Roche, Mannheim, Germany). Cholesterol levels were measured enzymatically with a commercial kit (Cholesterol CHOD-PAP, Roche, Mannheim, Germany). Plasmain LDL levels were calculated with Friedewald Equation which is represented as LDL = Cholesterol - High Density Lipoprotein-Triglyceride/5. Triglyceride levels were assessed with a commercial kit (Triglycerides GPO-PAP, Roche, Mannheim, Germany) and high density lipoprotein levels were mea-
Cardiac evaluation

Complete two dimensional and M-mode echocardiographic study was performed with an echocardiographic unit (Vivid Five, Expert Configuration) with a 2.5-5 MHz transducer. Recordings were made in a resting state when the patient was lying supine. Left ventricular end-diastolic, end systolic cavity dimensions, ejection fraction and fractional shortening were measured.

Left ventricular percentage of fractional shortening was calculated as follows:

\[
\frac{\text{LVEDD} - \text{LVESD}}{\text{LVEDD}}
\]

where LVEDD represents left ventricle internal end-diastolic diameter and LVESD represents internal end-systolic diameter. Twenty-five percent (25%) was accepted for the cut off between normal and abnormal fractional shortening. Left ventricular ejection fraction was derived from the biplane volumes expressed as a percentage of end-diastolic and end-systolic volumes expressed as a percentage of end-diastolic volume. Sixty percent (60%) was accepted for the cut off between a normal and abnormal left ventricular ejection fraction.

Posteroanterior X-ray films of the chest were also reviewed for assessment of cardiothoracic ratio.

Stress test

Symptom-limited-exercise test was performed according to the standard Bruce protocol, with a continuous 12-lead ECG monitoring. Test termination criteria included ST segment depression ≥ 2 mm, a significant decrease (≥ 10 mm) in systolic blood pressure, physical exhaustion, dangerous arrhythmia, progressive angina pectoris and limiting dyspnea. Exercise test was considered adequate if heart rate was ≥ 85% of the maximal predicted heart rate. The exercise ECG was interpreted as positive if ≥ 1 mm horizontal or downward or ≥ 1.5 mm upward sloping ST segment depression at 0.08 second after the J point in ≥ 3 consecutive complexes of the same lead was observed.

Myocardial perfusion scintigraphy

A two day stress-rest protocol was followed. Patients were injected 20 mCi of \(^{99m}\text{Tc}\) tetrofosmin at peak exercise if they were above 18 years. Dose was adjusted to patient weight if patients were below 18. Same doses were used for rest studies. \(^{99m}\text{Tc}\) tetrofosmin was prepared using a commercial kit (Myoview, Amersham) with \(^{99m}\text{Tc}\) pertechnetate freshly eluted from a \(^{99m}\text{Tc}\) generator (CIS international ELUMATIC III). After injection of the radiopharmaceutical at the peak heart rate, exercise was continued for 2 more minutes. SPECT acquisition was started at 30 minutes. Studies were performed with a double head rotating gamma camera (Siemens ECAM, Erlangen, Germany), equipped with low energy, high resolution, parallel hole collimator. A 10% symmetrical energy window, centered on the 140-keV peak was used. Thirty-two projections were recorded over a 180-degree arc starting from 45-degree right anterior oblique to 45-degree left posterior oblique and 64*64 matrix was used. Each projection’s acquisition time was 25 seconds and ECG gated images were acquired with 8 frames per cardiac cycle. Rest images were acquired 60 minutes after the injection of the radiopharmaceutical.

SPECT images were reconstructed by standard filtered back-projection algorithm without attenuation or scatter correction. A Butterworth filter (order 5, cutoff-frequency 0.5) was used to reconstruct transaxial images. Transaxial images were then reoriented into the short-axis, vertical and horizontal long axis images.

Image analysis and interpretation

Images were interpreted independently by two experienced nuclear medicine physicians unaware of the patients’ clinical status. A 5 point scoring system in which left ventricle was divided into 20 segments was used for the semi-quantification of the perfusion data. In this system each segment was given a score of 0 to 4 which represents to normal, mildly reduced, moderately reduced, severely reduced perfusion and no uptake respectively.

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Reversibility of radiotracer uptake was determined visually and semi-quantitatively. A reversible defect was considered if a score change ≥ 2 was present between rest and stress studies. A nonreversible or a fixed defect was considered if uptake was worse or the same in the rest compared with the stress image.

After examining the gated data, by using quantitative gated SPECT software (QGS), ejection fraction (EF), end systolic (ESV) and end diastolic volumes (EDV) of the left ventricle were calculated. Here 6 point scoring system was used in the same 20 segment model to evaluate wall motion in which 0,1,2,3,4,5 scores refers to normal, mild hypokinesia, moderate hypokinesia, severe hypokinesia, akinesia and dyskinesia respectively. Wall thickening was assessed by a 4 point scoring system where 0: represents normal, 1: mild reduction, 2: moderate reduction and 3: no detectable thickening.

Normal values for left ventricle EF, end systolic and end diastolic volumes were ≥ 50 %, 70 ml and 120 ml respectively.

Magnetic resonance imaging

Four patients with discordant results between echocardiography and gated myocard perfusion scintigraphy were further analyzed by magnetic resonance imaging (MRI). Patients were scanned with a 1.5 T Scanner (Philips Intera Archieva, Philips Medical Systems, Netherlands). Each scan lasted 15 minutes and included measurement of heart T2-star (T2*) value was 67 % with a standard deviation of 9.42. These patients EF ranged between 62-83 %, (mean: 70 %), fractional shortening was 35 % (range: 35-37 %).

In 33 patients echocardiography was normal. In these patients EF ranged between 62-83 %, (mean: 70 %), fractional shortening ranged between 31-52 %, (mean: 39 %), table 1. For all patients, the mean EF value was 67 % with a standard deviation of 9.42.

Echocardiography

Among 42 patients, echocardiography showed abnormality in 9. In 5 patients systolic dysfunction was observed where left ventricular ejection fraction ranged between 29 % and 59 % (mean 49.8 %). In this group fractional shortening ranged between 13 % and 35 % with a mean value of 24.8 %. In 4 patients echocardiography revealed increased left ventricle end diastolic diameter in 3 patients, left ventricle dilatation and hypertrrophy in 1 patient. In this group mean EF was 65 % (range: 63-67 %) and mean fractional shortening was 35 % (range: 35-37 %).

In 33 patients echocardiography was normal. In these patients EF ranged between 62-83 %, (mean: 70 %), fractional shortening ranged between 31-52 %, (mean: 39 %), table 1. For all patients, the mean EF value was 67 % with a standard deviation of 9.42.

Stress test and myocardial perfusion scintigraphy

Stress and rest myocardial perfusion scintigraphy was completed in 38 thalassemic patients. Three patients refused to undergo rest imaging and 1 patient died after stress imaging because of supraventricular arrhythmia.

Among thalassemic patients rest electrocardiogram revealed right bundle branch block in 3, first degree atrioventricular block in 3, 0.5-1 mm ST segment depression in 6 and left ventricle hypertrrophy in 6 patients. Only 1 patient who felt physical exhaustion, failed to reach the maximal heart rate. In

| Table 1 Results of Echocardiography in Thalassemic Patients |

<table>
<thead>
<tr>
<th>Values</th>
<th>Normal Echoangiography</th>
<th>Abnormal Echoangiography</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean EF ± SD (%)</td>
<td>70.00 ± 5.57</td>
<td>57.39 ± 11.00</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mean FS ± SD (%)</td>
<td>39.67 ± 5.00</td>
<td>30.80 ± 7.60</td>
<td>0.001</td>
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</table>

*Mann Whitney U test.
this patient stress test was stopped at 80 % of the maximal heart rate. In the remaining 41 patients 85 % or more of the maximal predicted heart rate was reached. No additional ECG changes or symptoms were observed during stress test.

In 41 of the 42 patients stress myocardial perfusion was normal without any sign of ischemia or infarct. One patient had a fixed perfusion defect in the inferior wall both on stress and rest images. This patient had an inferior wall perfusion defect involving 16 % of the myocardium which was calculated by quantitative perfusion SPECT software (QPS).

Stress and rest gated SPECT myocardial perfusion scintigraphy

Wall motion abnormalities were observed in 9 patients (21.4 %) on both stress and rest studies. There was global mild and moderate hypokinesia in 4, moderate and severe septal wall hypokinesia in 3, severe inferior wall hypokinesia in 1 and septal wall dyskinesia in one patient. Wall thickening abnormalities were observed in 6 patients (2 global, 2 inferolateral, 2 septal). In the remaining 33 patients results of gated study were normal.

In seven patients both stress and rest left ventricle EF was below 50 % (mean values for stress and rest left ventricle EF were 45 % and 43 % respectively). The results of gated SPECT in stress and rest studies are shown in table 2. Mean of the stress and rest left ventricle EF for all patients was 62 % and 60 % with standard deviations of 12.49 and 11.91 respectively.

In the control group (n = 34) gated SPECT studies were normal. The mean left ventricular EF value was 62 % with a range of 50 %-92 %. Thalassemia patients with normal wall motion had higher mean left ventricular EF values (66.8 %) compared with control subjects (62.0 %) which was not statistically significant (p: 0.198, t test for independent samples). Among 9 patients with wall motion abnormality, ferritin levels were within normal limits in 5, and increased in 4 (> 2000 ng/ml). In 16 of 33 patients with normal wall motion, ferritin levels were above 2000 ng/ml in 16 (48.4 %) and below 2000 ng/ml in 17 (51.5 %). The total number of blood transfusions given to the patients who had wall motion abnormality ranged from 192 to 342 with a mean value of 250. In 2 patients it was below 200 and in 7 it was above 200. In patients with normal wall motion, 14 had received less than 200 transfusions and 19 more than 200. No statistically significant relation was observed between ferritin levels, total number of transfusions, age, ALT, AST, LDL and cholesterol levels in patients with or without wall motion abnormalities. However 88.8 % of patients with reduced left ventricular EF and wall motion abnormality were male, p = 0.022. The distribution of patients with and without wall motion abnormalities according to clinical results and p values is summarized in table 3. Eight of 9 patients, who had wall motion abnormality on the gated study, had abnormal echocardiography as well. Among these, 5 had systolic dysfunction, 2 had increased left ventricular end diastolic diameter and 1 had left ventricular hypertrophy and dilatation. In 1 patient echocardiography was normal although gated study revealed septal dyskinesia. Further MRI of this patient showed reduced left ventricle function involving the septum. MRI also revealed deterioration of increased left ventricular function in 2 patients with abnormal wall motion on gated SPECT who showed only increased left ventricle end diastolic diameter on echocardiography in the absence of systolic dysfunction. In these patients, increased cardiovascular T2* (4 milisecond and 6 milisecond respectively) and reduced left ventricle EF (52.9 % and 38 % respectively) was calculated. These patients had

**Table 2**

<table>
<thead>
<tr>
<th>Results of Stress and Rest Gated SPECT in Thalassemic Patients</th>
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<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Mean EF in stress ± SD (%)</td>
</tr>
<tr>
<td>Mean ESV in stress ± SD (ml)</td>
</tr>
<tr>
<td>Mean EDV in stress ± SD (ml)</td>
</tr>
<tr>
<td>Mean EF in rest ± SD (%)</td>
</tr>
<tr>
<td>Mean ESV in rest ± SD (ml)</td>
</tr>
<tr>
<td>Mean EDV in rest ± SD (ml)</td>
</tr>
</tbody>
</table>

*p values were calculated by Mann Whitney U test.

n: number of patients

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global and septal wall motion abnormalities on the gated study. The other patient with global hypokinesia on gated study who only had left ventricle dilatation and hyperthrophy on echocardiography, was further evaluated by echocardiography after 24 months and global hypokinesia with reduced left ventricular EF of 44% was seen. The patient who had increased left ventricular end diastolic diameter on echocardiography with normal gated study, was also evaluated by cardiac MRI and no abnormality was reported.

DISCUSSION

Iron overload is inevitable in children with thalassemia major due to repeated blood transfusions and increased gastrointestinal absorption. Although recent improvements in iron removal have improved survival, cardiac damage is still the main cause of death in children10. In general, diagnostic tests have not been very useful in detecting early iron induced cardiac damage. Although rest echocardiography permits detection of anatomic and functional abnormalities in some patients before the onset of clinical symptoms,11 most patients without clinically evident congestive heart failure do not have echocardiographically detectable left ventricular dysfunction at rest. Leon et al emphasized the importance of ventricular reserve of left ventricle during exercise and reported rest echocardiography as an inadequate imaging modality for detecting preclinical cardiac dysfunction in iron overload.

The introduction of ECG gated SPECT imaging has allowed assessment of global and regional LV function in addition to perfusion.12-14. Direct comparisons between gated SPECT and echocardiography showed good correlations for the assessment of LV ejection fraction, volumes and regional wall motion.15,16. Also, gated SPECT has the advantage of providing information about left ventricular perfusion in addition to function and dimensions. In addition, agreement between EF and LV volumes measured from 16 interval and 8 interval gated SPECT was found excellent by Germano et al17. However, limited data is available on the utilization of gated SPECT in patients with thalassemia major.

In our study 9 patients had wall motion abnormalities on gated myocardial perfusion scintigraphy. Four patients had global, 4 had septal and 1 had inferior wall motion abnormality. Barosi et al18 have shown the inhomogenous nature of iron deposition in the myocardium which can explain the regional wall motion abnormalities in our patients. Septum might be involved in the preclinical phase of cardiac dysfunction due to earlier iron deposition which was suggested by Lattanzi et al19 and Vogel et al20. Among 9 patients with wall motion abnormality seen on MPS, only 5 had systolic dysfunction on echocardiography. Four patients who had normal systolic function on echocardiography had repeat examinations after one year which revealed deterioration of left ventricular function with a reduction of EF. One patient with normal echocardiography, had systolic dysfunction on magnetic resonance examination performed within one year. Thus it is possible that regional left ventricular dysfunction can be seen on gated SPECT prior to causing left ventricular EF reduction on echocardiography.

In our study, LVEF, obtained from 8-frame gated SPECT imaging have been noted to be smaller than those measured with echocardiography. By regression analysis we found a moderate correlation between gated SPECT and echocardiography. (r2: 0.44). As expected, compacting the16-interval data sets into 8 intervals leads to lower ejection fractions, because of smoothing the time-volume curve21.

Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients with wall motion abnormality (n = 9)</th>
<th>Patients with normal wall motion (n = 13)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (year)</td>
<td>19.7</td>
<td>17.1</td>
<td>0.077</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>5/4</td>
<td>14/19</td>
<td>0.022</td>
</tr>
<tr>
<td>Ferritin concentration &lt; 2000 ≥ 2000 mg/ml</td>
<td>5/4</td>
<td>17/16</td>
<td>1.00</td>
</tr>
<tr>
<td>Total number of transfusion &lt; 200 ≥ 200</td>
<td>2/7</td>
<td>14/19</td>
<td>0.442</td>
</tr>
<tr>
<td>ALT value &lt; 40 ≥ 40 U/L</td>
<td>3/4</td>
<td>22/11</td>
<td>0.698 **</td>
</tr>
<tr>
<td>AST value &lt; 33/ ≥ 33 U/L</td>
<td>3/4</td>
<td>20/13</td>
<td>1.00 **</td>
</tr>
</tbody>
</table>

*Mann Whitney U test; **Fischer’s Exact Test.
Exercise induced myocardial ischemia was not seen in any of our patients. A study by Lauffer\textsuperscript{21} showed significant correlation between iron stores and coronary artery disease. Iron is believed to promote coronary atherosclerotic disease (CAD) by increasing lipid peroxidation\textsuperscript{22-24}. In a study by Salonen et al\textsuperscript{25}, ferritin was reported as a risk factor for myocardial infarction. However, the relation between ferritin levels and myocardial infarction was higher in patients who had increased serum LDL and cholesterol levels.

In our study, there was only one patient with fixed perfusion defect involving the inferior wall. The absence of the elevation of LDL and cholesterol levels in 38 and 37 patients respectively and the normal scintigraphic findings in 41 patients suggests that iron overload is not solely enough to induce the formation of coronary atherosclerosis in thalassemic patients. LDL and iron probably play a synergistic role in the formation of atherosclerosis and must both be elevated as suggested by Salonen et al\textsuperscript{25}. The patient who had a fixed perfusion defect was a 30 year old male patient with normal LDL and cholesterol levels. He was hospitalized 3 months after the scintigraphy because of chest pain but coronary angiography was not performed. The possible explanation for a fixed defect accompanied by reduced wall motion is myocardial infarction which might have occurred due to increased hematocrit levels following transfusion. There is a case in the literature which recurred due to increased hematocrit following transfusion which was confirmed by electrocardiography that showed ST elevations\textsuperscript{28}. Since coronary angiography revealed normal coronary arteries, infarction was attributed to thromboembolic events that may have occurred due to the rise in hematocrit following transfusion.

Although there were more patients with wall motion abnormality in patients with thalassemia major compared to control patients, our findings show that laboratory and clinical parameters are not adequate to predict cardiac dysfunction in patients with thalassemia major which is discordant with the results of Scopinaro et al\textsuperscript{22} who reported a significant correlation with the total number of blood transfusions and left ventricle EF. In our study no significant correlation was found between wall function and serum ALT, AST and ferritin levels. This finding can be due to the adequate control of serum ferritin levels and effective chelation therapy. Cumulative blood transfusion load, which has a strong relation to cardiac iron content\textsuperscript{3}, was also not associated with reduced in myocardial perfusion or function in this study. These findings suggest that mechanical dysfunction or myocardial ischemia is not only related to iron overload.

Interestingly, high left ventricular EF values were observed in thalassemic patients with normal wall motion. This can be attributed to their chronic anemia which causes increase in cardiac output to maintain a normal mean systemic blood pressure which has already been reported\textsuperscript{21-22,25}. Another interesting finding in our study was the predominance of boys who had impaired left ventricle EF (p = 0.022). This difference might be due to the preventive role of menstrual iron loss in women\textsuperscript{26}.

In conclusion, our results indicate that gated SPECT myocardial perfusion scintigraphy is clinically reliable and has the added advantage of evaluating ventricular perfusion in addition to function. It has a role in monitoring early cardiac dysfunction which can not be shown by echocardiography. Laboratory results such as ALT, AST and ferritin values are not adequate to predict the cardiac damage.

REFERENCES


