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Thalassemic Cardiomyopathy: Echocardiographic Difference Between Major and Intermediate Thalassemia at Rest and During Isometric Effort: Yearly Follow-Up

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Summary: Left ventricular (LV) performance was studied in young patients with severe chronic anemia due to β-thalassemia major, intermedia, and in healthy control subjects. M-mode echocardiograms were recorded in each patient and semiautomatic computerized analysis of the tracings provided data relating to LV performance. Then a statistical analysis of the difference between each specific thalassemic group and the normal subjects was made using Student's *t*-test for unpaired data. The study showed that cardiac dysfunction is more serious in major than in intermediate β thalassemia. A follow-up one year later showed a progressive deterioration of the cardiac indices, in spite of treatment with desferrioxamine. A handgrip test was performed in the follow-up study, which permitted us to distinguish different groups relative to the changes in LV performance indices. Our findings indicate that echocardiography provides a simple noninvasive means for assessing changes in the cardiac structure and function, which should also prove useful in the serial evaluation of patients at risk of developing myocardial iron deposition.

Key words: thalassemia, cardiomyopathy, echocardiography, isometric effort, chelating therapy, hemosiderosis, desferrioxamine

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Introduction

Mediterranean anemia, or thalassemia, leads to hemosiderosis as a consequence of a pathological destruction of red blood cells, increased intestinal absorption of iron, and as a consequence of frequent hemotransfusions. In this situation, the myocardium gradually develops infiltrative cardiomyopathy with dilatative evolution.[1-7] Thalassemia major (M), a homozygous recessive autosomal inborn error, leads to marked clinical manifestations, such as defects in physical development.[8-11] In thalassemia intermedia (I), there is less severe clinical damage.[12-15]

The aim of our study was to verify whether there are echocardiographic parameters suitable to distinguish thalassemia major from thalassemia intermedia, and to evaluate left ventricular performance by means of semiautomatic computerized analysis of M-mode echocardiographic tracings in subjects affected by major and intermediate thalassemia compared with normal control (N) subjects. A one-year follow-up permitted us to determine the evolution of the disease; the handgrip test permitted us to establish patterns of differentiation based on the changes in left ventricular performance indices.

Material and Methods

Of 32 patients studied, 22 (13 males, 9 females; mean age 16.2±3.7 years) had thalassemia major and 10 (4 males, 6 females; mean age 23.5±10 years) had thalassemia intermedia. Fourteen healthy subjects (mean age 23.9±5.5 years) served as controls. All thalassemia major patients had received hemotransfusions in the past and were transfused during the first echocardiographic evaluation (from 117 to 503 total units from birth).

All subjects had splenectomy at an early age. Only 3 of 10 thalassemia intermedia patients received two or more transfusions, and 7 of 10 had undergone splenectomy. Fewer transfusions and splenectomies were performed at later ages compared with thalassemia major patients.

All patients had undergone slow subcutaneous infusion of chelating desferroxamine for some years and ferritin was periodically measured as an index of severity of the illness. M-mode chocardiographic evaluation (SKE Ekoline 21) was carried out at a paper speed of 100 mm/s and simultaneous electrophonocardiographic tracings were recorded.

All tracings were then analyzed by the semiautomatic computerized method (Cardio 70 Kontron, Instant Program). Each tracing was analyzed at three RR intervals. The results were submitted for statistical analysis (Student's *t*-test for unpaired data).

The following year, the same subjects (except one who had died from an untreatable cardiac heart failure) were echocardiographically monitored following the same methods and were then subjected to isometric effort. Echocardiogram recordings during the handgrip test were obtained at rest, and at 30 s, 1, 2, 3 min after beginning and at 1, 2, 3 min after the end of testing. Simultaneous pressure values were recorded. The effort expended by the patients was 33% of the maximal effort to which each patient had previously been submitted. The parameters considered are shown in Tables I–VI.

Results

The initial body surface area (BSA) was 1.32 m^2 in thalassemia major, 1.55 m^2 in thalassemia intermedia, and

TABLE I Modifications of echocardiographic parameters at the first control and after one year

Parameter	1983			1984		
	Major	Intermediate	Normal	Major	Intermediate	Normal
EDD	47.2±5.1	53.1±7.0	47.7±5.7	48.3±5.2	49.5±4.3	49.1±4.5
ESD	32.2±4.0	37.1±5.0	30.4±5.8	36.5±4.3	37.2±4.1	32±4.1
EDD/m^2	35.8±4.0	33.6±4.2	27.2±1.9	35±4.5	31.5±3.8	27.8±1.8
ESD/m^2	23.9±3.9	23.8±3.3	17.3±2.2	26.4±3.4	23.7±3.0	17.9±1.9
V%	32.5±4.2	31.1±3.7	36.2±6.2	27.7±4.2	25±4.0	35.1±5.9
VCFSP	2.3±0.4	2.4±0.7	2.5±0.6	1.9±0.6	1.5±0.2	2.4±0.5
VCFDP	3.5±0.7	3.4±1.4	3.7±1.6	2.4±0.9	2±0.4	3.7±1.5
IVS%	36.8±12.1	41.6±10.8	59.2±12.4	36.2±12.2	36.3±12.5	57.3±10.9
IVSSP	4.5±1.7	4.5±1.7	4.4±1.7	2.4±0.8	4.1±1.1	4.5±1.6
IVSDP	3.8±1.3	3.9±1.0	4.4±1.6	3.0±1.6	2.8±1.1	4.5±1.5
IVSST	11.3±2.7	12.8±1.8	9.8±1.0	10.7±1.8	11.1±1.1	9.7±1.0
IVSDT	7.3±2.0	8.2±0.7	5.9±0.9	7.3±1.5	7.3±1.3	6.0±0.9
PW%	81.9±22.9	89.3±21.9	95.3±18.4	60.4±20.6	64.1±19.3	92.4±15.3
PWSP	7.6±3.3	7.2±2.9	7.0±2.1	4.6±2.4	3.8±1.2	7.0±1.9
PWDP	4.5±2.0	4.2±1.5	4.4±1.2	3.5±1.5	3.5±0.9	4.5±1.1
PWEX	33.1±4.6	44.5±5.1	57.1±10.9	62.1±12.5	52.6±10.9	59.3±9.4
BSA	1.32±0.1	1.55±0.2	1.75±0.2	1.38±0.2	1.57±0.1	1.79±0.2
AGE	16.2±3.7	23.5±10.1	23.9±5.5	18.1±3.4	25.3±5.3	24.9±5.5
FERR	2877±2159	1157±1108	—	3025±2515	828±808	—
HR	83.5± —	76.2± —	68.5± —	82.4± —	73.4± —	67.1± —
Hb	11.8±0.6	8.8±0.9	—	11.6±0.6	8.9±1.0	—
IRT	51.7±14.8	52±18.2	56.7±25	53.7±12.1	51.5±16.2	55.4±20

Abbreviations: EDD = end-diastolic diameter (mm); ESD = end-systolic diameter (mm); EDD/m^2 = end-diastolic diameter in relation to body surface (mm/m^2); ESD/m^2 = end-systolic diameter in relation to body surface (mm/m^2); V% = percentage diameters decrease of left ventricule; VCFSP = systole peak velocity of circumferential fiber shortening; VCFDP = diastolic peak velocity of circumferential fiber shortening; IVS% = interventricular septum systolic percentage increase; IVSSP = interventricular septum systolic peak velocity; IVSDP = interventricular septum diastolic peak velocity; IVSST = interventricular septum systolic thickening (mm); IVSDT = interventricular septum diastolic thickening (mm); PW% = posterior wall systolic percentage increase; PWSP = posterior wall systolic peak velocity; PWDP = posterior wall diastolic peak velocity; PWST = posterior wall systolic thickening (mm); PWDT = posterior wall diastolic thickening (mm); PWEX = posterior wall systolic percentage excursion; IRT = isovolumetric relaxation; SBP = systolic blood pressure (mmHg); DBP = diastolic blood pressure (mmHg); MP = mean pressure (mmHg); HR = heart rate (beats/min); AGE (years); BSA = body surface (m^2); FERR = ferritin (mg/ml); Hb = hemoglobin (g/dl); IVSST/m^2 = interventricular septum systolic thickening in relation to body surface; IVSDT/m^2 = interventricular septum diastolic thickening in relation to body surface; PWST/m^2 = posterior wall systolic thickening in relation to body surface; PWDT/m^2 = posterior wall diastolic thickening in relation to body surface.

1.75 m² in normals. Serum ferritin concentration was 2877±2158 mg/ml in the major syndrome, and 1157±1108 mg/dl in the intermediate syndrome. Hemoglobin mean was 11.9±0.6 g/dl in major patients and 8.9±1 g/dl in intermediate patients. The end-diastolic and the end-systolic diameters relative to body surface (EDD/m²−ESD/m²) were statistically higher in thalassemia patients (Table I) compared with normal subjects ($p<0.001$), and higher in the major compared with intermediate syndrome (Fig. 1). The same behavior was observed with regard to posterior wall and septum thickening relative to body surface (IVSST/m²-IVSDT/m²-PWDT/m²). The systolic percentage septum increase (IVS%) did not show any considerable difference between the two thalassemic groups; on the contrary, there was quite a significant difference between thalassemia major patients and normals ($p<0.01$), and between intermediate patients and normals ($p<0.01$) (Fig. 2). Posterior wall systolic percentage increase (PW%) demonstrated a similar behavior, though not statistically significant (Fig. 3). The percentage diameter decrease (V%) was reduced ($p<0.01$) in all thalassemics compared with normal subjects with no significant difference between the thalassemic groups (Fig. 2). The systolic septum and posterior wall peak velocities (IVSSP-PWSP) were slightly increased in thalassemics, more so in those with the major syndrome compared with normals ($p<0.05$). Isovolumetric relaxation (IRT) did not show relevant variations in the three groups. Heart rate (HR) was shown to be higher in majors compared with intermediates, and intermediates as compared with normals (Fig. 4). After one year, left ventric-

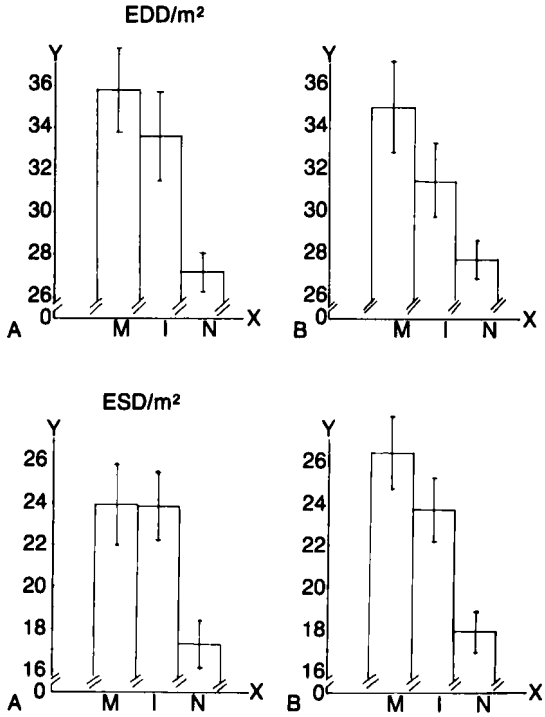

FIG. 1 Changes of EDD/M² and ESD/M² in thalassemia major (M), intermedia (I), and in normal subjects (N): (A) first recording (1983); (B) control after one year (1984)

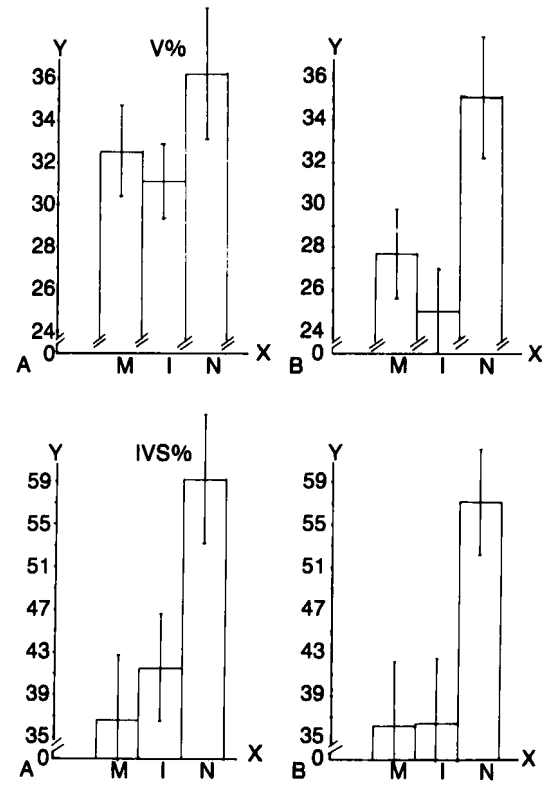

FIG. 2 Changes of V% and IVS% in M, I, and N.

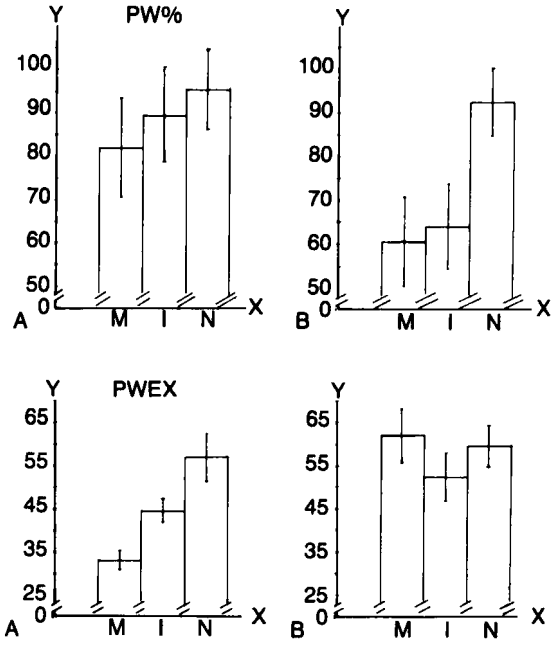

FIG. 3 Changes of PW% and PWEX in M, I, and N.

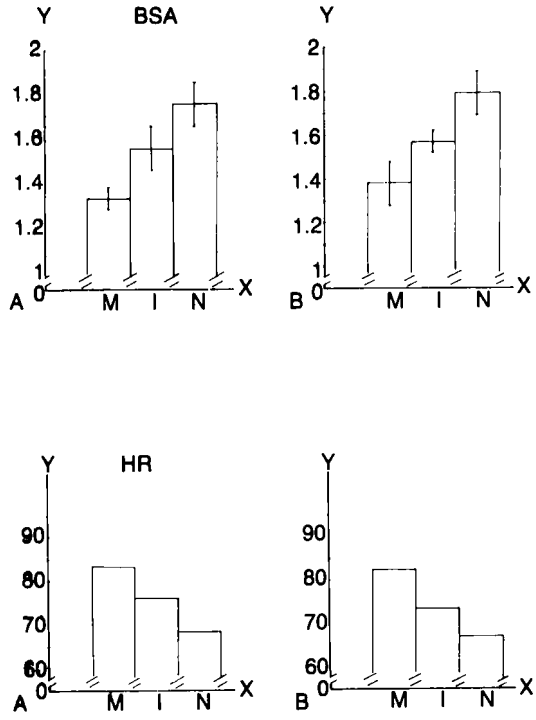

FIG. 4 Changes of BSA and HR in M, I, and N.

ular function indices usually deteriorate in both thalassemia groups (Table II). Body surface (area) (BSA) increased both in normal and thalassemic subjects as consequence of increased weight (Fig. 4). EDD/m² and ESD/m² showed marked statistical alteration in both thalassemics. Percentage diameter decrease, percentage posterior wall increase (V%-PW%), and systolic peak velocities showed a more marked decrease in the major syndrome. Systolic percentage increase of intraventricular septum (IVS%) increased in intermediates, according to the values obtained in the first study on major patients. Posterior wall systolic percentage excursion (PWEX) was considerably increased in the major syndrome and slightly increased in the intermediate. Heart rate variation was not significant. Serum ferritin concentration was lower than at the previous year's measurements: in I:828±251; M:3050±2000.

After handgrip performance, all subjects were further divided into three major groups (MA, MB, MC) and two intermediate groups (IA, IB) according to principal behavior parameters of the ventricular function observed during echocardiographic monitoring.

In the MA group, percentage decrease of ventricular diameters (V%), systolic percentage septum increase (IVS%), posterior wall systolic percentage increase (PW%), and diastolic-systolic peak velocities (IVSSP-IVSDP and PWSP-PWDP) indicated a steady decrease during the test, which was then followed by an increase

TABLE II Modifications of echocardiographic parameters during handgrip in thalassemia major (group with moderate increase of left ventricular parameters)

Parameter	B	½	1	2	3	A 1	A 2	A 3
EDD	48.3±5.2	46.5±4.0	48.0±2.6	49.1±3.0	49.1±4.6	49.1±4.8	49.3±4.2	49.1±3.1
ESD	36.5±4.3	34.6±3.9	34.8±3.8	35.5±3.3	36.1±4.1	35.6±4.2	35.6±3.3	37.6±2.0
EDD/m²	35.0±4.5	33.7±4.7	34.8±5.8	35.6±6.4	35.6±5.0	35.5±5.7	35.7±5.3	35.6±5.9
ESD/m²	26.4±3.4	25.1±2.5	25.2±2.7	25.7±3.5	26.1±2.8	25.8±4.5	25.8±3.0	27.2±4.0
V%	27.7±4.2	29.5±4.5	30.6±5.4	29.8±2.7	30.5±5.3	30.5±5.8	29.3±2.5	25.8±2.2
VCFSP	1.9±0.6	2.1±0.7	2.4±0.6	2.4±0.8	2.0±0.3	2.1±0.5	2.0±0.6	1.7±0.3
VCFDP	2.4±0.9	2.5±0.5	2.8±0.8	2.5±0.4	2.5±0.4	2.6±1.1	2.4±0.7	2.2±0.5
IVS%	36.2±12.2	39.5±16.0	53.0±18.7	54.3±13.3	48.8±12.9	52.6±20.1	43.3±12.6	40.5±7.6
IVSSP	2.4±0.8	2.7±0.6	3.9±1.8	4.8±1.2	2.6±0.5	2.7±1.1	3.3±1.0	2.5±0.8
IVSDP	3.0±1.6	3.0±0.8	3.3±0.9	4.7±2.0	2.7±0.8	3.3±1.1	2.9±1.5	2.3±0.5
IVSST	10.7±1.8	10.5±2.5	10.1±2.3	10.3±1.9	10.1±1.4	10.0±2.2	10.0±2.3	10.1±1.6
IVSDT	7.3±1.5	6.6±1.4	6.1±1.3	6.5±1.3	6.3±1.4	6.5±1.8	6.3±1.6	7.0±0.9
PW%	60.4±20.6	69.1±21.2	65.0±20.0	71.6±23.5	75.6±19.0	69.8±18.1	65.8±19.5	62.6±14.4
PWSP	4.6±2.4	5.1±2.2	4.8±2.1	5.7±3.4	4.2±1.5	4.2±1.7	4.8±2.1	4.0±0.8
PWDP	3.5±1.5	3.5±1.6	4.3±2.1	5.0±2.5	3.3±1.6	3.2±0.5	4.2±2.8	3.0±0.7
PWEX	62.1±12.5	70.1±16.6	74.1±26.0	76.6±23.3	79.3±22.5	65.3±17.8	72.1±18.1	68.3±22.5
SBP	117.1±10.3	129.1±8.3	131.9±6.4	133.8±8.5	139.6±9.2	120.8±7.4	117.0±6.2	115.5±5.2
DBP	78.3±9.2	85.0±6.4	86.4±5.6	89.1±6.3	85.7±5.2	83.1±5.8	79.7±4.3	80.1±4.8
MP	91.4±9.4	89.8±7.2	101.5±6.1	103.7±7.8	100.6±6.4	95.6±6.5	92.1±5.8	91.9±5.1
HR	82.4± —	93.8± —	93.8± —	91.1± —	86.6± —	79.4± —	80.7± —	81.0± —

Abbreviations: See Table I.

TABLE III Modifications of echocardiographic parameters during handgrip in thalassemia major (group with no significant variations of left ventricular parameters)

Parameter	B	½	1	2	3	A 1	A 2	A 3
EDD	48.3±5.2	46.8±4.6	47.8±5.0	46.6±3.9	47.8±5.7	46.6±4.8	48.2±5.4	48.0±5.2
ESD	36.5±4.3	36.0±3.8	36.4±3.5	34.8±5.2	36.4±4.0	34.4±5.0	35.0±3.8	34.6±3.6
EDD/m²	35.0±4.5	33.9±3.8	34.6±3.8	33.8±3.1	34.6±4.1	33.8±4.0	34.9±4.2	34.8±4.4
ESD/m²	26.4±3.4	26.8±3.3	26.3±2.9	25.2±4.0	26.4±3.2	24.9±3.9	25.4±3.1	25.1±3.1
V%	27.7±4.2	25.6±3.9	27.4±2.9	29.6±5.4	26.6±4.8	29.2±5.8	30.6±2.9	31.6±2.9
VCFSP	1.9±0.6	1.7±0.1	1.7±0.3	2.2±0.5	1.7±0.3	1.8±0.2	1.9±0.2	1.8±0.1
VCFDP	2.4±0.9	2.0±0.4	2.0±0.5	2.3±0.6	2.1±0.4	2.1±0.4	2.3±0.2	2.3±0.3
IVS%	36.2±12.2	44.6±24.8	38.6±23.7	45.6±21.3	35.5±21	37.2±17.7	37.0±18.3	30.4±19.1
IVSSP	2.4±0.8	2.8±0.7	3.0±1.2	2.5±0.5	2.3±0.8	2.0±0.6	2.2±1.1	2.2±0.4
IVSDP	3.0±1.6	3.3±1.4	2.8±1.5	2.7±0.3	2.2±0.6	2.4±0.5	2.1±0.8	2.2±0.7
IVSST	10.7±1.8	10.2±1.2	9.8±0.8	10.0±1.4	9.6±0.8	9.2±1.0	10.0±1.2	9.4±0.8
IVSDT	7.3±1.5	6.7±0.8	6.2±0.8	6.4±1.1	6.8±1.1	6.4±1.5	7.0±1.5	6.4±1.1
PW%	60.4±20.6	50.6±8.6	62.4±16.9	57.8±15.9	58.0±16.5	63.6±14.0	68.8±15.7	66.0±8.6
PWSP	4.6±2.4	3.6±1.2	3.5±1.1	4.2±1.7	4.1±1.4	3.8±1.6	3.9±1.4	4.3±1.4
PWDP	3.5±1.5	2.5±0.5	3.3±0.1	3.9±1.6	2.9±0.5	2.9±1.0	3.7±1.0	3.4±0.4
PWEX	62.1±12.5	58.4±8.7	72.4±11.0	69.0±13.0	65.8±14.1	59.4±11.4	63.6±12.6	72.4±10.2
SBP	117.7±10.3	129.1±8.3	131.9±6.4	133.8±8.5	130.6±9.2	120.8±7.4	117.0±6.2	115.5±5.2
DBP	78.3±9.2	85.0±6.4	86.4±5.6	89.1±6.3	85.7±5.2	83.1±5.8	79.7±4.3	80.1±4.8
MP	91.4±9.4	89.8±7.2	101.5±6.1	103.7±7.8	100.6±6.4	95.6±6.5	92.1±5.8	91.9±5.1
HR	82.4± —	93.8± —	93.8± —	91.1± —	86.6± —	79.4± —	80.7± —	81.0± —

Abbreviations: See Table I.

during the recovery phase. However, absolute values were lower than those observed in normals.

The MB group did not show significant variations when compared with basal tracings, whereas in subdivision MC, a marked increase of the indices during maximum effort was noted, with subsequent gradual return to the basal condition during the recovery phase (Table III) though not reaching the levels of healthy patients.

End-diastolic diameter decreased in all thalassemia major subdivisions in contrast with that observed in the normal group. The two groups demonstrated similar behavior to MA and MC.

Discussion and Conclusions

In our study on thalassemia major patients, we found it seems appropriate to relate end-systolic and end-diastolic values to body surface, since absolute values were similar to those obtained in normal subjects, as confirmed by other authors. Hemoglobin values were significantly greater in the major syndrome; this is due to the greater frequency of hemotransfusions which maintained Hb values steady at medium-high levels. The wide standard deviation referred to ferritin values in the major syndrome is due to the presence of one subject whose values were well above 10,000 mg/ml.

Echocardiography demonstrated a very useful noninvasive method for serial evaluation of myocardial damage in these subjects. Furthermore, echocardiography allows the identification of patients' families having different degrees of severity of the illness in relation to this pathology.

The use of isometric effort with the handgrip allows further classification of groups according to different stages of illness (see Figs. 5, 6, 7).

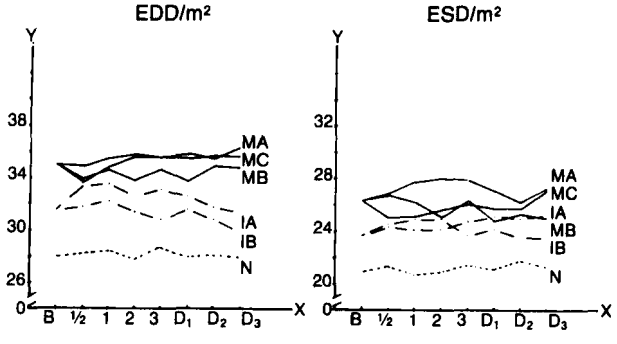

FIG. 5 Changes of EDD/M² and ESD/M² during handgrip. B: resting recording; 1/2, 1, 2, 3: recordings at 1/2, 1, 2, 3 min; D1, D2, D3: recording at 1, 2, 3 min after stopping test. MA = major group with left ventricular parameters decrease, MB = major group with no significant variations (compared with basal tracings), MC = major group with left ventricular parameters increase, IA = intermediate group with left ventricular parameters increase, IB = intermediate group with left ventricular parameters increase, N = control group.

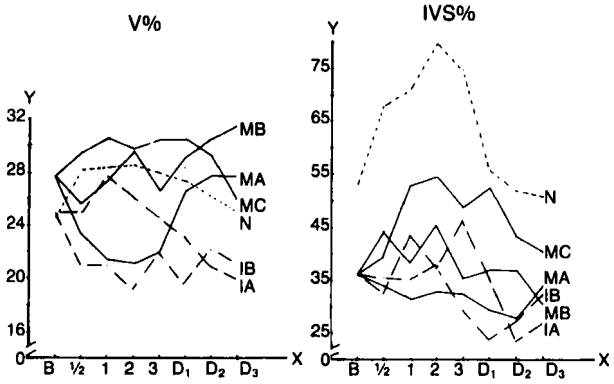

FIG. 6 Changes of V% and IVS% during handgrip.

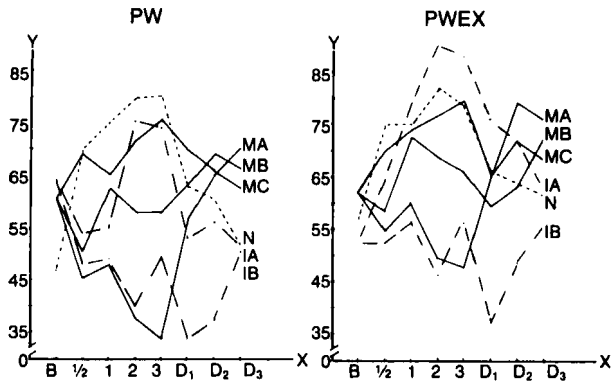

FIG. 7 Changes of PW% and PWEX during handgrip.

TABLE IV Modifications of echocardiographic parameters during handgrip in thalassemia major (group with moderate decrease of left ventricular parameters)

Parameter	B	½	1	2	3	A 1	A 2	A 3
EDD	48.3±5.2	48.2±4.5	49.0±4.4	49.4±4.5	49.2±5.1	49.5±3.2	49.0±4.5	50.1±4.7
ESD	36.5±4.3	37.2±5.4	38.4±4.8	38.8±4.8	38.7±4.8	37.5±4.8	36.4±4.5	37.8±3.9
EDD/m²	35.0±4.5	34.9±3.0	35.5±3.3	35.8±3.7	35.6±3.7	35.8±3.1	35.5±3.6	36.3±3.1
ESD/m²	26.4±3.4	26.9±3.1	27.8±2.6	28.1±3.3	28.0±3.5	27.2±5.0	26.3±2.8	27.4±2.8
V%	27.7±4.2	23.4±8.9	21.5±5.4	21.2±4.5	22.0±4.3	26.7±4.6	27.8±3.3	27.8±2.5
VCFSP	1.9±0.6	1.5±0.5	1.5±0.6	1.4±0.3	1.5±0.3	1.8±0.5	1.7±0.1	1.6±0.2
VCFDP	2.4±0.9	1.7±0.6	1.6±0.8	1.6±0.5	1.5±0.2	2.1±0.7	2.1±0.2	1.9±0.5
IVS%	36.2±12.2	34.0±21.5	31.7±18.5	33.2±17.6	32.7±17.4	29.5±13.3	28.1±5.4	33.8±10.3
IVSSP	2.4±0.8	2.6±1.0	2.5±2.5	2.1±1.0	2.9±1.4	3.5±2.0	2.3±1.7	2.5±1.1
IVSDP	3.0±1.6	2.7±1.0	2.8±2.3	2.2±0.7	3.0±1.0	2.6±1.2	2.7±0.6	2.6±1.0
IVSST	10.7±1.8	9.8±1.8	9.8±1.4	9.8±1.3	10.2±1.7	10.1±1.9	10.0±1.8	9.3±1.7
IVSDT	7.3±1.5	6.5±1.7	6.5±1.7	7.0±1.6	6.7±1.5	7.2±1.9	7.7±1.8	7.5±2.3
PW%	60.4±20.6	45.5±18.3	47.8±18.5	38.1±18.3	34.0±18.4	56.4±24.0	64.8±23.5	70.0±21.5
PWSP	4.6±2.4	3.5±0.7	3.4±1.1	3.5±1.4	3.4±1.4	4.3±2.3	4.3±1.1	3.8±1.1
PWDP	3.5±1.5	3.7±0.6	3.5±1.0	2.5±0.6	3.0±1.2	3.7±1.8	3.9±0.9	3.8±0.7
PWEX	62.1±12.5	55.0±16.9	60.1±19.2	49.8±22.1	48.1±23.1	64.8±18.4	79.0±18.8	75.7±13.3
SBP	117.7±10.3	129.1±8.3	131.9±6.4	133.8±8.5	130.6±9.2	120.8±7.4	117.0±6.2	115.5±5.2
DBP	78.3±9.2	85.0±6.4	86.4±5.6	89.1±6.3	85.7±5.2	85.1±5.8	79.7±4.3	80.1±4.8
MP	91.4±9.4	89.8±7.2	101.5±6.1	103.7±7.8	100.6±6.4	95.6±6.5	92.1±5.8	91.9±5.1
HR	82.4± —	93.8± —	93.8± —	91.1±—	86.6± —	79.4± —	80.7± —	81.0± —

Abbreviations: See Table I.

TABLE V Modifications of echocardiographic parameters during handgrip in thalassemia intermediate (group with moderate increase of left ventricular parameters)

Parameter	B	½	1	2	3	A 1	A 2	A 3
EDD	49.5±4.3	52.3±4.7	52.6±5.5	51.3±5.6	52.0±6.2	51.3±5.6	50.0±6.0	49.3±3.5
ESD	37.2±4.1	38.3±1.5	38.0±2.0	38.0±0.5	39.0±1.0	39.6±1.1	39.3±1.5	39.6±2.0
EDD/m²	31.5±3.8	33.3±4.7	33.5±4.8	32.6±5.2	33.1±5.6	32.6±5.2	31.8±5.0	31.4±3.4
ESD/m²	23.7±3.0	24.4±1.3	24.2±1.2	24.2±1.4	24.8±1.2	25.2±1.5	25.0±2.5	25.2±3.0
V%	25.0±4.0	25.0±7.8	27.8±9.5	26.3±9.1	24.6±9.6	23.3±9.8	21.0±7.5	20.0±4.3

(continued)

TABLE V *(continued)*

Parameter	B	½	1	2	3	A 1	A 2	A 3
VCFSP	1.5±0.2	1.4±0.2	1.5±0.4	1.5±0.4	2.2±0.6	1.5±0.5	1.3±0.2	1.0±0.2
VCFDP	2.0±0.4	1.7±0.2	1.8±0.8	1.8±0.6	2.2±1.2	1.8±0.6	1.4±0.2	1.4±0.2
IVS%	36.3±12.5	32.3±15.3	43.3±12.1	37.6±14.6	47.0±12.6	35.3±4.6	23.6±8.1	27.0±15.1
IVSSP	4.1±1.1	3.3±0.3	2.1±1.0	2.1±0.3	3.8±1.6	2.8±0.9	3.2±1.3	2.4±1.1
IVSDP	2.8±1.1	2.6±0.8	2.1±0.7	1.8±0.2	2.9±0.3	2.8±0.3	2.9±0.5	1.7±0.6
IVSST	11.1±1.1	12.0±1.0	13.0±1.0	12.6±1.1	13.3±0.5	12.3±0.5	11.3±0.5	11.6±1.2
IVSDT	7.3±1.3	8.0±1.0	8.0±1.0	8.0±1.0	8.6±0.5	8.0±1.0	7.6±1.1	8.3±0.5
PW%	64.1±19.3	54.0±14.5	55.0±10.1	75.0±23.0	74.0±25.0	53.0±21.1	56.0±20.5	51.6±20.0
PWSP	3.8±1.2	2.8±1.2	3.6±0.3	4.2±1.3	4.6±2.3	3.5±1.3	2.9±0.9	3.1±0.8
PWDP	3.5±0.9	3.0±0.8	4.0±1.3	4.0±1.4	4.5±1.3	3.5±1.4	3.5±0.9	2.8±0.6
PWEX	52.6±10.9	64.3±5.1	79.0±13.3	90.0±20.5	88.0±18.0	76.0±13.8	72.3±16.9	62.3±17.5
SBP	125.0±6.3	134.1±7.2	137.5±6.4	137.3±5.8	139.1±7.9	130.5±8.3	126.6±6.4	123.0±6.3
DBP	82.5±4.1	84.1±5.3	85.8±4.9	88.3±4.3	90.8±6.1	85.0±5.4	84.1±3.6	81.5±3.9
MP	96.6±4.4	100.7±6.3	103.0±5.5	104.6±6.5	106.9±6.4	100.1±6.5	98.2±4.9	95.3±5.7
HR	73.4± —	72.0± —	68.5± —	73.9± —	75.0± —	70.8± —	69.5± —	72.1± —

Abbreviations: See Table I.

We can explain the different behaviors of the left ventricular function indices according to several factors in this disease such as thalassemia major or intermedia, number and frequency of hemotransfusions, age at splenectomy, and age at the start of chelating therapy as well as hemoglobin ferritin levels (Figs. 8, 9, and 10).

Thalassemia major subjects who suffered from severe anemia prior to 1970, because of outdated transfusion methods and different chelating therapy compliance, presented an obstacle to drawing definite conclusions.

The importance of our work probably lies in having found a follow-up method which will determine whether

TABLE VI Modifications of echocardiographic parameters during handgrip in thalassemia intermediate (group with moderate decrease of left ventricular parameters)

Parameter	B	½	1	2	3	A 1	A 2	A 3
EDD	49.5±4.3	50.0±6.5	50.6±7.0	49.3±5.1	48.3±5.1	49.6±6.6	48.3±7.5	47.0±8.5
ESD	37.2±4.1	38.6±5.5	39.3±5.8	39.3±4.9	37.3±6.1	39.0±7.0	37.3±8.5	37.0±7.8
EDD/m²	31.5±3.8	31.8±3.9	32.2±3.6	31.4±2.5	30.8±2.5	31.6±3.4	30.8±6.7	29.9±4.6
ESD/m²	23.7±3.0	24.6±2.9	25.0±3.1	25.0±2.6	23.7±3.2	24.2±3.9	23.7±4.9	23.6±4.3
V%	25.0±4.0	21.0±1.7	21.0±1.0	19.3±1.1	22.0±2.6	19.6±4.0	22.3±6.2	21.3±7.5
VCFSP	1.5±0.2	1.1±0.5	1.3±0.2	1.3±0.2	1.3±0.4	1.1±0.3	1.3±0.5	1.2±0.3
VCFDP	2.0±0.4	1.4±0.3	1.4±0.5	1.4±0.1	1.1±0.5	1.4±0.5	1.3±0.6	1.4±0.4
IVS%	36.3±12.5	35.6±18.9	35.3±16.0	38.0±15.0	29.3±12.5	24.0±9.5	27.6±12.0	32.3±12.6
IVSSP	4.1±1.1	3.2±1.6	3.7±2.2	2.1±0.8	1.5±0.1	2.5±1.2	1.9±0.6	1.5±0.2
IVSDP	2.8±1.1	2.1±1.6	1.9±0.8	2.4±0.2	1.6±0.2	1.7±0.7	2.1±0.6	1.3±0.1
IVSST	11.1±1.1	11.0±1.0	11.6±1.5	11.0±2.0	11.3±2.0	11.0±2.0	10.3±2.0	10.6±2.2
IVSDT	7.3±1.3	7.0±1.7	7.6±2.3	7.6±2.0	8.3±2.0	8.3±2.5	7.3±1.1	8.0±1.7
PW%	64.1±19.3	48.0±10.5	49.0±12.1	40.0±12.8	49.3±11.0	34.0±12.0	37.6±11.5	50.6±13.1
PWSP	3.8±1.2	3.7±1.9	5.4±2.8	2.6±0.9	2.9±0.9	5.0±1.7	2.4±0.6	3.5±1.6
PWDP	3.5±0.9	3.2±1.5	3.8±1.6	2.4±0.7	2.4±0.3	3.9±1.8	2.4±0.4	3.8±0.8
PWEX	52.6±10.9	52.6±11.6	56.6±9.0	46.3±11.0	56.6±11.0	37.5±17.2	49.0±6.9	56.0±14.9
SBP	125.0±6.3	134.1±7.2	137.5±6.4	137.3±5.8	139.1±7.9	130.5±8.3	126.6±6.4	123.0±6.3
DBP	82.5±4.1	84.1±5.3	85.8±4.9	88.3±4.3	90.8±6.1	85.0±5.4	84.1±3.6	81.5±3.9
MP	96.6±4.4	100.7±6.3	103.0±5.5	104.6±6.5	106.9±6.4	100.1±6.5	98.2±4.9	95.3±5.7
HR	73.4± —	72.0± —	68.5± —	73.9± —	75.0± —	70.8± —	69.5±—	72.1± —

Abbreviations: See Table I.

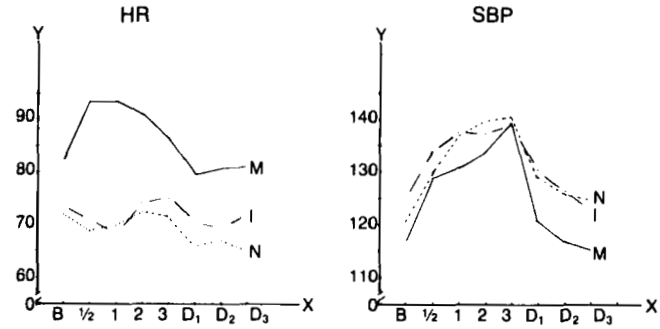

FIG. 8 Changes of HR and SBP during handgrip.

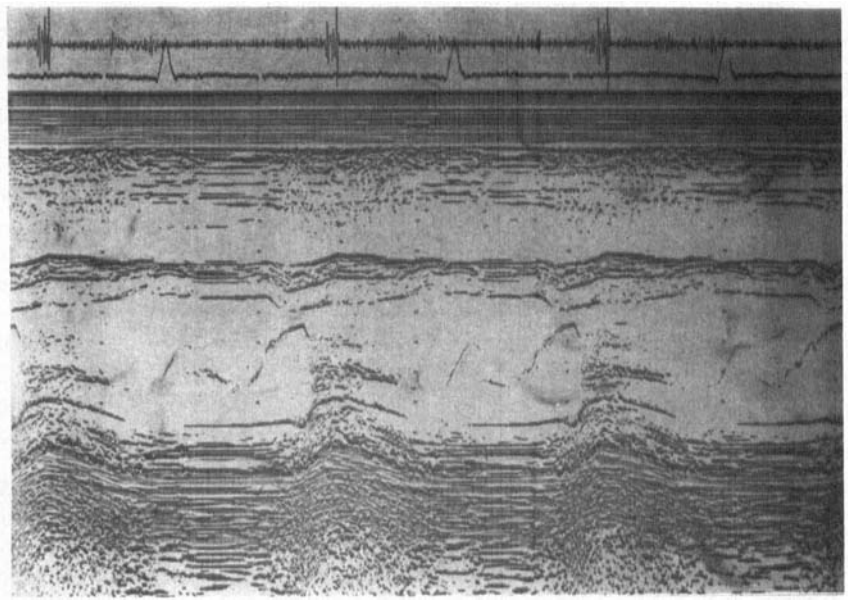

FIG. 9 Echo-strip of thalassemia major patient which represents an increasingly thick interventricular septum.

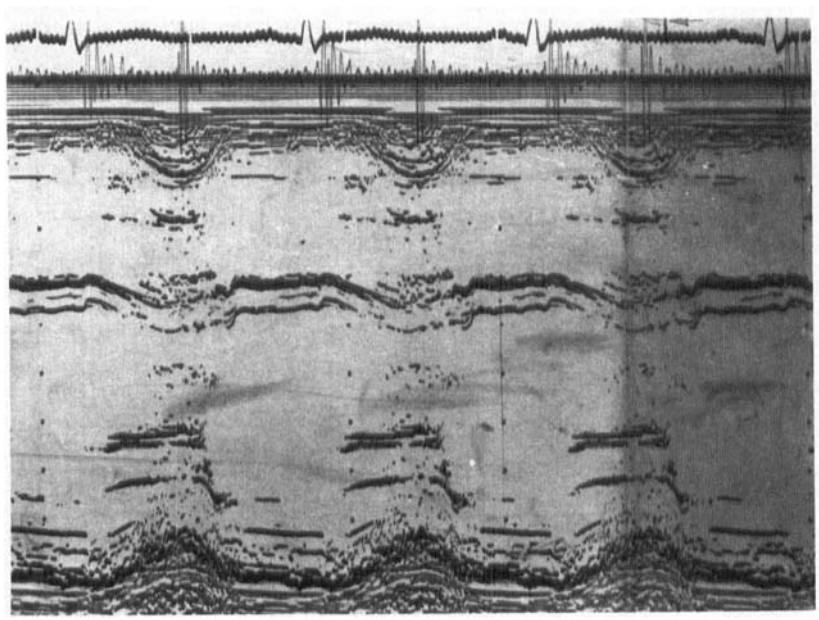

FIG. 10 Echo-strip of major subject which respresents a dilatation of left ventricle.

thalassemia major treated from 1979 onward according to a rigid transfusion protocol and chelating therapy may avoid or significantly reduce myocardiopathy in the near future.

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