Quebec Cooperative Study of
Friedreich's Ataxia

Echocardiographic Findings in Friedreich's Ataxia

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SUMMARY: *Echocardiographic examination of 21 patients with Friedreich's ataxia (age 7 to 28 years) showed cardiac abnormalities in 90% of the cases. They were characterized by varying degrees of septal hypertrophy in 81%, left ventricular free wall hypertrophy in 61%, and a slight reduction of left ventricular internal dimension in 57% of the cases. Asymmetric septal hypertrophy (ASH) with a septal/left ventricular free wall ratio of over 1.3 was found in 29% of the cases, and systolic anterior motion (SAM) of the mitral valve in three patients. Two other patients showed evidence of a different type of cardiomyopathy with marked symmetric left ventricular hypertrophy and marked left ventricular enlargement.*

RÉSUMÉ: *L'examen échocardiographique de 21 patients avec ataxie de Friedreich (âge 7 à 28 ans) montre des anomalies dans 90% des cas. Ces anomalies incluent des degrés divers d'hypertrophie septale (81%), d'hypertrophie de la paroi libre du ventricule gauche (61%) et une légère réduction des dimensions ventriculaires internes dans 57% des cas. Une hypertrophie septale asymmétrique avec un rapport septum/paroi ventriculaire gauche libre dépassant 1.3, furent trouvés chez 29% des cas et un mouvement antérieur en systole de la valvule mitrale chez trois patients. Deux autres patients montrent cependant un type différent de cardiomyopathie avec hypertrophie ventriculaire gauche symmétrique marquée et agrandissement du ventricule gauche.*

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INTRODUCTION

Echocardiography is a diagnostic method utilizing ultrasound to measure dimensions of various cardiac structures and to track their motions faithfully. It has become an accepted diagnostic tool in cardiology for the non-invasive assessment of cardiac size and function (Feigenbaum, 1972; Lalani, 1976).

Cardiac involvement is found in up to 55% of cases with Friedreich's ataxia (Boyer et al., 1962). Echocardiography therefore seems to be a promising method for non-invasive detection and evaluation of possible cardiac abnormalities in patients with Friedreich's ataxia.

SUBJECTS AND METHODS

Echocardiographic examination was performed as part of a cooperative study of patients with Friedreich's ataxia. There was no selection of patients because of suspected cardiac involvement. Satisfactory echocardiographic records were available from 21 patients who were divided into two groups: thirteen individuals (age 7 to 16 years) formed a group of pediatric patients with Friedreich's ataxia and were compared with a group of 28 normal subjects (age 7 to 16 years) without heart disease. Eight individuals (age 17 to 28 years) formed a group of adult patients with Friedreich's ataxia whose echocardiographic data were compared with normal published values (Henry, 1973; Popp, 1969). All these patients were from Groups Ia and Ib.

Echocardiograms were obtained and analyzed in a standard fashion according to the technique described (Feigenbaum, 1972; Henry et al., 1973; Popp et al., 1969). A Smith-French Ekoline 20 echocardiograph with a 2.25 MHz C14 transducer focused at 7.5 cm. and a Honeywell 1856 or a Cambridge recorder were used.

The following echocardiographic parameters were utilized:

$LVID_{(D)}$ — Left ventricular internal dimension in diastole

$LVWT_{(D)}$ — Left ventricular free wall thickness in diastole

$ST_{(D)}$ — Interventricular septal thickness in diastole

$ST_{(D)}/LVWT_{(D)}$ — Septal thickness/posterior left ventricular free wall thickness ratio

PWMV — Posterior wall maximal velocity, obtained by drawing a tangent to the steepest portion of the systolic endocardial excursion and measuring the slope.

An estimation of the left ventricular volume in diastole ($LVVol_{(D)}$) was obtained by $LVID_{(D)}^3$. The ejection fraction was calculated by:

$$EF = \frac{(LVID_{(D)}^3 - LVID_{(S)}^3) \times 100}{LVID_{(D)}^3}$$

$LVID_{(S)}$ — Left ventricular internal dimension in systole

Mean value ±S.D. (standard deviation) were calculated for the echocardiographic data of the group of pediatric patients and normals, and statistical analysis was done by a Student's t-test.

RESULTS

Age and body surface area

There was no significant difference in age and body surface area between the group of pediatric patients with Friedreich's ataxia and normal subjects, age 7 to 16 years (Table 1).

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TABLE 1

ANTHROPOMETRIC AND ECHOCARDIOGRAPHIC DATA

	Patients with Friedreich's ataxia (N = 13)	Normal subjects (N = 28)	
Age (years)	11.9 ± 2.8 (range 7-16)	10.5 ± 2.9 (range 7-16)	NS
BSA (m^2)	1.06 ± 0.19	1.13 ± 0.28	NS
$LVID_{(D)}I$ (cm/m^2)	3.18 ± 0.83	3.85 ± 0.72	*
$LVWT_{(D)}I$ (cm/m^2)	0.89 ± 0.24	0.62 ± 0.14	**
$ST_{(D)}$ I (cm/m^2)	1.01 ± 0.31	0.73 ± 0.18	**
ST/LVWT	1.13 ± 0.21	1.18 ± 0.13	NS
$LVVol_{(D)}I$ (ml/m^2)	35.18 ± 15.66	65.77 ± 12.18	**
EF (%)	71.90 ± 17.70	74.66 ± 7.26	NS
PWMV (cm/sec)	5.15 ± 1.23	5.05 ± 0.76	NS

Abbreviations:

*: $P < 0.05$

**: $P < 0.01$

NS: Not significant

BSA: Body surface area

$LVID_{(D)}I$: Left ventricular internal dimension in diastole index

$LVWT_{(D)}I$: Left ventricular free wall thickness in diastole index

$ST_{(D)}I$: Interventricular septal thickness in diastole index

ST/LVWT: Septal thickness/posterior wall thickness ratio in diastole

$LVVol_{(D)}I$: Left ventricular volume in diastole index

EF: Ejection fraction

PWMV: Posterior wall maximal velocity

Echocardiographic data

Left ventricle and interventricular septum

Individual values of patients with Friedreich's ataxia were compared with normal values (Mean values ± S.D. [standard deviation] were accepted as the range of normal values.) and showed that 13/21 patients had an increase in left ventricular free wall thickness, and 17/21 patients an increase in interventricular septal thickness. Asymmetric septal hypertrophy (ASH) with a septal/left ventricular free wall ratio over 1.3 (range: 1.33 to 1.7, mean 1.43) was found in 6/21 patients with Friedreich's ataxia. Twelve/21 patients showed a decrease in left ventricular internal dimension.

Two patients with Friedreich's ataxia, age 8 and 7 showed an increase in left ventricular internal dimension index (4.64 and 5.16 cm/m^2) and a marked increase in left ventricular free wall thickness index (1.5 and 1.32 cm/m^2) with a septal/left ventricular free wall ratio of 1.1 and 1.0.

Comparison of two groups of pediatric subjects are summarized in Table 1 and Figures 1 and 2.

The mean $LVWT_{(D)}$ index was 43% ($p<0.01$) larger in patients with Friedreich's ataxia than in normal subjects. The mean $ST_{(D)}$ index was 38% ($p<0.01$) thicker in patients with Friedreich's ataxia than in normal subjects. The mean $ST_{(D)}/LVWT_{(D)}$ ratio showed no significant difference between patients with Friedreich's ataxia and normal subjects. The mean $LVID_{(D)}$ index was 17% ($p < 0.05$) smaller in patients with Friedreich's ataxia than in normal subjects.

The estimated mean $LVVol_{(D)}$ was 46% ($p<0.01$) smaller in patients with Friedreich's ataxia than in normal subjects.

There was no significant difference in the estimated mean EF and mean PWMV between patients with Friedreich's ataxia and normal subjects.

Mitral valve

Systolic anterior motion (SAM) was found in three patients (Table II, Figures 3 and 4). Mitral valve prolapse was found in one patient (No. 23). Two patients, age 15 and 12, were normal on echocardiographic examination.

DISCUSSION

Echocardiographic examination of 21 patients with Friedreich's ataxia showed evidence of cardiac abnormalities in 90% of the cases. These abnormalities were: varying degrees of interventricular septal hypertrophy in 81%, left ventricular free wall hypertrophy in 62%, and slight reduction of the left ventricular internal dimension in 57%.

Asymmetric septal hypertrophy (ASH) with a septal/left ventricular free wall ratio over 1.3 was found in 29% of the cases.

Three patients showed evidence of systolic anterior motion (SAM) of the mitral valve. They all had a

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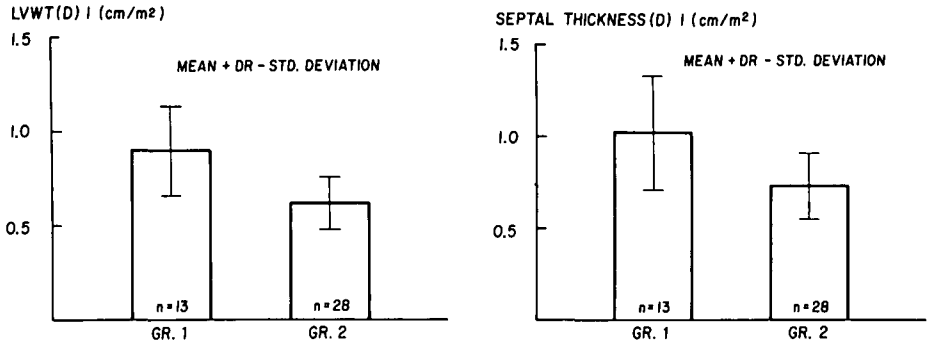
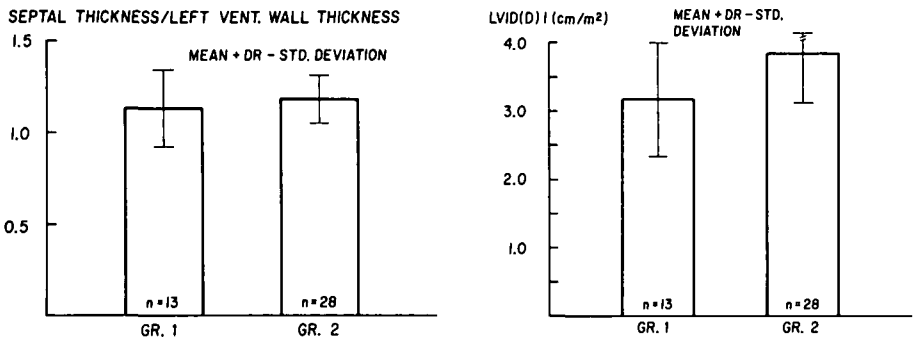


Figures 1a & 1b — Echocardiographic determination of $LVWT_{(D)}I$ (left) and $ST_{(D)}I$ (right) in 13 patients with Friedreich's ataxia (GR 1) and 28 normal subjects (GR 2).



Figures 2a & 2b — Echocardiographic determination of $ST_{(D)}/LVWT_{(D)}$ (left) and $LVID_{(D)}I$ (right) in 13 patients with Friedreich's ataxia (GR 1) and 28 normal subjects (GR 2).

marked septal hypertrophy, but only two had ASH of a minor degree. The third patient had symmetric left ventricular hypertrophy. The interventricular septum contracted poorly in all three patients, and an echocardiographic diagnosis of probable obstructive cardiomyopathy was made in the two patients with ASH. Obstruction could not be ruled out completely in the third patient with symmetric left ventricular hypertrophy. Hemodynamic examination showed evidence of a pressure gradient within the left ventricle of 60 mmHg at rest in one patient and of 38 mmHg only on provocation with isoproterenol in the other patients, who showed ASH. No gradient, either at rest or on provocation, was present in the patient without ASH.

It should be noted that two of our youngest patients with Friedreich's ataxia showed evidence of a different type of cardiomyopathy characterized by marked left ventricular enlargement and concentric left ventricular hypertrophy with a normal/left ventricular free wall ratio. It is not known if this represents a different type of cardiomyopathy or only a different stage in the development of the usual

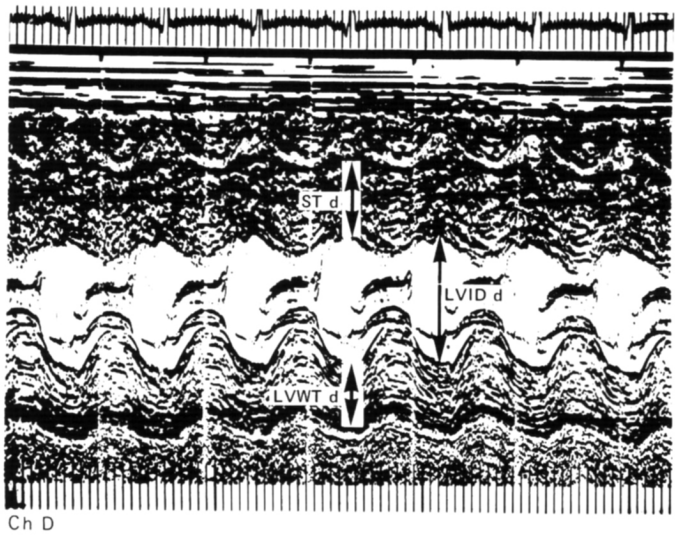


Figure 3 — Left ventricular echocardiogram from patient No. 18 (Group Ia) (Ch. D.) showing asymmetric septal hypertrophy (ASH) of slight degree. $LVID_{(D)}$ — left ventricular internal dimension in diastole. $ST_{(D)}$ — Septal thickness in diastole. $LVWT_{(D)}$ — Left ventricular free wall thickness in diastole.

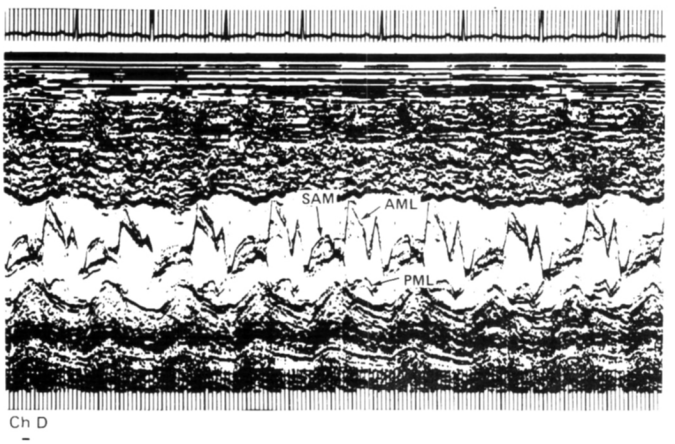


Figure 4 — Mitral valve echocardiogram from the same patient, No. 18, Group Ia (Ch.D), showing systolic anterior motion (SAM) of the anterior leaflet of the mitral valve. SAM — Systolic anterior motion of the anterior mitral valve leaflet. AML — Anterior mitral valve leaflet. PML — Posterior mitral valve leaflet.

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TABLE 2

ECHOCARDIOGRAPHIC DATA OF PATIENTS

WITH SYSTOLIC ANTERIOR MOTION (SAM) OF THE MITRAL VALVE

Patient	S.T. No. 19	Ch. D. No. 20	G.M. No. 35
Age (years)	13	14	12
$ST_{(D)}{}^{I}$ (cm/m^2)	1.32	1.16	1.17
ST/LVWT	1.19	1.36	1.5
Septal thickening (%) in systole	16.7	13.3	16.7

cardiomyopathy found in the other patients with Friedreich's ataxia.

The only report on echocardiographic examination of patients with Friedreich's ataxia that we could find was an abstract by E. R. Smith (1975), who examined 10 patients with Friedreich's ataxia and found ASH in four patients with a septal/posterior wall ratio of 1.4 to 1.9 (mean: 1.66).

In conclusion, echocardiography appears capable of providing qualitative and quantitative information on abnormalities of left ventricular dimension and function and on mitral valve motion. Echocardiographic screening of family members of patients with Friedreich's ataxia should help to detect and define more precisely early cardiac involvement and aid in clarifying the relationship between cardiac and neurological manifestations of this disease. Because of its non-invasive nature, echocardiography can be used repeatedly in the same patient. Echocardiographic follow-up examination of patients with Friedreich's ataxia should give valuable information on the natural history and prognosis of established cardiomyopathy.

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