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EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN CHILDREN WITH ACUTE RHEUMATIC FEVER

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ABSTRACT

This work was planed to evaluate the left ventricular diastolic function in children with acute rheumatic carditis. The study comprised 30 children with acute rheumatic fever 17 males (56.7%) and 13 females (43.3%) their ages ranged from 6 to 15 years. They were divided into two groups. Group I which consists of 20 cases with rheumatic carditis and group II, they were 10 cases with acute rheumatic fever (ARF) without clinical carditis. Twenty children of age and sex matched to patients group were taken as a control. They were divided into two other groups, group III were 10 patients with chronic quiescent rheumatic heart disease, compared to group I and 10 healthy children, group IV were compared to group II. All patients were subjected to full history taking, full clinical examination and laboratory investigations, standard 12 leads ECG, plane x-ray and echocardiography emphasis on left ventricular diastolic function. There was great affection of LV diastolic function indices among patients with acute rheumatic carditis GI when compared with GIII (quiescent RHD). There was significant decrease of E velocity and E/A ratio indices which measured respectively 88.71 ± 30.85 cm/sec and 1.43 ± 0.67 in GI while in group III were 120.10 ± 29.35 cm/sec and 2.00 ± 0.59 . As regard

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deceleration time (DT) the mean value in GI was 133.35 ± 32.79 m/sec and in GIII was 100.00 ± 28.28 m/sec and the difference between both groups was statistically significant. Also, isovolumic relaxation time (IVRT) mean value in GI was 90.60 ± 28.34 msec and was 49.25 ± 12.12 msec in GIII and the difference between both groups was statistically significant. Also there was prolongation of the IVRT duration as the only parameter of diastolic function of LV among ARF patients without carditis (GII) when compared with GIV and the difference was statistically significant. The results revealed that the systolic function of left ventricle as evaluated by fractional shortening (FS) in ARF patients with carditis (Group I) was $34.7 \pm 6.2\%$ and in patients with chronic quiescent RHD (Group III) was $33.1 \pm 5.97\%$ and there was no significant statistical difference between both groups. Also, FS in ARF patients without carditis GII was $35.3 \pm 3.4\%$ and in normal control children G IV was $37.7 \pm 6.5\%$ and there was no significant statistical difference between both groups.

Conclusion: Doppler echocardiography proved to be of great value in detecting diastolic function indices as IVRT which may be used as early sensitive parameter for diagnosis of carditis in subclinical carditis. Also, diastolic function can be used for the early detection of myocardial involvement in patients with acute rheumatic fever.

INTRODUCTION

Rheumatic fever is an inflammatory disease occurs as a delayed non suppurative sequel of upper respiratory infection with group A beta-hemolytic streptococci (*Bezold and Brecker, 1995*). Rheumatic heart disease, an important sequel to rheumatic fever remains the most common acquired heart disease among children worldwide and is the major

cause of cardiovascular death during the first five decades of life in developing countries (*Eisenberg, 1993*).

Normal diastolic function may be clinically defined as the ability of left ventricle to accommodate an adequate filling volume to maintain cardiac output while operating in low pressure (*Smith, 1997*).

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E/A ratio mean value also showed statistical significant difference between both groups (ARF patient with carditis and chronic quiescent rheumatic heart patients).

As regard DT the mean value in G1 was 133.35 ± 32.79 m/sec and in GIII was 100.00 ± 28.28 m/sec and the difference between both groups was statistically significant. Also IVRT mean value in G1 was 90.60 ± 28.34 m sec and was 49.25 ± 12.12 m sec in GIII and the difference between both groups was statistically significant (Table 3).

But when studying diastolic function between GII and GIV (ARF patients without carditis and normal control children) the only parameter showing significant difference between both groups was IVRT the mean value in GII was 72 ± 6.93 m sec and in GIV was 55.30 ± 15.43 m sec.

This difference may be explain that the prolongation of IVRT is an early marker for cardiac involvement in ARF. This was in agreement with *Douglas et al. (1989)* who stated that diastolic function may produce a tool for early diagnosis of cardiac involvement. Also the use of IVRT

as an index of diastolic impairment in patients with ARF has the advantage that it is unlike the other diastolic indices not affected by moderate alteration in haemodynamic load (*Starling et al., 1987*).

This study showed that there was no significant difference in diastolic function between ARF patients with mitral or aortic regurgitation and those without mitral or aortic regurge. In conclusion: Doppler echocardiography proved to be of great value in detecting diastolic function indices as IVRT which may be used as early sensitive marker for diagnosis of carditis in silent carditis. Also there is significant impairment in diastolic function in patients with acute rheumatic carditis if compared with chronic quiescent RHD who have similar loading alternation.

So we recommend echocardiography as a routine investigation in order to evaluate early sequel of ARF. Diastolic function can be used for the early detection of myocardial involvement in patients with acute rheumatic fever.

Systolic and diastolic functions must be distinct as each of their dysfunction affects the decision of management.

DISCUSSION

The management of patients with primarily systolic or diastolic dysfunction is very different and it is critical to make the distinction (Goldsmith and Dick, 1993).

Diastolic dysfunction can be an early manifestation of impaired LV function and may occur long before the systolic performance starts to fail. Diastolic dysfunction impairs ventricular filling by diminishing relaxation or reducing compliance of the ventricle or both. The haemodynamic consequences include elevation of left ventricular filling pressure, left atrial pulmonary venous and pulmonary capillary pressure. If uncorrected, an eventual increase in pulmonary artery pressure and right heart failure occurs (Verdi et al., 1983).

In this study systolic function as evaluated by fractional shortening (FS) in ARF patients with carditis (GI) was $34.7 \pm 6.2\%$ and in patients with chronic quiescent (RHD) GIII was $33.1 \pm 5.97\%$ and there was no significant statistical difference.

Also FS in ARF patients without carditis (GII) was $35.3 \pm 3.4\%$ and in normal control children (GIV) was $37.7 \pm 6.5\%$ and there was no significant statistical difference between both groups. This in agreement with Verdi et al. (1983)

who stated that the majority of patients with rheumatic carditis have normal left ventricular systolic function, as inflammation of the myocardium is insufficient to cause any detectable change in the indices of left ventricular systolic function.

Our patients showed mitral valve thickening in 14 cases (46.7%) of patients with ARF there were 11 of 20 cases with clinical carditis (55%) and were 3 of 10 cases without clinical carditis (30%). There is also 15 of 30 studied cases of ARF (50%) having mild mitral regurge and mild aortic regurgitation was found in 5 of 30 ARF patients (16.7%). This was in agreement with Vasani et al. (1996) who stated that mitral valve is the most frequently involved in patients with rheumatic fever either first attack or recurrent episodes. It is associated with aortic valve involvement but less commonly (Table I, 2).

Alteration in LV diastolic function may reduce the height of E-wave and increase height of A-wave and decrease E/A ratio. It is usually accompanied by prolongation of IVRT and DT (Brecker et al., 1992). In this study the mean value of E-wave velocity in GI was 88.71 ± 30.85 cm/sec and in GIII was 120.10 ± 29.35 cm/sec and there was significant difference between both groups ($P < 0.05$).

Table (4): Statistical comparison between patients without carditis and normal control group as regard diastolic function.

Diastolic function	ARF without carditis group (n =20)	Normal control group (n =10)	t (unpaired)	P-value
E- velocity	82.80 ± 14.49	87.90 ± 15.49	0.76	> 0.05
A velocity	43.00 ± 9.68	52.20 ± 12.35	1.85	> 0.05
E/A ratio	1.99 ± 0.44	1.73 ± 0.35	1.45	> 0.05
DT	111.10 ± 31.41	111.20 ± 19.55	0.01	> 0.05
IVRT	72.60 ± 6.93	55.30 ± 15.43	3.23	< 0.01*

* Significant

Table (5): Statistical comparison between ARF patients with mitral regurge, and those without as regard diastolic functions.

Diastolic functions	Patients with MR (n =15)	Patients without MR (n = 15)	t (unpaired)	P-value
E- velocity	90.80 ± 31.26	82.67 ± 20.77	0.84	> 0.05
A velocity	62.79 ± 20.86	57.17 ± 24.26	0.68	> 0.05
E/A ratio	1.58 ± 0.67	1.65 ± 0.66	0.32	> 0.05
DT	133.73 ± 33.73	118.13 ± 32.58	1.29	> 0.05
IVRT	87.00 ± 27.28	82.20 ± 22.76	0.52	> 0.05

Table (6): Statistical comparison between ARF patients with aortic regurge, and those without as regard diastolic functions.

Diastolic functions	Patients with AR (n = 5)	Patients without AR (n = 25)	t (unpaired)	P-value
E- velocity	100.02 ± 35.28	84.08 ± 24.30	1.24	> 0.05
A velocity	52.30 ± 16.22	61.52 ± 23.42	0.84	> 0.05
E/A ratio	2.03 ± 0.73	1.53 ± 0.62	1.57	> 0.05
DT	129.40 ± 34.06	125.24 ± 34.10	0.25	> 0.05
IVRT	62.40 ± 23.08	89.04 ± 23.06	2.36	< 0.05*

* Significant

Table (2): Statistical comparison between patients without carditis and normal control group as regard clinical, lab and echo findings.

	No carditis (n = 10)	Normal (n = 10)	Statistics	P-value
Age	8.9 ± 2.8	8.9 ± 2.6	t = 0.00	> 0.05
Sex:				
Male	5 (50.0%)	4 (40.0%)	Fisher	>0.05
Female	5 (50.0%)	6 (60.0%)		
ESR	71.7 ± 28.9	14.9 ± 5.5	t = 6.10	< 0.001*
ASOT	10 (100.0%)	0 (0.0%)	Fisher	< 0.001*
CRP			$\chi^2 = 20.00$	< 0.001*
-	0 (0.0%)	10 (100%)		
+	7 (70.0%)	0 (0.0%)		
++	2 (20.0%)	0 (0.0%)		
+++	1 (10.0%)	0 (0.0%)		
LVEDD	3.8 ± 0.5	4.3 ± 0.6	t = 1.75	> 0.05
LVESD	2.6 ± 0.4	2.6 ± 0.4	t = 0.17	> 0.05
AO	2.0 ± 0.2	2.2 ± 0.3	t = 1.43	> 0.05
LA	2.5 ± 0.5	2.9 ± 0.6	t = 1.59	> 0.05
FS	35.3 ± 3.4	37.7 ± 6.5	t = 1.03	> 0.05
Arthritis	8 (80.0%)	0 (0.0%)	Fisher	< 0.001*
Chorea	2 (20.0%)	0 (0.0%)	Fisher	> 0.05
Mitral thickness	3 (30.0%)	0 (0.0%)	Fisher	> 0.05
Mitral prolapse	0 (0.0%)	0 (0.0%)	Fisher	> 0.05
MR	4 (40.0%)	0 (0.0%)	Fisher	> 0.05
AR	0 (0.0%)	0 (0.0%)	Fisher	> 0.05

Fisher = Fisher exact test

* Significant

Table (3): Statistical comparison between patients with carditis and quiescent RHD as regard diastolic function.

Diastolic function	ARF with carditis group (n = 20)	Quiescent RHD group (n = 10)	t (unpaired)	P-value
E- velocity	88.71 ± 30.85	120.10 ± 29.35	2.67	< 0.05*
A velocity	68.47 ± 22.24	62.80 ± 16.51	0.71	> 0.05
E/A ratio	1.43 ± 0.67	2.00 ± 0.59	2.27	< 0.05*
DT	133.35 ± 32.79	100.00 ± 28.28	2.74	< 0.05*
IVRT	90.60 ± 28.34	49.25 ± 12.12	5.58	< 0.001*

* Significant

Doppler transducer positioned at the cardiac apex (Park, 1996). Generally IVRT is prolonged when relaxation becomes impaired. Its normal values approximating 65 ± 20 m sec (Rahko et al., 1986).

Statistical methods: All results were presented and analysed using mean, standard deviation, student t-test, chi-square test, fisher exact test and linear correlation coefficient (Knapp and Miller, 1992).

RESULTS

The results of the present study are illustrated in tables (1-6).

Table (1): Statistical comparison between ARF patients with carditis and children with quiescent RHD as regard clinical, lab and echo findings.

	Carditis (n = 20)	Quiescent (n = 10)	Statistics	P-value
Age	10.5 ± 3.0	12.3 ± 2.1	t = 1.69	>0.05
Sex:				
Male	12 (60.0%)	6 (60.0%)	Fisher	>0.05
Female	8 (40.0%)	4 (40.0%)		
ESR	81.5 ± 25.8	14.0 ± 5.5	t = 11.21	< 0.001*
ASOT	20 (100.0%)	0 (0.0%)	Fisher	< 0.001*
CRP				
-	0 (0.0%)	10 (100%)	$\chi^2 = 30.00$	< 0.001*
+	13 (65.0%)	0 (0.0%)		
++	4 (20.0%)	0 (0.0%)		
+++	3 (15.0%)	0 (0.0%)		
LVEDD	4.9 ± 0.8	5.1 ± 0.4	t = 0.37	> 0.05
LVESD	3.5 ± 0.6	3.7 ± 0.4	t = 0.95	> 0.05
AO	2.5 ± 0.4	2.7 ± 0.3	t = 1.39	> 0.05
LA	3.8 ± 1.3	3.3 ± 0.4	t = 1.66	> 0.05
FS	34.7 ± 6.2	33.1 ± 5.97	t = 0.65	> 0.05
Arthritis	11 (55.0%)	3 (30.0%)	Fisher	> 0.05
Chorea	2 (10.0%)	0 (0.0%)	Fisher	> 0.05
Mitral thickness	11 (55.0%)	6 (60.0%)	Fisher	> 0.05
Mitral prolapse	4 (20.0%)	4 (40.0%)	Fisher	> 0.05
MR	11 (55.0%)	6 (60.0%)	Fisher	> 0.05
AR	5 (25.0%)	2 (20.0%)	Fisher	> 0.05

Fisher = Fisher exact test

* Significant.

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hypertension, diabetes mellitus, renal impairment or any factors affecting left ventricular diastolic function will be excluded from this study.

All children were subjected to the following:

1- Thorough history taking with special concern on history of recent sore throat, previous attacks of rheumatic fever, symptoms of rheumatic activity e.g. arthritis, orthopnea, heart failure and abnormal movement.

2- Complete physical examination, general and cardiac examination. The presence of two major criteria or one major and two minor manifestations strongly favors the diagnosis of ARF (*Dajani et al., 1993*).

3- Laboratory investigations including ESR, CRP and ASOT.

4- Standard 12 leads ECG.

5- Plain x-ray chest and heart postero-anterior and lateral views.

6- Echocardiography examination including M-mode, 2-D and Doppler study. Using Hewlett Packard (HP) 21200 ultrasound imaging system with 3.5 and 5 MHz transducers.

At M-mode and 2-D studies, conventional variables were measured, also the morphology of valves and subvalvular apparatus were evaluated for valve thickening, mobility prolapse vegetations and

rupture chordae. Pericardial space was looked for pericardial effusion.

At Doppler echo study:

- Valvular regurgitations were studied and graded.

- Left ventricular diastolic function were studied as follows. Sample volume placed near the tip of mitral leaflets while it is fully opened. The following were measured.

- Peak velocity of early filling (E) wave, normal range of 70-100 cm/s.

- Peak velocity of late filling (A) wave, normal range of 45-70 cm/s.

- E/A ratio > 1.

- Deceleration time (DT) of early filling which is the interval from the early peak velocity to the zero intercept of the extrapolated deceleration slope (*Yamamoto et al., 1996*).

The normal deceleration time range from 160-220 m/sec (*Smith, 1997*).

- Isovolumic relaxation time (IVRT), which is the interval between the end of LV outflow velocity and the onset of mitral inflow. It is measured from the end of LV ejection to the onset of mitral inflow i.e. defined as the time between aortic closure and mitral opening. It was measured by simultaneous recording of the aortic and mitral flow by continuous wave

The heart of patients with acute rheumatic fever is mildly enlarged, flabby and edematous. The cardiac chambers are dilated and one or more of the cardiac valves are more obviously abnormal, retracted thickened and deformed and incompetent. Their commissures may be fused and chordae tendeneae may be retracted and fused. These features results in loss of ventricular heterogeneity or diastolic asynergy, also the loss of ventricular ability to relax quickly alter mitral opening. These account for prolonged relaxation and shift of diastolic filling to late diastole with enhanced atrial contribution (*Braunwald, 1997*). Of the available methods for non-invasive assessment of the pattern of diastolic filling the Doppler echocardiography is currently the technique of choice (*De Bruyne et al., 1989*). So the Doppler transmitral flow recording shows reduced peak velocity of early filling (E) wave, predominant late mitral flow (A) wave, reduced E/A ratio and prolonged deceleration time of early filling. The IVRT was also prolonged (*Hirota, 1980*).

SUBJECTS AND METHODS

This study was conducted on 30 children with acute rheumatic fever (ARF). They were selected

from pediatric cardiology outpatient clinic or admitted in pediatrics department of Benha University Hospital. Their ages ranged from 6-15 years, they were 17 males and 13 females.

They were divided into two groups:

Group I: They were 20 cases presented with acute rheumatic carditis.

Group II: They were 10 cases with acute rheumatic fever without clinical carditis.

The diagnosis of ARF was based on revised Jones criteria and laboratory investigations.

Twenty children of age and sex matched to patients groups were taken as control. They were divided into two other groups.

Group III: 10 patients with chronic quiescent rheumatic heart disease (RHD) without clinical evidence of activity, they were compared with group I. Both groups were matched as regard age, sex and severity of valvular lesion.

Group IV: 10 healthy children, this group was compared with group II.

Exclusion criteria:

Patients with heart failure, more than mild mitral regurge or mitral stenosis and mild aortic regurge or stenosis will be excluded from this study. Also patients with

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