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ROLE OF GATED SPECT USING TC 99 SESTAMIBI IN EARLY DETECTION OF SUBCLINICAL HCV RELATED CIRRHOTIC CARDIOMYOPATHY

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ABSTRACT

Background: HCV is one of the health priority in Egypt due to its high prevalence. Cirrhotic cardiomyopathy in manifest stage can affect the patient's prognosis. This study aimed to evaluate the ability of gated SPECT in detection of early HCV related cirrhotic cardiomyopathy

Methods: We studied forty Child A HCV cirrhotic patients with no other cardiac risk factors by conventional echocardiography and Tc99 sestamibi gated SPECT and twenty normal persons as controls.

Results: the studied group showed blunted response to stress no ischemic changes and normal right ventricular measures.

Conclusions: HCV had an early effect on the heart in the form of chronotropic impairment with stress.

Keywords: *Gated SPECT, Cirrhotic cardiomyopathy, HCV*

INTRODUCTION

Hepatitis C is found worldwide. The most affected regions are WHO Eastern Mediterranean and European Regions, with the prevalence of 2.3% and 1.5% respectively.[(1)] It is considered a major health problem in Egypt as it had the highest prevalence rate worldwide. Its prevalence was estimated up to 40% in some areas.[(2)] The Egyptian national viral hepatitis treatment program made a successful and effective public health impact. It successfully established a strong infrastructure for controlling hepatitis C in Egypt.[(3)] In addition to hepatic complications, Two-thirds of patients with HCV infection experienced extrahepatic manifestations. Which vary from common to infrequent.[(4)]

Cirrhotic cardiomyopathy (CCM) is the term used to describe structural and functional cardiac changes that occur in patients with cirrhosis. It includes electrophysiological abnormalities, impairment of systolic and/or diastolic function as well as chronotropic failure, all of which in the absence of known cardiac disease. CCM occur in two stages: a subclinical one, which can be underestimated for a long time, being accidentally discovered by the doctor during a routine exam, and another clinically manifest, the cardiac affection dominating the clinical picture, raising the problem for both the diagnosis as well as treatment.[(5)]

A patient complaining of dyspnea, presenting with ascites, without pathological jugular swelling, normal ECG, ECHO with normal ejection fraction, but with elevated B-type natriuretic peptide (BNP) – a condition that may be suggestive of CCM. Rather than classic presentations of HF, clinical suspicion for early identification, to prevent its evolution to related complications, such as suprarenal insufficiency and hepatorenal syndrome (HRS) is of great value.[(5)]

Because CCM is asymptomatic, except during situations of stress, prevalence studies are limited. Heart failure (HF) secondary to CCM is frequent in patients who undergo liver transplant, in which half the patients presents HF, and up to 21% die from cardiac causes.[(5)]

Cardiac imaging role in the management of cardiovascular diseases has been increasing nowadays. Non-invasive stress testing, echocardiography provides valuable information regarding the development of clinically important systolic and diastolic dysfunction. Trans-thoracic echocardiography is non-invasive, available at the bedside, and low-cost relative to other imaging modalities. [(6)] Three-dimensional echocardiography (3DE) is becoming more available and increasingly used in clinical practice. Cardiac magnetic resonance (CMR) is a fully automated software allowing fast online measurements and better reproducibility. [(7)] Nuclear imaging provides a very well-validated test for proper diagnosis of disease pathophysiology, prognosis and guidance towards optimal therapy. [(8)] It is the preferred technique for risk stratification and prognostication in

patients in whom prior revascularization has been performed. Pharmacological stress may also be combined with either echocardiography or CMR, where after LV function is evaluated. These methods have similar diagnostic accuracy for viable myocardium.[9])

AIM.

To evaluate the ability of gated SPECT in detection of early HCV related cirrhotic cardiomyopathy

STUDY POPULATION AND METHEDOLOGY:

Forty patients with Child A HCV related liver cirrhosis diagnosed clinically, laboratory and by abdominal ultrasonography and twenty normal persons as controls. All the patients and the controls were subjected to complete clinical examination and assessment of liver and kidney functions with measurement of cardiac enzymes and tumor marker. Resting ECG, pulse and blood pressure were recorded. Conventional echocardiographic assessment of the right and left ventricles as regard dimensions and systolic and diastolic function. Gated SPECT study using Treadmill stress modality to assess the cardiac parameters in rest and stress states using Tc99 sestamibi.

STATISTICAL ANALYSIS

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

The used tests were:

1 - Chi-square test
For categorical variables, to compare between different groups

2 - Student t-test
For normally distributed quantitative variables, to compare between two studied groups

3 - Pearson coefficient
To correlate between two normally distributed quantitative variables

4 - Mann Whitney test
For abnormally distributed quantitative variables, to compare between two studied groups

RESULTS:

This study was held on forty patients (26 males and 14 females) with age ranged between 24 - 72 years with a mean of 51years. Laboratory tests were within normal reference ranges in both groups.

Echocardiographic results revealed: first degree diastolic dysfunction was observed in patients while diastolic function was preserved in control group. Assessment of EF (Ejection Fraction) by M-mode was within normal reference ranges in both groups. Right ventricular dimensions, systolic and diastolic functions were within normal reference ranges in both groups. (Table 1)

Gated SPECT studies showed normal resting and stress parameters as regard heart rate, systolic and diastolic blood pressure in both groups. Metabolic Equivalent measurements recording was within average functional capacity for all patients and controls. Stress termination was due to reaching target heart rate in both groups. Blunted chronotropic response to stress was observed in the patients due to the presence of left ventricular dilatation. While normal response to stress was observed in patients group. No filling defects were detected, with no lung uptake, No right ventricular uptake and Calculated ischemic scores were below ischemic ranges in both groups. (Figure 1-3)

Table (1): The demographic data, laboratory results, echocardiographic findings and gated SPECT results for patients and controls

	HCV (n = 40)		**Control (n = 20)**		**Test of Sig.**	**p**
	No.	**%**	**No.**	**%**		
Sex						
Male	26	65.0	13	65.0	χ^2= 0.0	1.000
Female	14	35.0	7	35.0		
Min. – Max.	24.0 – 72.0		24.0 – 72.0		t= 0.127	0.900
Mean ± SD.	50.97 ± 14.97		51.50 ± 15.52			
Median	54.50		53.50			
HB (gm/dl)						
Min. – Max.	16.0 –12.0		16.0 –12.0		t= 1.318	0.193
Mean ± SD.	1.26 ±14.10		1.22 ±13.65			
Median	14.0		13.50			
RBC(10^6/mm^3)						
Min. – Max.	6.0 –4.0		6.0 –4.0		t= 0.595	0.554
Mean ± SD.	0.69 ±5.02		0.73 ±5.14			
Median	5.0		5.30			
WBC(10^3/mm^3)						
Min. – Max.	9.50 –4.50		10.50 –4.0		t= 0.5 71	0.573
Mean ± SD.	1.54 ±7.14		2.22 ±7.45			
Median	7.40		7.60			

	HCV (n = 40)	Control (n = 20)	Test of Sig.	p
	No.	%	No.	%
PLT(10^3/mm^3)				
Min. – Max.	460.0 –150.0	460.0 –150.0	U= 382.0	0.777
Mean ± SD.	300.4 ±100.4	306.5 ±105.8		
Median	300.0	320.0		
PT(seconds)				
Min. – Max.	10.0 –13.0	10.0 –13.0	t= 0.0	1.000
Mean ± SD.	11.25 ±1.16	11.25 ±1.18		
Median	11.0	11.0		
INR				
Min. – Max.	0.70 –1.30	0.70 –1.30	t= 0.428	0.670
Mean ± SD.	0.21 ±1.0	0.22 ±0.97		
Median	1.0	0.95		
Serum sodium (mEq/L)				
Min. – Max.	140.0 –145.0	135.0 –146.0		
Mean ± SD.	142.2 ±1.62	141.7 ±2.75	0.712	0.483
Median	142.0	142.0		
Serum potassium (mEq/L)				
Min. – Max.	3.50 –5.0	3.50 –5.0		
Mean ± SD.	4.16 ±0.51	4.21 ±0.50	0.323	0.748
Median	4.20	4.20		
Urea(mg/dL)				
Min. – Max.	9.0 –20.0	7.0 –20.0		
Mean ± SD.	14.25 ±3.48	14.05 ±4.32	t= 0.193	0.847
Median	14.0	14.0		
Creatinine(mg/dL)				
Min. – Max.	0.80 –1.30	0.80 –1.30		
Mean ± SD.	1.01 ±0.17	0.99 ±0.16	t=0.503	0.617
Median	0.98	0.95		
Bilirubin(mg/dL)				
Min. – Max.	0.10 –1.20	0.10 –1.20		
Mean ± SD.	0.61 ±0.36	0.70 ±0.30	U=338.0	0.329
Median	0.60	0.75		
Albumin(g/dL)				
Min. – Max.	5.50 –3.50	5.50 –3.50		
Mean ± SD.	0.70 ±4.48	0.67 ±4.54	0.277	0.783
Median	4.50	4.60		
AST(IU/L)				
Min. – Max.	39.0 –18.0	37.0 –20.0		
Mean ± SD.	8.87 ±23.10	4.92 ±28.30	2.916*	0.005*
Median	21.0	27.50		
ALT(IU/L)				
Min. – Max.	55.0 –7.0	55.0 –8.0	1.903	0.062
Mean ± SD.	13.68 ±29.50	17.06 ±37.25		
Median	27.50	42.50		
Albumin(g/dL)				
Min. – Max.	5.50 –3.50	5.50 –3.50		
Mean ± SD.	0.70 ±4.48	0.67 ±4.54	0.277	0.783
Median	4.50	4.60		
AST(IU/L)				
Min. – Max.	39.0 –18.0	37.0 –20.0		
Mean ± SD.	8.87 ±23.10	4.92 ±28.30	2.916*	0.005*
Median	21.0	27.50		

	HCV (n = 40)	Control (n = 20)	Test of Sig.	p
	No.	%	No.	%
ALT(IU/L)				
Min. – Max.	55.0 –7.0	55.0 –8.0		
Mean ± SD.	13.68 ±29.50	17.06 ±37.25	1.903	0.062
Median	27.50	42.50		
αFP(ng/mL) Min. – Max.	9.0 –2.0	9.0 –2.0		
Mean ± SD.	2.49 ±5.45	2.43 ±5.75	0.444	0.659
Median	5.0	6.0		
CK-MB(IU/L)				
Min. – Max.	24.0 –5.0	24.0 –6.0		
Mean ± SD.	5.27 ±13.85	5.64 ±15.30	t= 0.982	0.330
Median	14.0	15.50		
Trop I(ng/ml)				
Min. – Max.	0.39 –0.10	0.39 –0.10		
Mean ± SD.	0.11 ±0.25	0.11 ±0.25	U= 400.0	1.000
Median	0.25	0.25		
Pro BNP (pg/ml)				
Min. – Max.	20.60 – 125.0	46.0 – 110.0	1.675	0.100
Mean ± SD.	69.65 ± 27.87	80.05 ± 19.57		
Median	64.50	86.0		
E (cm/s)				
Min. – Max.	59.0 – 88.80	53.0 – 89.0		
Mean ± SD.	63.75 ±16.23	68.20 ±9.21	1.353	0.181
Median	65.90	68.50		
A (cm/s)				
Min. – Max.	65.0 – 94.0	38.0 – 65.0		
Mean ± SD.	73.25 ±18.51	50.15 ±7.64	6.817*	<0.001*
Median	74.30	48.50		
E/A				
Min. – Max.	0.54 – 1.40	1.14 – 1.84		
Mean ± SD.	0.90 ±0.22	1.37 ±0.18	8.274*	<0.001*
Median	0.84	1.30		
E\ (cm/s)				
Min. – Max.	5.03 – 16.0	8.0 – 16.0		
Mean ± SD.	10.64 ±2.98	11.41 ± 2.34	1.087	0.283
Median	10.0	11.40		
E/E				
Min. – Max.	4.59 – 15.01	4.17 – 8.33		
Mean ± SD.	6.47 ±2.61	6.18 ± 1.28	0.585	0.561
Median	6.28	6.58		
EF%				
Min. – Max.	54.0 – 75.0	53.0 – 78.0	0.382	0.704
Mean ± SD.	63.38 ± 6.62	64.05 ± 6.07		
Median	62.50	63.50		
TAPSI(mm)				
Min. – Max.	19.0 – 26.0	19.0 – 26.0		
Mean ± SD.	22.75 ± 1.84	22.70 ± 2.11	0.095	0.925
Median	23.0	22.50		
S RV(cm/s)				
Min. – Max.	12.70 – 15.0	11.0 – 18.0		
Mean ± SD.	13.67 ± 0.64	14.20 ± 2.09	1.114	0.278
Median	13.73	14.0		

	HCV (n = 40)	Control (n = 20)	Test of Sig.	p
	No.	%	No.	%
E RV (cm/s)				
Min. – Max.	42.0 – 66.0	49.0 – 67.0		
Mean ± SD.	55.83 ± 6.47	58.45 ± 5.58	1.548	0.127
Median	57.0	60.0		
A RV(cm/s)				
Min. – Max.	32.0 – 66.0	33.0 – 55.0		
Mean ± SD.	48.15 ± 8.68	48.20 ± 6.13	0.023	0.982
Median	48.0	50.0		
E/A				
Min. – Max.	1.0 – 1.63	1.0 – 1.53		
Mean ± SD.	1.18 ± 0.14	1.23 ± 0.14	1.260	0.213
Median	1.16	1.20		
Annular RV(mm)				
Min. – Max.	23.0 – 40.0	25.0 – 33.0		
Mean ± SD.	31.33 ± 4.26	30.25 ± 2.73	1.183	0.242
Median	30.0	31.0		
Mid Cavity RV(mm)				
Min. – Max.	20.0 – 40.0	27.0 – 33.0		
Mean ± SD.	5.91 ±29.58	1.84 ±29.65	0.073	0.942
Median	32.0	30.0		
Long RV(mm)				
Min. – Max.	45.0 – 79.0	60.0 – 71.0		
Mean ± SD.	64.58 ± 7.39	66.7 ± 3.61	1.496	0.140
Median	65.0	67.50		
Rest EF by SPECT				
Min. – Max.	60.0 – 78.0	55.0 – 75.0		
Mean ± SD.	67.38 ± 5.29	64.6 ± 5.95	1.836	0.071
Median	67.50	65.0		
Stress EF by SPECT				
Min. – Max.	55.0 – 77.0	65.0 – 90.0		
Mean ± SD.	68.25 ± 5.90	74.9 ± 8.8	3.072*	0.005*
Median	68.0	71.50		

t: Student t-test
p: p value for comparing between the two studied groups
*: statistically significant at p ≤0.05

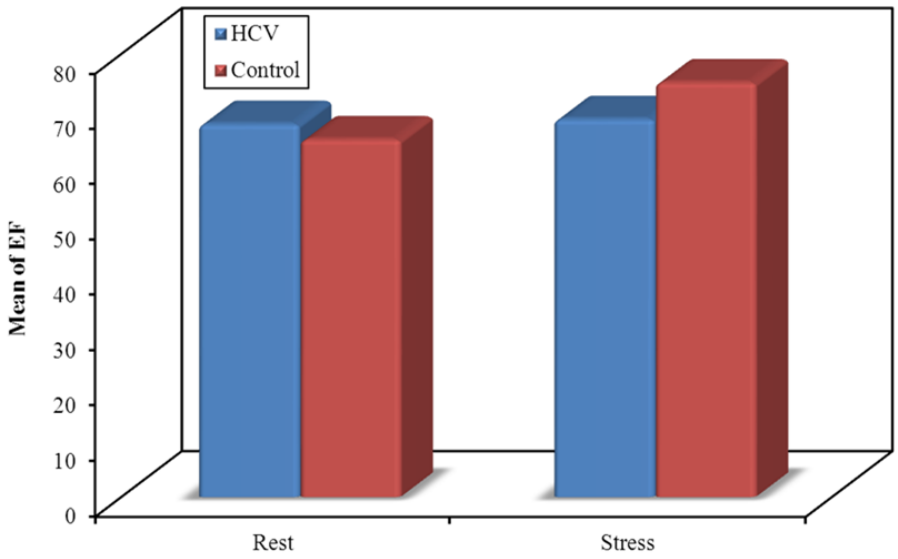

Figure (1): Estimated EF during rest and stress by Gated SPECT

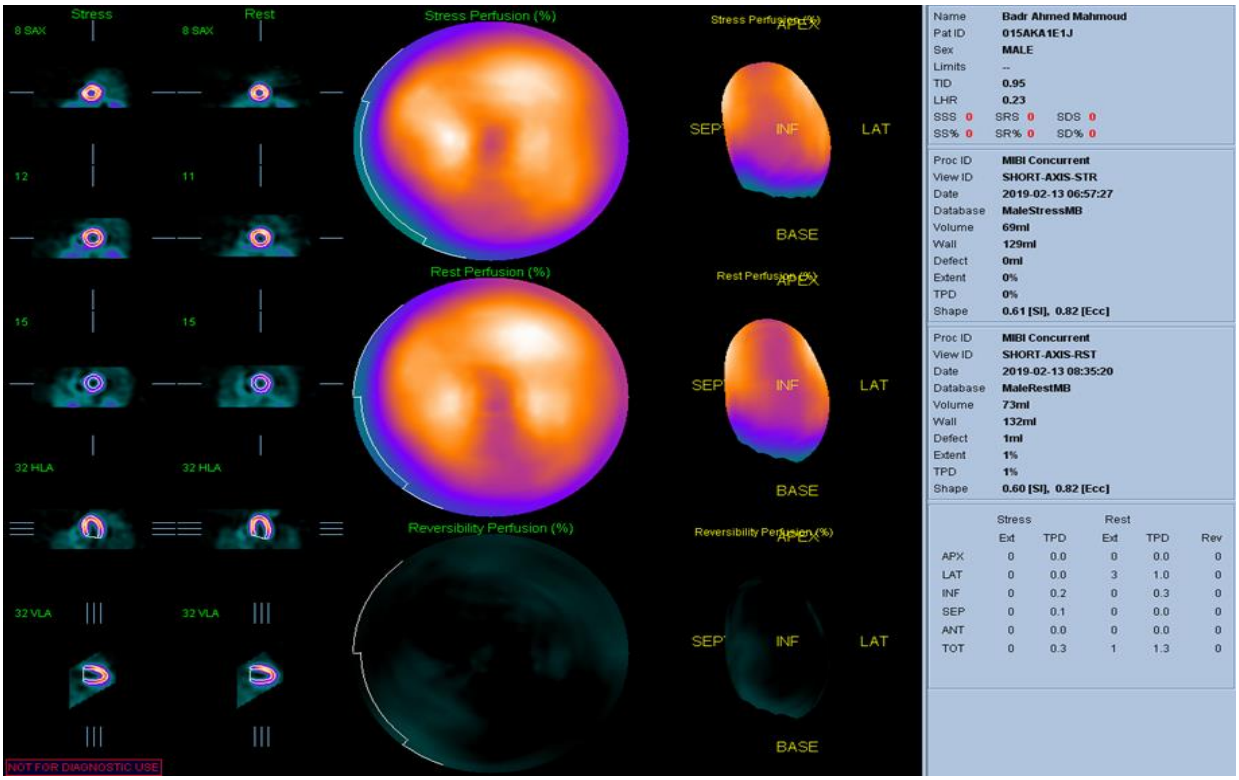

Figure (2): Gated SPECT study of one of our patients

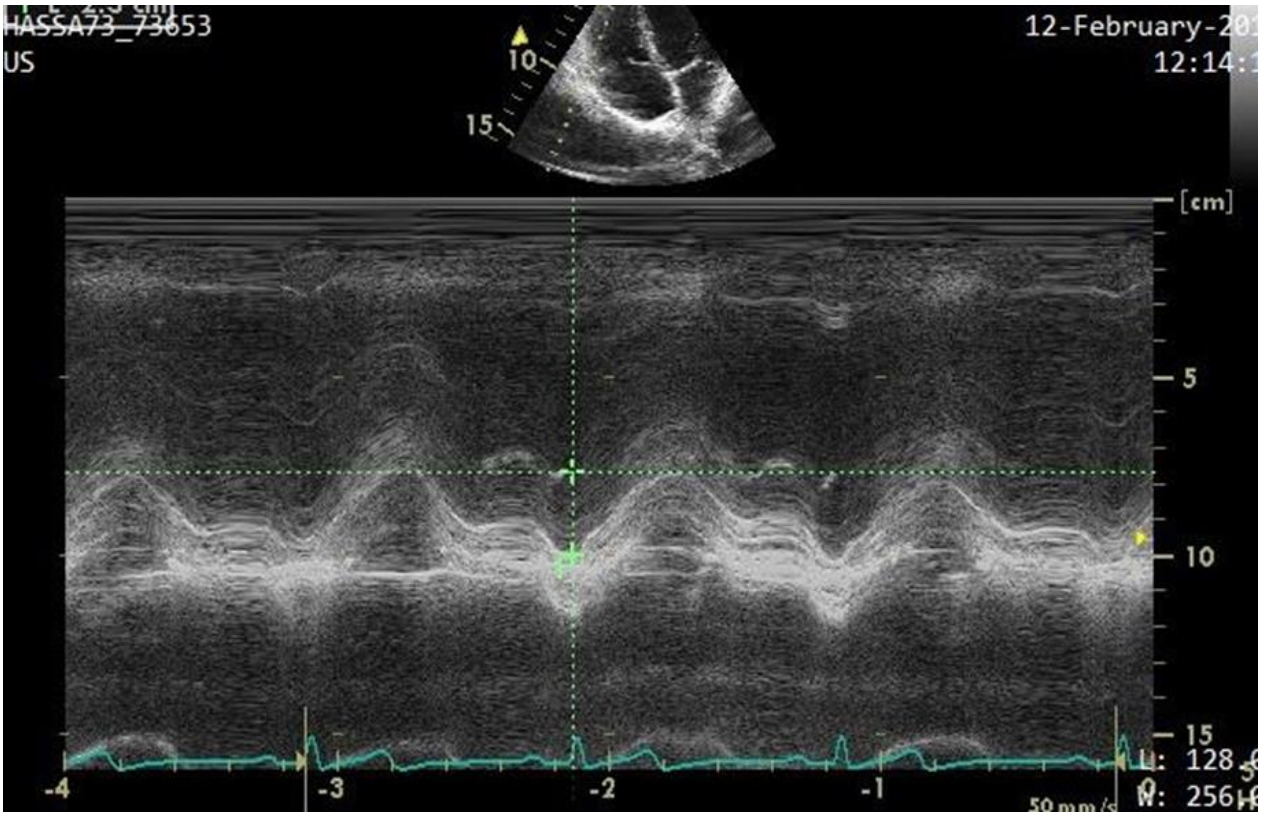

Figure 3: Assessment of right ventricular function by TAPSI

DISCUSSION:

Cirrhotic cardiomyopathy (CCM) is characterized by an impaired contractile response to stress, diastolic dysfunction and the presence of electrophysiological abnormalities, and it may be diagnosed at rest in some patients or demasked by physiological or pharmacological stress. CCM is associated with an impaired survival.[10] In this study, we included 40 HCV patients diagnosed by PCR and a 20 normal persons as a control group. The patients were collected from the newly discovered cases in a national campaign held in Egypt in 2019 for detection and treatment of HCV patients. The patients and the controls were subjected to laboratory testing and abdominal ultrasonography to ensure their compatibility to the study criteria.

In our study there were no significant differences between patients' group and control group as regard E and A waves values, but in E/A ratio the patients group was lower than control group which indicates grade I diastolic dysfunction in patients group. The measurements of E\ did not differ significantly between both groups which was reflected on E/E\ ratio in both groups did not differ significantly. In Sampaio *et al* study.[6] assessment of diastolic functions were done by E, A, E/A ratio, deceleration time, E\ and E/E\ ratio. The results in this study showed significant differences in all the parameters. In our study the ejection fraction assessed by echocardiography was within normal reference ranges in patients and control groups with no significant differences between both groups. In Sampaio *et al*.[6] The ejection fraction measurements were within normal reference ranges in both patients and control groups with no significant difference between both groups as in our study. Assessment of systolic functions using TAPSI revealing perseveration of systolic functions of the right ventricle in patients group. Measurement of right ventricular dimensions (annular, mid cavity and longitudinal) revealed normal reference ranges. In Sampaio *et al*.[6] Right ventricular function evaluated by tricuspid annulus plane systolic excursion (TAPSE) was not different between patients and controls as in our study.

In our study, the gated SPECT studies were done, all were subjected to treadmill stress till reaching target heart rate. Resting heart rate, systolic blood pressure and diastolic blood pressure were within normal reference ranges. The cause of test terminations was reaching target heart rate and no other causes detected. Metabolic equivalents measurement showed good functional capacity. Peak heart rate and systolic and diastolic blood pressure measurements were with normal reference ranges. The ejection fraction calculation by gated SPECT in resting images showed normal values. While ejection fraction calculation at stress images showed lower values. Left ventricular dilatation with stress was observed in patients. Calculated SSS, SRS and SDS were below ischemic ranges. No signs of right ventricular ischemia or lung uptake were observed. In Wong *et al*.[11] EF and cardiac volumes were analyzed. The patient was seated upright on an automated exercise cycle, the study showed reduced cardiac response to exercise. When increase in EF with exercise in cirrhotic was compared with controls, this was significantly reduced as in our study. Consequently, both the absolute and percentage increases in cardiac output in cirrhotic patients were also significantly decreased compared with controls.

CONCLUSIONS:

1. Hepatitis C virus had a subclinical effect on the heart.
2. Gated SPECT is a good modality in detection of subclinical cirrhotic cardiomyopathy as it showed the chronotropic abnormalities.
3. Subclinical cirrhotic cardiomyopathy does not affect the right side of the heart.
4. Conventional echocardiography is not the modality of choice in subclinical cirrhotic cardiomyopathy detection.

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