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Anti-inflammatory treatment with cetirizine improves refractory heart failure in patients with hepatitis C virus-induced myocarditis

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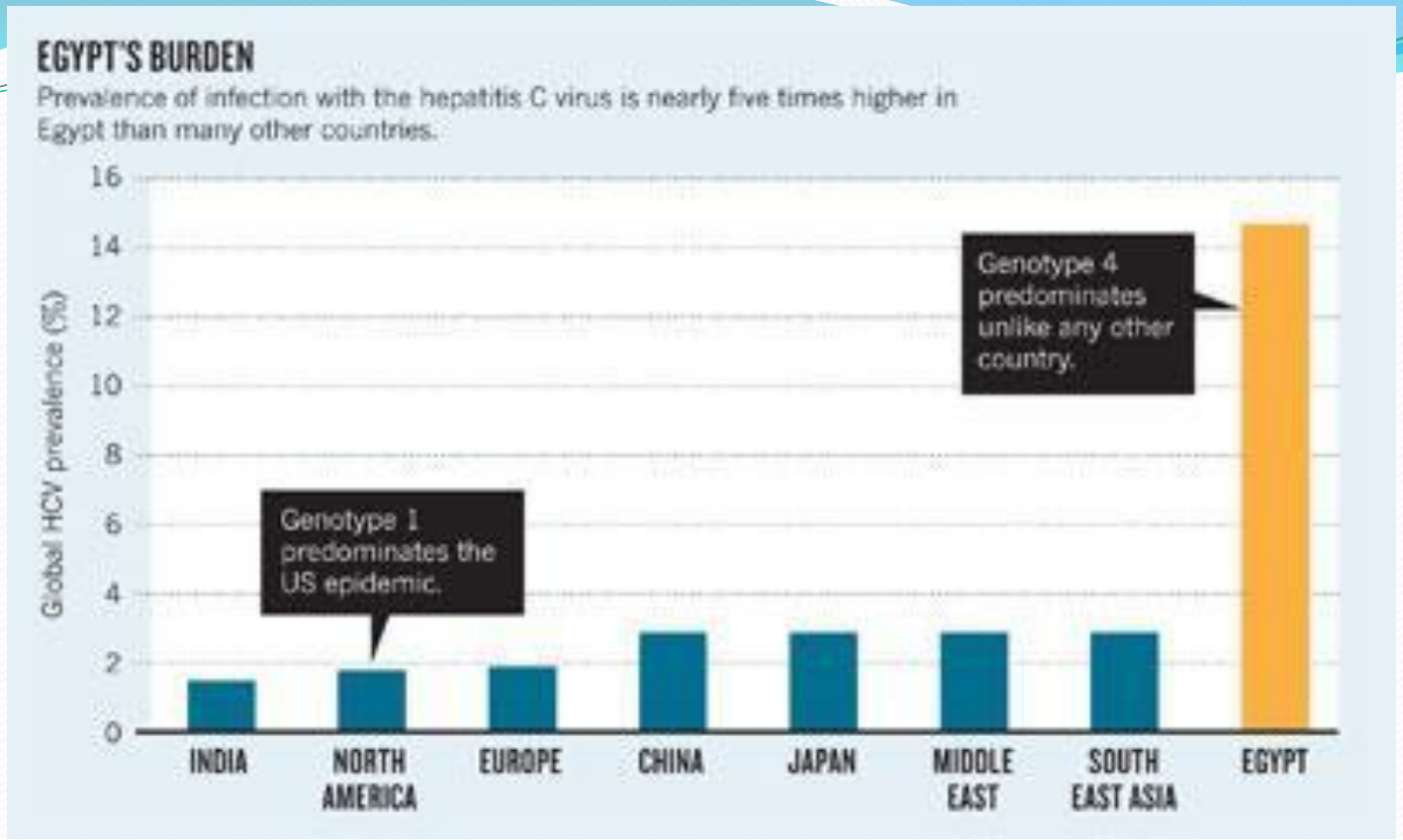
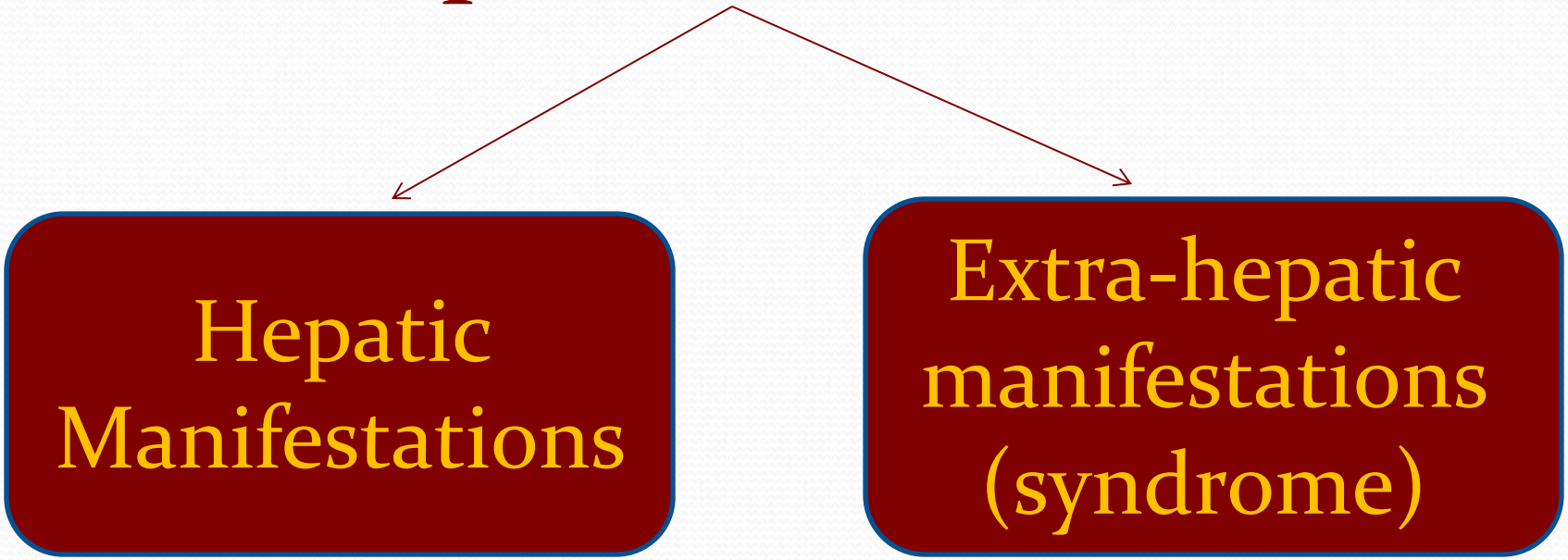


Egypt has the highest prevalence of hepatitis C virus (HCV) in the world, apparently because disposable needles and syringes were not used for the intravenous treatment of schistosomiasis during the widespread national eradication campaigns until 1980.

(Deuffic et al; 2006)

Predominant HCV genotypes in different parts of the world (Tibbs&Smith; 2001).

Hepatitis C infection



HCV: Extrahepatic Manifestations

Autoimmune Phenomena
- CRST Syndrome[2]

Dermatologic
- Cutaneous Necrotizing Vasculitis[2]
- Lichen Planus[1]
- Porphyria Cutanea Tarda[1]

Hematologic
- Aplastic Anemia[1]
- Mixed Cryoglobulinemia[1]
- Non Hodgkin's B-Cell Lymphoma[1]
- Thrombocytopenia[1]

Endocrine
- Diabetes Mellitus[2]
- Hypothyroidism[2]

Neuromuscular
- Arthritis/Arthralgia[3]
- Myalgia/Weakness[3]
- Peripheral Neuropathy[3]

Neuropsychiatric
- Depression[4]

Ocular
- Corneal Ulcer[2]
- Uveitis[2]

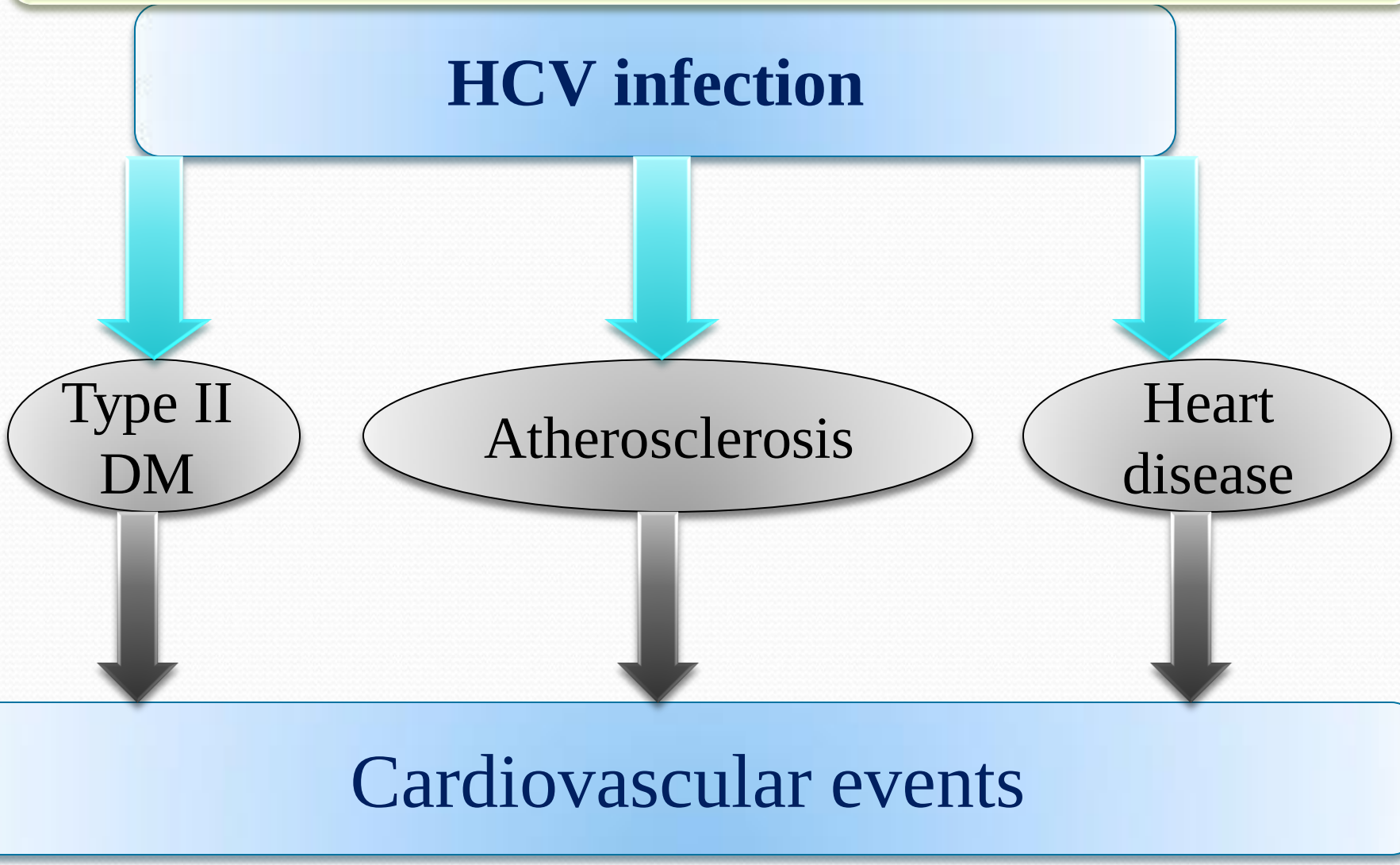
Renal
- Glomerulonephritis[1]
- Nephrotic Syndrome[2]

Vascular
- Necrotizing Vasculitis[3]
- Polyarteritis Nodosa[3]

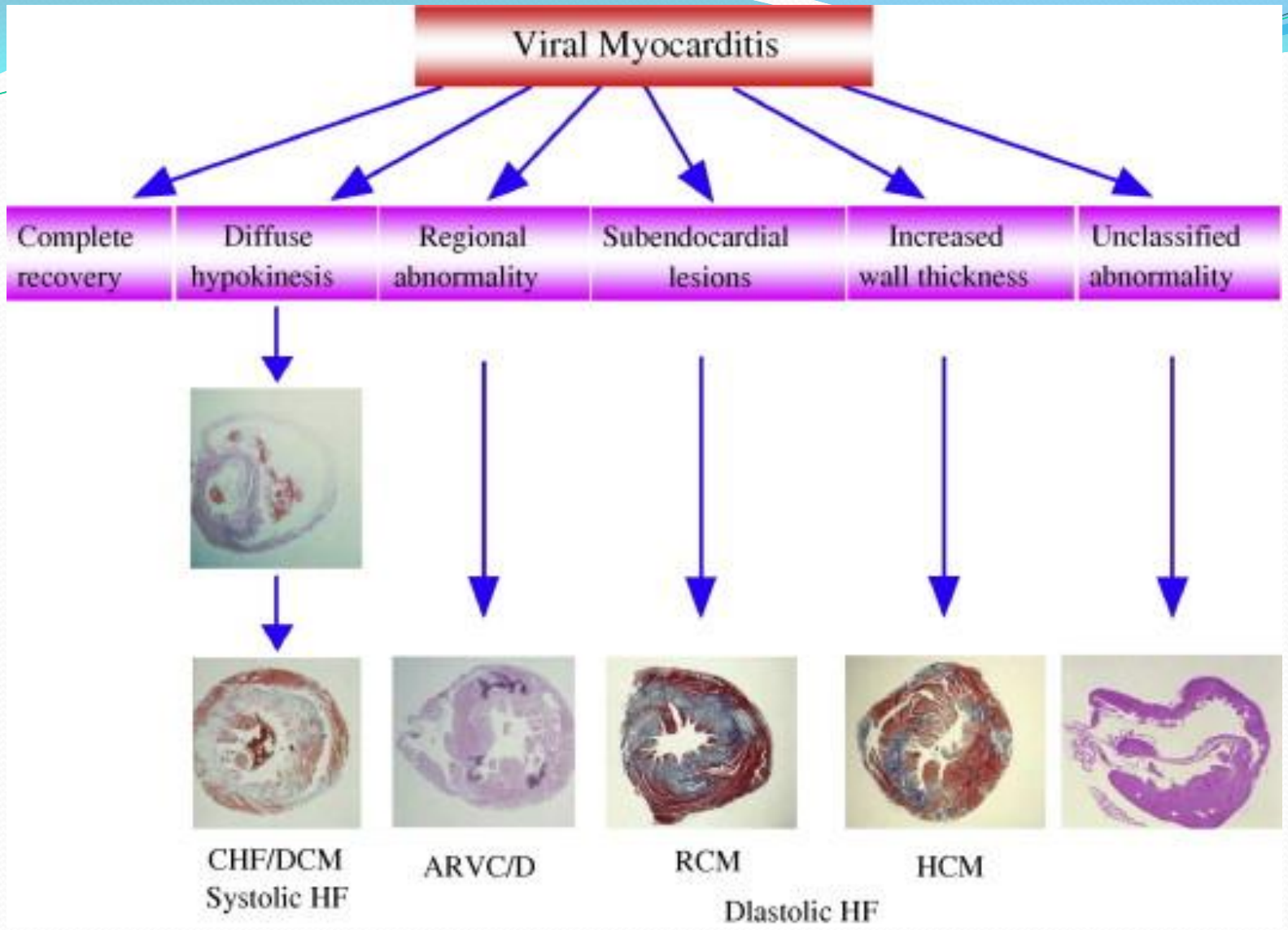
CRST = Calcinosis, Raynaud's phenomenon, Sclerodactyly and Telangiectasis

1. Angello V, et al *Journal of Hepatology*. 2004;40:341-352
2. Galossi A, et al. *J Gastrointestin Liver Dis*. 2007;16:65-73
3. NIH. *NIH Consens State Sci Statements* 2002; 19(3):1-46
4. Scene D, et al. *Metab Brain Dis*. 2004;19: 357-381

Pathways of cardiovascular affection in HCV patients



Matsumori; 2007



(Matsumori; 2009)

Hepatitis C virus (HCV) causes cardiomyopathy as a complication of HCV myocarditis.

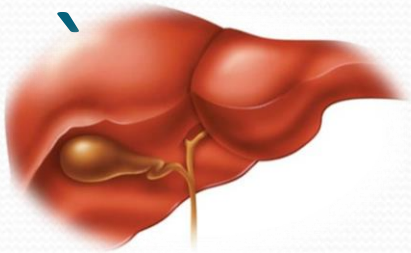
This may be due to:-

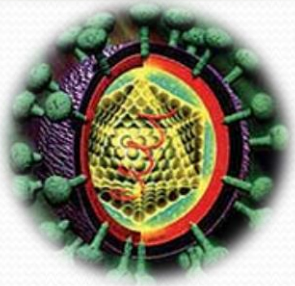
1- An inflammatory response, which induces growth or death of cardiac cells.

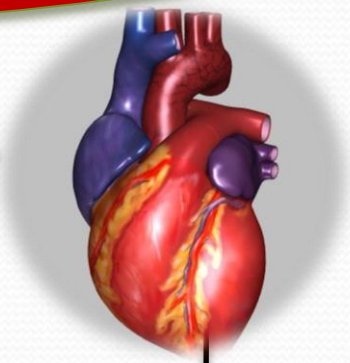
2- HCV may directly induce cardiomyopathy, via viral products that lead to cardiomyopathy through damage of the cardiac cells.

(Matsumori; 2010)

HCV infection







Acute Hepatitis

Chronic hepatitis 85%

Liver cirrhosis 20%

Hepatic failure 6%

Hepatocellular carcinoma 4%

Acute myocarditis

Chronic myocarditis 85%

Myocardial fibrosis 20 %

Dilated cardiomyopathy 6%

Hypertrophic cardiomyopathy 4%

Matsumori; 2007

In 2007

About 600 patients were screened for HCV Abs in the out patient clinic of Cardiovascular and Ultrasonography Research Unit (CURU)

24 % (144 patients) are HCV Abs +ve

In 2007

Haykal et al; have studied CV effects of HCV in 50 HCV patients compared to 50 healthy controls

Echocardiography results

	Echocardiographic measurement	Control group (n=50)	HCV group (n=50)	P value	Significance
1.	**IVSDd**	0.84(±0.11)	0.905(±0.2)	<0.001	VHS
2.	**LVPWDd**	0.855(±0.13)	1.0(±0.2)	<0.01	HS
3.	**LVEDd**	4.94(±0.43)	4.78(±0.86)	>0.05	NS
4.	**RVEDd**	1.61(±0.47)	2.0(±0.4)	<0.01	HS
5.	**LA**	3.645(±0.45)	3.925(±0.6)	> 0.05	NS

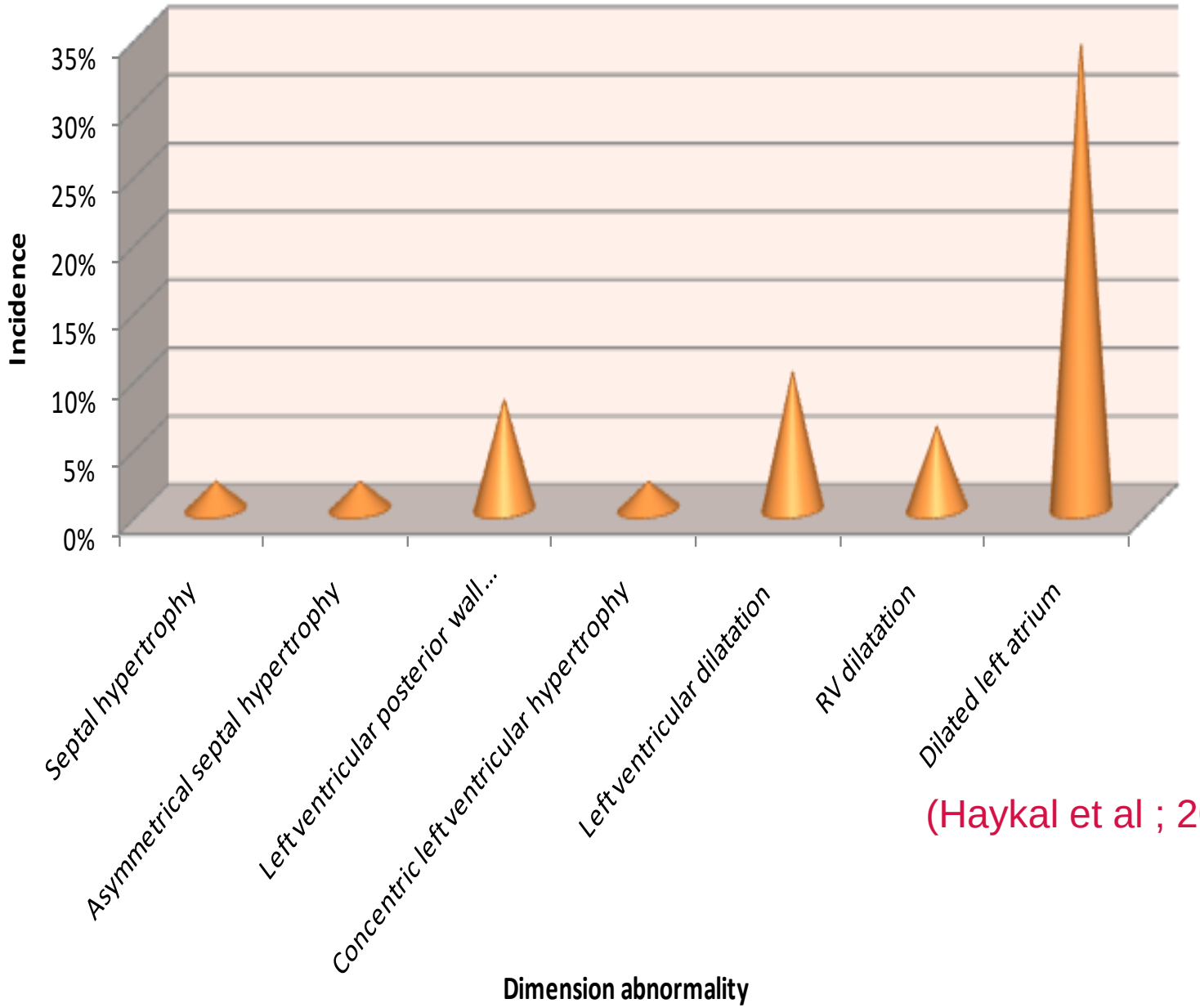
Cardiac dimensions in HCV group compared to control group (Haykal et al; 2007)

Echocardiography results

	Echocardiographic feature	Control group (n=50)	Patients with HCV (n=50)	P value	Significance
1	**FS**	35.23(±4.45)	33(±8.47)	< 0.05	S
2	**EF**	65(±6.02)	62.425(±12.9)	<0.001	VHS
3	**E/A ratio of mitral inflow.**	1.38(±0.31)	0.855(±0.43)	<0.001	VHS
4	**E/A ratio of tricuspid inflow.**	1.45(±0.32)	0.835(±0.48)	<0.001	VHS

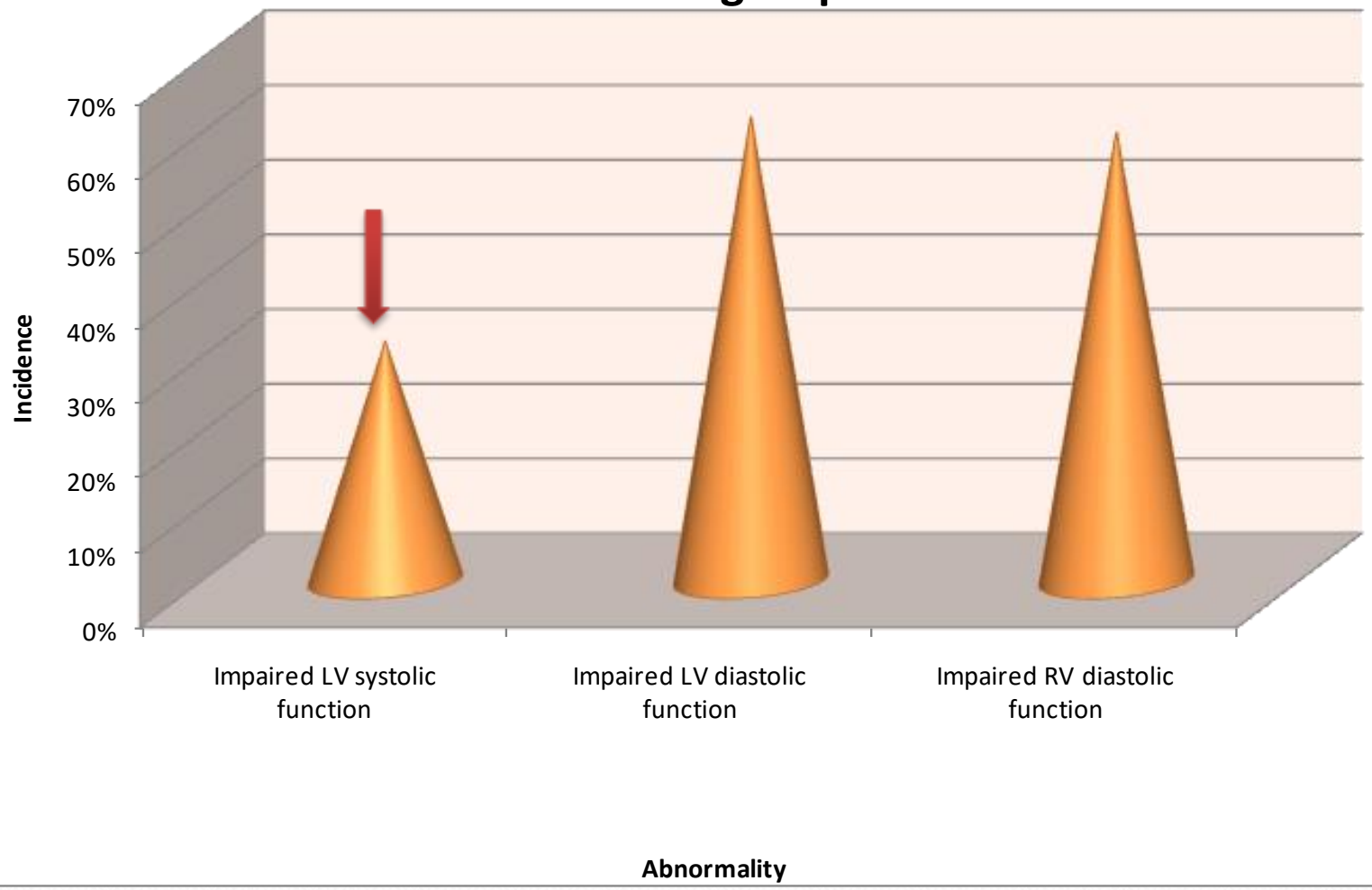
Systolic and diastolic functions in HCV group compared to control group
(Haykal et al; 2007)

Incidence of echocardiographic abnormalities in HCV group



(Haykal et al ; 2007)

Incidence of impaired systolic and diastolic functions in HCV group



(Haykal et al ; 2007)

ECGresults

	Electrocardiogra-phic feature	Control group (n=50)	HCV group (n=50)	P value	Significance
1.	QTc interval	350(±27.5)	360(±34.92)	<0.05	S
2.	P-R interval	160(±19.22)	160(±33.03)	>0.05	NS

Comparison of P-R and QTc intervals between HCV group and control group.

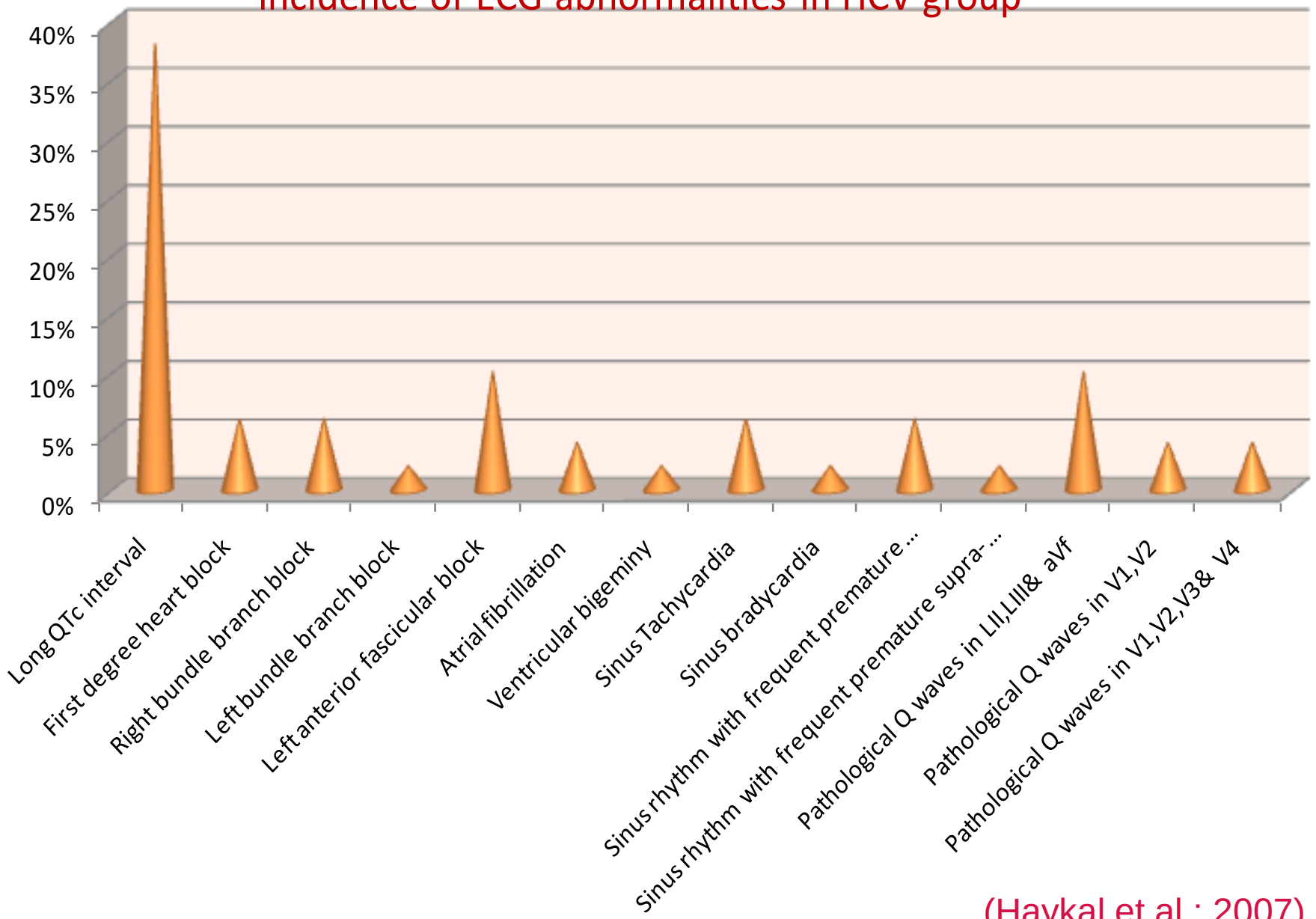
(Haykal et al ; 2007)

	Electrocardiographic abnormality	Incidence
1.	Long QTc interval	38%
2.	First degree heart block	6%
3.	Right bundle branch block	6%
4.	Left bundle branch block	2%
5.	Left anterior fascicular block	10%
6.	Atrial fibrillation	4%
7.	Ventricular bigeminy	2%
8.	Sinus Tachycardia	6%
9.	Sinus bradycardia	2%
10.	Sinus rhythm with frequent premature ventricular complexes	6%
11.	Sinus rhythm with frequent premature supra-ventricular complexes	2%
12.	Pathological Q waves in LII,LIII& aVf	10%
13.	Pathological Q waves in V1,V2	4%
14.	Pathological Q waves in V1,V2,V3& V4	4%

Incidence of electrocardiographic abnormalities in HCV group.

(Haykal et al ; 2007)

Incidence of ECG abnormalities in HCV group



(Haykal et al ; 2007)

Heart failure is an inflammatory process

Mast cells also are found in the human heart and have been implicated in cardiovascular diseases. Mast cells increase in number in the failing heart, including dilated or ischemic cardiomyopathy and acute myocardial infarction.

(Matsumori; 2010)

Cetirizine

(a second generation anti-histaminic)

An agent that stabilizes mast cells and an H-1 receptor antagonist has been shown to improve heart failure caused by pressure overload and viral myocarditis in an animal model.

(Matsumori; 2010)

Patients and methods

Inclusion criteria :- HCV patients with systolic dysfunction and heart failure not associated with other causative or contributing factor of HF including valvular, CAD, DM, HTN.....etc. **(only 9 patients)**

Exclusion criteria:- any HCV patient associated with other possible cause of HF.

All patients were subjected to clinical evaluation, ECG, NTpro BNP and echocardiographic assessment including speckle tracking initially and during follow up visits.

Patients and methods

Standard anti-failure therapy including B- blocker, ACEIs, Diuretics ± digixin were prescribed to the 9 patients >>>>>> Still NYHA III/IV after 1 month of ttt.

Cetirizine therapy was added to the standard anti-failure therapy in dose 10 mg once daily at bed time for three months

After three months of Cetirizine therapy

The 9 patients improved on both clinical, ECG , Echo and NT-Pro BNP basis.

Clinically >> all patients improved form NYHA III/IV to NYHA I

Results

1- ECG

QTc interval

Before Cetirizine (n =9)	After Cetirizine (n=9)	P value
465.56 ± 49.27	435.56 ± 41.57	0.005

Results

2- Conventional echocardiography

Parameter	Before Cetirizine (n =9)	After Cetirizine (n =9)	P Value
Left atrial diameters (mm)	48.78 ± 5.26	46.11 ± 4.34	0.001
LV end diastolic diameter (mm)	61.33 ± 15.58	59 ± 15.01	0.019
LV end systolic diameter (mm)	47.44 ± 16.95	42.89 ± 13.94	0.005
EF %	46.89 ± 16.59	54 ± 10.62	0.013

Results

3- speckle tracking

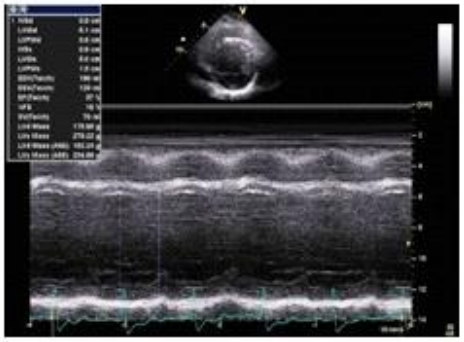
Average LV Strain %Global (GS)	Before Cetirizine (n =9)	After Cetirizine (n =9)	P value
	-11.9 ± 6.24	- 13.29 ± 6.07	0.009

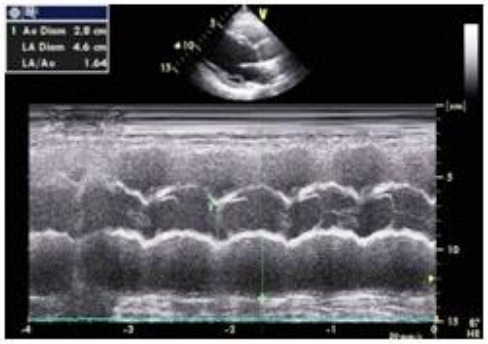
Results

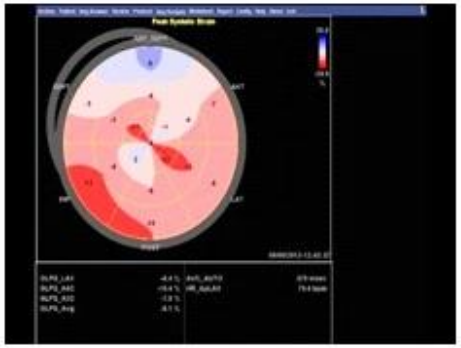
4- NT proBNP

NT Pro BNP	Before Cetirizine (n =9)	After Cetirizine (n =9)	P wave
pg/dL	1217.33 ± 1189.19	591.56 ± 644.88	0.021

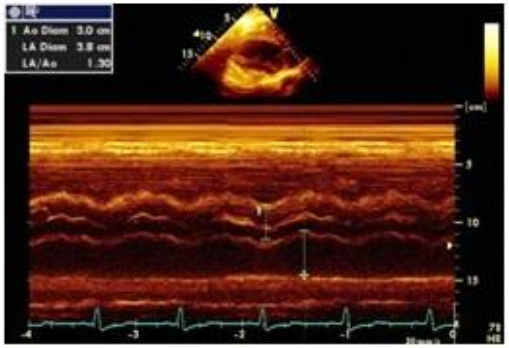
HCV patient with systolic dysfunction before cetirizine therapy (EF 37%, LA 46 mm& GS – 8.1 %)

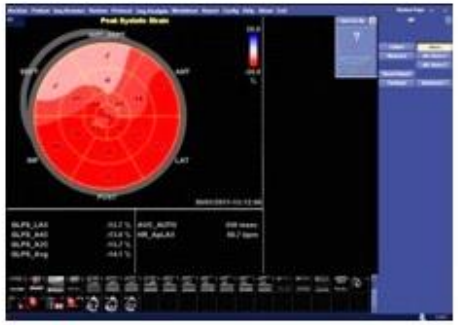






The same HCV patient after 3 months of cetirizine therapy (EF 50 %, LA 38 mm & GS – 14.1 %)





Conclusion

1- Our study is the first to investigate the role of an antihistamine, cetirizine, in the treatment of HCV cardiomyopathy in human. Our results confirm those from an experimental study of viral myocarditis in mice, which showed the role of inflammatory cytokines and metalloproteinases in cardiac remodeling

Conclusion

2- Cetirizine represents a new adjuvant drug that is effective for the treatment of refractory heart failure in HCV cardiomyopathy

Conclusion

3- Cetirizine might be considered as a bridge therapy for HCV-induced myocarditis and heart failure until the HCV patient becomes eligible for interferon-ribavirin eradication therapy aimed at complete hepatic and extrahepatic viral clearance.


Thank you!