CARDIAC CHANGES IN CIRRHOTIC PATIENTS WITH CHRONIC HCV

Thesis

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Abstract

Cirrhotic cardiomyopathy is a clinical syndrome in patients with liver cirrhosis characterized by an abnormal and blunted response to physiologic, pathologic or pharmacologic stress but normal to increased cardiac output and contractility at rest. In this study, we demonstrate the cardiac changes in cirrhotic patients with chronic HCV by echocardiography and electrocardiogram.

Keyword:

Cirrhosis – cardiomyopathy – cirrhotic cardiomyopathy

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List of abbreviations

ALKM	Anti-liver kidney microsomal antibodies
ALT	Alanine transaminase
AMA	Antimitochondrial antibodies
ANA	Anti-nuclear antibody
ANP	Atrial natriuretic peptide
Anti HCV-Ab	Anti-Hepatitis C antibody
ASMA	Anti-smooth muscle antibodies
AST	Aspartate transaminase
AT	Angiotensin
BH_4	Tetrahydrobiopterin
BNP	Brain natriuretic peptide, B-type natriuretic peptide
bpm	Beats per minute
Ca^{++}	Ionized calcium
CBC	Complete blood count
cGMP	Cyclic guanosine mono-phosphate
CM	Cardiomyopathy
CNP	C-type natriuretic peptide
CO	Carbon monoxide
COPD	Chronic obstructive pulmonary disease
CT	Computed Tomography
CTP	Child -Turcotte-Pugh
(D)	Diastole
Dbh	Dopamine β-hydroxylase

DNA	Deoxyribonucleic acid
DNP	Dendroaspis natriuretic peptide
DT	Deceleration time
E/A ratio	Ratio of early to late (atrial) phases of ventricular filling
ECG	Electrocardiogram
EEG	Electroencephalography
EF	Ejection fraction
eNOS	Endothelial nitric oxide synthase
ETs	Endothelins
FS	Fractional shortening
HBV	Hepatitis B virus
HBs-Ag	Hepatitis B surface antigen
HCV	Hepatitis C virus
HFE	High iron Fe
HO	Haeme-oxygenase
HR	Heart rate
HSC	Hepatic stellate cells
IHD	Ischemic heart disease
IHVR	Intrahepatic vascular resistance
IVRT	Isovolumetric relaxation time
IVST	Interventricular septal thickness
iNOS	Inducible nitric oxide synthase
INR	International normalized ratio
LT	Leukotrienes.
LV	Left ventricle
LVDD	Left ventricular diastolic diameter

LVEF	Left ventricular ejection fraction
LVSD	Left ventricular systolic diameter
MELD	Model for End-Stage Liver Disease
MRI	Magnetic resonance imaging
n	number
NADPH	Nicotinamide adenine dinucleotide phosphate
NAFLD	Non-alcoholic fatty liver disease
NASH	Nonalcoholic steatohepatitis
NE	Norepinephrine
nNOS	Neurons nitric oxide synthase
NO	Nitric oxide
NPR-A	Natriuretic peptide receptor A
NT-proBNP	N-terminal prohormone of brain natriuretic peptide
ΔP	Pressure difference, also means pressure gradient
PAP	Pulmonary artery pressure
PCR	Polymerase chain reaction
PCWP	Pulmonary capillary wedge pressure
PDGF	Platelet-derived growth factor
PHT	Portal hypertension
PWT	Post wall thickness
Q	Flow
QTc	QT interval corrected for HR
R	Resistance
RAA	Renin-angiotensin-aldosterone
RAAS	Renin-angiotensin-aldosterone system
RAP	Right atrial pressure

RNA	Ribonucleic acid
ROS	Radical oxygen species
(S)	Systole
SD	Standard deviation
SNS	Sympathetic nervous system
T.Bil	Total bilirubin
D.Bil	Direct bilirubin
TGFß$_1$	Transforming growth factor ß$_1$
TIBC	Total iron binding capacity
TIPS	Transjugular intrahepatic portosystemic stent-shunt
TNF-α	Tumour necrosis factor - alpha
TTE	Transthoracic echocardiography
Us	Ultrasound
VP	Vasopressin
vs	Versus

Introduction

Patients with liver cirrhosis are reported to have a hyperdynamic circulation, which is manifested primarily as high cardiac output, decreased systemic vascular resistance and widespread arterial vasodilatation.[1]

Cirrhotic cardiomyopathy is the term used to describe a constellation of features indicative of abnormal heart structure and function in patients with cirrhosis. [2,3]

In the absence of consensus definitions, the term "cirrhotic cardiomyopathy" is defined at present as:

- baseline increased cardiac output but blunted ventricular response to stimuli
- systolic and/or diastolic dysfunction
- absence of overt left ventricular failure at rest
- electrophysiological abnormalities including prolonged QT interval on electrocardiography and chronotropic incompetence.[4,5]

The disease is generally latent and shows itself when the patient is subjected to stress such as exercise, drugs, hemorrhage and surgery.[6] In the majority of cases, diastolic dysfunction precedes systolic dysfunction, which tends to manifest only under conditions of stress.[7]

Generally, cirrhotic cardiomyopathy with overt severe heart failure is rare. Major stresses on the cardiovascular system such as liver transplantation, infection and procedures such as insertion of transjugular intrahepatic portosystemic stent-shunts (TIPS) can convert latent to overt heart failure. It may also contribute to the pathogenesis of hepatorenal syndrome.[8]

Pathogenic mechanisms of cirrhotic cardiomyopathy are multiple and include abnormal membrane biophysical characteristics, impaired β-adrenergic receptor signal transduction and increased activity of negative-inotropic pathways mediated by cGMP. Other mechanisms include increased inducible nitric oxide synthase (iNOS) activity with overproduction of NO.[9,10]

To date, there is no single diagnostic test that can identify patients with this condition. Diagnosis and differential diagnosis require a careful assessment of patient history, physical examination and appropriate diagnostic tests.[11]

Tissue Doppler imaging has been suggested to be able to describe changes in myocardial performance that go beyond the limitations of simple measurements of EF or myocardial motion. It showed additional value in describing changes in LV function both in systemic and regional myocardial diseases. [12-14]

Levels of brain natriuretic peptide, also called B-type natriuretic peptide (BNP), are elevated in systolic and diastolic dysfunction, ventricular hypertrophy and myocardial ischemia.[15,16]

In cirrhotic patients, levels of atrial natriuretic peptide (ANP) and BNP are elevated due to increased cardiac release and not because of impaired hepatic extraction.[17,18] Several studies have shown increased plasma levels of brain natriuretic peptide (BNP) in some patients with cirrhosis, suggesting cardiac dysfunction.[19]

NT-proBNP has recently suggested been to be an even better indicator of early cardiac dysfunction than BNP because of its stability and longer biological half-life.[20,21]

The exact role of BNP and NT-proBNP in the noninvasive diagnosis of cardiac dysfunction in cirrhotic patients remains to be fully clarified. This study was undertaken to investigate the prevalence of cirrhotic cardiomyopathy in cirrhotic patients with chronic HCV by means of echocardiography and ECG as well as the predictive value of BNP and NT-proBNP levels in detecting cardiac dysfunction assessed by Echocardiography.

Aim of the work

This study was undertaken to assess the cardiac structural and functional changes as well as electroconductance abnormalities in cirrhotic patients with chronic HCV by means of transthoracic echocardiography and 12-lead ECG.

To correlate these changes with levels of BNP and N-terminal pro-BNP and determine the predictive value of BNP and N terminal-proBNP levels in detecting cardiac dysfunction assessed by Echocardiography and ECG.

Review of literature

Liver Cirrhosis and portal hypertension

Cirrhosis is the result of chronic liver disease that causes scarring of the liver (fibrosis – nodular regeneration) and liver dysfunction.[24]

Fibrosis is not synonymous with cirrhosis, it may be in zone 3 (e.g. in heart failure) or in zone 1 (e.g. in bile duct obstruction and congenital hepatic fibrosis) or interlobar (in granulomatous liver disease), but without a true cirrhosis. However, nodule formation without fibrosis (as in partial transformation) is not cirrhosis.[25]

Classification of cirrhosis

I. Morphological classification

The most common histologic classification divides cirrhosis into micronodular, macronodular and mixed forms.[26] However, there is no functional or prognostic value to the nodule size.[27]

a. Micronodular cirrhosis

It is characterized by thick, regular fibrous septa, by regenerating small nodules (less than 3mm) which involve every lobule. The micronodular liver may represent impaired capacity for regrowth as in alcoholism, malnutrition, old age or anemia.

b. Macronodular cirrhosis

It is characterized by septa and large nodules. The size of nodules are more than 3mm.[25]