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Insight HEART

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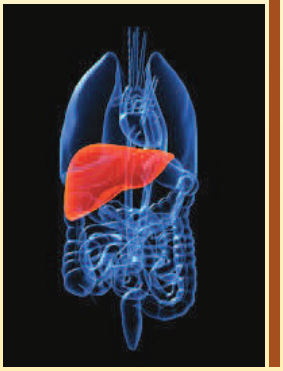


Hepato-Cardiac Disorders

The heart and liver are organs that are closely related both in health and disease. Chronic liver diseases may affect cardiac functions in the absence of other heart disease. These effects are called cirrhotic cardiomyopathy and may aggravate the course during orthotropic liver transplantation (OLT). In case of ischemic hepatitis, patients with severe heart failure usually remain asymptomatic, while for patients with congestive hepatopathy, signs of right-sided heart failure could mask hepatic injury. The evaluation of cardiac and hepatic function is very important in patients with severe heart failure and hepatic injury.

LIVER DISEASES AFFECTING THE HEART

Chronic hepatitis C virus

In hepatitis C virus (HCV) heart disease, most patients develop chronic inflammation of the myocardium and, later, dilated cardiomyopathy attributable to necrosis and loss of myocytes. However, because myocytes do not replicate, the proliferative stimuli induced by HCV infection may promote myocyte hypertrophy and hypertrophic cardiomyopathy. Cardiac damage is a rare manifestation of HCV-related mixed cryoglobulinemia vasculitis. Despite favourable early outcomes, patients with cardiac damage had poorer survival than those without. Chronic hepatitis C viral infection is independently associated with presence of metabolic conditions (insulin resistance, type 2 diabetes mellitus and hypertension) and congestive heart failure.

The connection between hyperlipidemia and atherosclerosis is not linear in people with hepatitis C. Although chronic HCV infection was associated with severe insulin resistance, the patients only had mild atherosclerosis, suggesting a unique characteristic of HCV-related metabolic abnormality. Chronic HCV-associated steatosis was suggested as a leading cause of coronary artery diseases through the modulation of atherogenic factors. Interestingly, interferon-based therapies in patients with chronic HCV were found to reduce the long-term risk of stroke. Thus, atherosclerosis in patients with hepatitis C is likely due to an inflammatory process rather than to a lipid related source. Thus, even patients having healthy cholesterol and triglyceride levels in the presence of chronic hepatitis C infections should not engage in activities that could further increase the disease risk of their cardiovascular vessels.

Liver cirrhosis

Patients with liver cirrhosis (LC) frequently experience autonomic cardiovascular dysfunction. Patients with liver cirrhosis have an enhanced activity of the sympathetic nervous system and hyperdynamic circulation showing increased cardiac output and reduced systemic vascular resistance. These changes may induce myocardial remodelling and LV hypertrophy (LVH), resulting in systolic and diastolic functional abnormalities and cardiomyopathy. The criteria for the diagnosis of cirrhotic cardiomyopathy are shown in Table 1.

Systolic dysfunction is related to the inability of the heart to meet its demands with respect to the generation of an adequate arterial blood pressure and cardiac output. This dysfunction can be unveiled by physical exercise that increases left ventricular pressure, volume, and left ventricular ejection fraction and heart rate in some cirrhotic patients. Similarly, the administration of vasoconstrictors, such as angiotensin II and terlipressin, increases the SVR and thereby the left ventricular afterload unmasking a latent left ventricular dysfunction in cirrhosis. In contrast, vasodilators, such as angiotensin-converting enzyme inhibitors and other afterload-reducing agents, should be used with caution due to the risk of further aggravation of the vasodilatory state. Systolic dysfunction may have an impact on the development of complications, such as sodium and water-retention and ascites formation, as well as development and prognosis of renal dysfunction.

Diastolic dysfunction in cirrhosis is due to an increased stiffness of the myocardial wall owing to myocardial hypertrophy, fibrosis, and

subendothelial edema. The prevalence of diastolic dysfunction has been reported to range from 45% to 56%. Diastolic dysfunction is most prominent in patients with severe decompensation, in whom, the combination of myocardial hypertrophy, contractile dysfunction, changes in heart volumes, and diastolic dysfunction may represent an essential element in cirrhotic cardiomyopathy. The diastolic dysfunction may adversely affect the prognosis of patients with cirrhosis, by favouring the occurrence of complications and impairing the outcomes of manoeuvres that lead to rapid increases in preload, such as transjugular intrahepatic porto-systemic shunt (TIPS) insertion.

Patients with advanced cirrhosis usually exhibit tachycardia. The inability to increase the heart rate further contributes to an impaired ability to keep the cardiac output at a level adequate to meet the needs of systemic circulation. At this point, the effective volemia suddenly worsens, similar to the events of post-paracentesis circulatory dysfunction and hepatorenal syndrome. The prolongation of the electrocardiographic QT interval is common in cirrhosis, with a prevalence that exceeds 60% in patients with an advanced disease. Systemic and cardiac changes in patients with liver cirrhosis are shown in Figure 1.

Nonalcoholic fatty liver disease

It has been shown that the leading cause of death in patients with nonalcoholic fatty liver disease (NAFLD) is coronary events. In patients with diabetes mellitus, NAFLD is associated with cardiovascular disease (CVD) independent of the classical risk factors, glycaemic control, medications, and metabolic syndrome features. When diabetic patients with and without NAFLD were compared, those with NAFLD had a higher prevalence of coronary vascular disease, hypertension, central obesity, poor glycaemic control, and dyslipidaemia and greater carotid intimal thickness. Furthermore, with the development of steatohepatitis, the degree and severity of CVD became directly proportional to the severity of inflammation on liver biopsy. Cardiovascular mortality is also increased at least two-fold in non-alcoholic steatohepatitis (NASH). NASH is not simply a marker of CVD but may also be involved in its pathogenesis. Steatosis has been found to be the strongest independent risk predictor of vascular damage, followed by age and blood pressure. Patients with NAFLD and systolic BP ≥ 130 mmHg are 4.7 times more likely to have a positive treadmill test.

Primary biliary cirrhosis

Circulating cholesterol levels are elevated in most with primary biliary cirrhosis. Hypercholesterolemia in patients with primary biliary cirrhosis should be considered a cardiovascular risk factor only when other factors are present. Ursodeoxycholic acid, the standard treatment for primary biliary cirrhosis, improves cholestasis, thereby lowering the circulating levels of cholesterol. Hypercholesterolemia in the absence of other cardiovascular risk factors does not require specific therapeutic interventions in patients with primary biliary cirrhosis. Autonomic dysfunction has been seen in PBC and was associated with an increased cardiac mortality risk in

Table 1 :Proposal for diagnostic and supportive criteria for cirrhotic cardiomyopathy agreed upon at a working party held at the 2005 World Congress of Gastroenterology

A working definition of cirrhotic cardiomyopathy
A cardiac dysfunction in patients with cirrhosis characterised by impaired contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease
Diagnostic criteria
Systolic dysfunction
Blunted increase in cardiac output with exercise, volume challenge or pharmacological stimuli
Resting EF < 55%
Diastolic dysfunction
E/A ratio < 1.0 (age-corrected)
Prolonged deceleration time (> 200 ms)
Prolonged isovolumetric relaxation time (> 80 ms)
Supportive criteria
Electrophysiological abnormalities
Abnormal chronotropic response
Electromechanical uncoupling/dyssynchrony
Prolonged QTc interval
Enlarged left atrium
Increased myocardial mass
Increased BNP and pro-BNP
Increased troponin I

BNP: Brain natriuretic peptide; E/A: Early diastolic/atrial filling ratio; LVEF: Left ventricular ejection fraction.

non-liver chronic disease states.

Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of affecting the large bile ducts and is characterized by periductal fibrosis and stricture formation. It has been hypothesized that PSC represents "arteriosclerosis of the bile duct".

Hepatocellular carcinoma

Cardiac complications of hepatocellular carcinoma are rare. Cases of right atrial invasion of HCC had been reported.

Budd-chiari syndrome

Primary Budd-chiari syndrome (BCS) is a rare clinical entity characterized by hepatic venous outflow obstruction at various levels from the small hepatic veins to the inferior vena cava.

Portal hypertension

Three important complications are associated with portal hypertension: hepatopulmonary syndrome, portopulmonary hypertension, and hepatic hydrothorax.

The hepatopulmonary syndrome: This entity is defined by an oxygenation defect caused by the development of intrapulmonary vascular dilation in patients with either advanced liver disease and/or portal hypertension. Patients with the hepatopulmonary syndrome (HPS) may present with the insidious onset of dyspnea or remain completely asymptomatic during the early stages. Dyspnea upon standing (platypnea) and hypoxemia exacerbated in the upright position (orthodeoxia) are present in almost 25% of HPS patients. Patients with severe HPS may display digital clubbing and cyanosis.

Chest radiographs may be normal or show bibasilar nodular or reticulonodular opacities, reflecting diffuse vascular pulmonary dilation. Pulmonary function tests typically demonstrate a reduced diffusion capacity for carbon monoxide. There is no established medical therapy currently available for HPS. In patients with PaO2 <60 mmHg at rest or with exertion, the administration of supplemental oxygen is appropriate, because chronic hypoxemia itself may contribute to the mortality in HPS.

Portopulmonary hypertension: Portopulmonary hypertension (POPH) is characterized by pulmonary arterial hypertension (PAH) that occurs in the setting of portal hypertension, with or without advanced liver disease. The severity of POPH does not correlate with the degree of liver dysfunction or the severity of portal hypertension. Dyspnea on exertion is the most common initial symptom of POPH and fatigue, orthopnea, chest pain, peripheral edema, syncope, and dyspnea at rest may develop as the disease progresses. Medical treatment includes the following: prostacyclin analogs (prostanoids), Endothelin receptor antagonist and Phosphodiesterase-5 inhibitors. β-blockers was associated with worsening exercise capacity.

Hepatic hydrothorax: This entity is characterized by a transudative pleural effusion in the absence of underlying cardiac or pulmonary disease. Its prevalence has been estimated to be 5%-10% in cirrhotics. The most important mechanism leading to the passage of ascitic fluid from the peritoneal into the pleural cavity is the presence of diaphragmatic defects. These defects were corroborated by showing passage of 99mTc-human albumin from the abdominal into the pleural cavity, even in the absence of

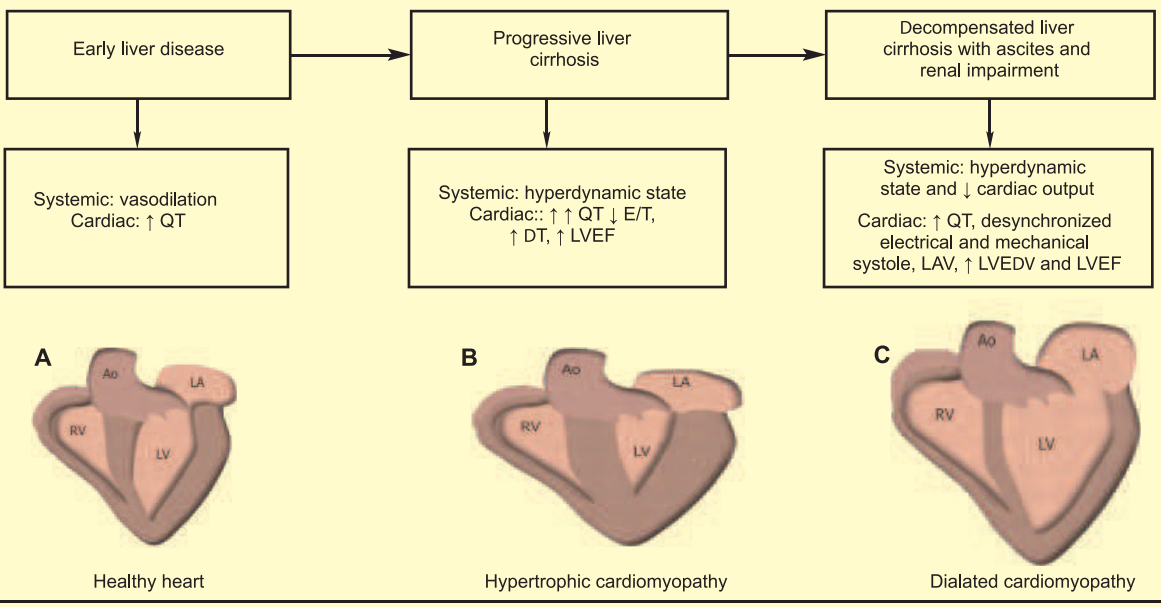


Figure 1 Proposal of changes in cardiac output during the course of the liver disease.
DT: Deceleration time; LAV: Left atrial volume; LVEDV: Left ventricular end-diastolic volume; LVEF: Left ventricular ejection fraction.

underlying ascites. Symptoms include cough, dyspnea, chest discomfort, hypoxia, and in the most severe cases respiratory failure with or without ascites. Spontaneous bacterial pleuritis (SBPL) results when hepatic hydrothorax (HH) becomes infected in the absence of pneumonia. Symptoms in SBPL vary from fever and pleuritic chest pain to subtle worsening of encephalopathy or renal function, necessitating a high index of suspicion. A PMN >500 cells/mm^3 is diagnostic for SBPL in a pleural effusion, although SBPL with PMN between 250-500 cells/mm^3 is documented by positive pleural fluid culture. Chest tube placement is contraindicated in SBPL, in the absence of empyema, due to the risk of protein loss, prolonged drainage, secondary infection and hepatorenal syndrome. Treatment of HH includes the restriction of sodium intake with the administration of diuretics. This approach is effective in controlling HH, although fluid mobilization from the pleural cavity may be slower than from the peritoneal cavity and approximately 20% of patients develop refractory HH. Percutaneous drainage, and chest tube placement can be used in some cases. The standard of care treatment for refractory HH is TIPS placement with response rates of 70% to 80%. Video assisted thoracoscopy (VATS) with pleurodesis is a alternative for patients with refractory HH, who are not eligible for or who have failed TIPS.

Liver transplantation

Patients with cirrhosis requiring liver transplantation (LT) usually demonstrate increased cardiac output. Low systemic vascular resistance and bradycardia are also commonly seen in cirrhosis and can be aggravated by beta-blocker use. These physiologic changes increase the risk of cardiovascular complications, in addition to altered hemodynamic stresses that LT patients face in the immediate post-operative period. Post-transplant reperfusion may result in cardiac death due to a multitude of causes, including arrhythmia, acute heart failure (HF), and myocardial infarction.

The unusually high perioperative mortality in transplant patients with CAD warrants a systematic evaluation in every patient that thought to have a greater risk of atherosclerotic coronary disease. Almost all cardiovascular abnormalities can be reversed 6 to 12 months after liver transplantation.

CARDIAC CAUSES OF HEPATIC DISORDERS

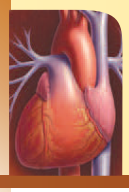
Heart failure

The cardiac causes of hepatic dysfunction include constrictive pericarditis, severe pulmonary arterial hypertension (PAH), mitral stenosis, tricuspid regurgitation (TR), corpulmonale, ischemic cardiomyopathy, and postoperative consequences of the Fontan procedure for pulmonary atresia and hypoplastic left heart syndrome. All of

Table 2 :Comparison between acute and chronic hepatic complications of cardiac failure

	Chronic congestive hepatopathy	Acute ischemic hepatitis
Aetiology	Chronic heart failure	Acute heart failure
Pathophysiology	Perisinusoidal edema Increased lymph flow Zone 3: alternating necrosis and hemorrhage Sinusoidal thrombosis	Tissue hypoxia Zone 3 necrosis
Manifestations	Right hypochondrial pain Edema, ascites, jaundice	Asymptomatic or nonspecific (nausea, vomiting, jaundice, right hypochondrial pain)
Laboratory data		
Bilirubin	Mild increase	Marked elevation
ALT and AST	Normal mild elevation	Marked elevation
LDH	Normal or mild elevation	Marked elevation
Prothrombin time	Prolonged	Normal or prolonged
ALP	Normal or mild elevation	Increased
Albumin	Hypoalbuminemia	Normal
Treatment	ACE inhibitors β-blockers Diuretic Amiodarone Statins with caution	Oxygen therapy Avoid precipitating factors Inotropic agents with caution Vasopressor with caution Diuretics in hypervolemia
Prognosis	Slowly progressive course	Benign and usually self limited

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactic dehydrogenase; ALP: Alkaline phosphatase; ACE: Angiotensin-converting enzyme.



postoperative consequences of the Fontan procedure for pulmonary atresia and hypoplastic left heart syndrome. All of these causes can lead to passive congestion due to the elevated right ventricular (RV) pressure and right sided heart failure.

Clinical presentations: As for the acute ischemic hepatitis, no specific symptoms but patients may present with symptoms of nausea, vomiting, anorexia, malaise, right-upper quadrant pain, jaundice, oliguria, and flapping tremors representing cerebral hypoperfusion rather than hepatic encephalopathy. Ischemic hepatitis is usually benign and self-limited. The clinical diagnosis of liver injury is almost always incidental when liver enzymes are found to be massively elevated 1 to 3 d after an episode of systemic hypotension. This condition may be associated with increased serum creatinine level from acute tubular *necrosis.*

Congestive hepatopathy: The term congestive hepatopathy replaced cardiac cirrhosis. Patients experience mild, dull right upper quadrant pain caused by the stretching of the liver capsule. Hepatomegaly with a firm, tender liver edge and peripheral edema are typically the most prominent findings in patients with chronic right-sided HF, but these may also occur rapidly in acute HF. Ascites may be present in up to 25% of these patients and splenomegaly is characteristically absent. Jaundice is not commonly reported. In patients with considerable TR, a prominent systolic pulsation of the liver, attributable to an enlarged right atrial V wave, is often noted. A presystolic pulsation of the liver, attributable to an enlarged right atrial A wave, can occur in tricuspid stenosis, constrictive pericarditis, restrictive cardiomyopathy involving the RV, and pulmonary hypertension.

Laboratory data: As for the acute ischemic hepatitis, severe jaundice is common, with a bilirubin level as high as 15 to 20 mg/dL, elevation of AST to more than 10 times the upper reference range limit, a marked increase in serum LDH, an elevated ALP level, and prolongation of the prothrombin time. Increases in LDH tend to be massive and an ALT/LDH ratio of less than 1.5 helps distinguishing ischemic injury from other forms of acute hepatitis.

As for the congestive hepatopathy, the usual findings are moderate elevations of the biochemical parameters of liver function 2 to 3 times the upper normal reference level. These parameters include AST, ALT, LDH, gamma-glutamyl transpeptidase (GGT), and alkaline phosphatase (ALP). Hyperbilirubinemia, secondary to an increase in both the direct and indirect bilirubin, is also common. The total bilirubin level is rarely greater than 3 mg/dL. In patients with long-standing HR, albumin synthesis may be impaired, leading to hypoalbuminemia and intensifying the accumulation of fluid.

Treatment: Treatment of the cardiac problem is the key to improvement in hepatic dysfunction. As for the AHF and ischemic hepatitis, correcting underlying circulatory or respiratory disturbances is the main treatment. It is recommended that doctors identify and remove any precipitating cause, such as medications with negative inotropic or hypotensive effects (certain antiarrhythmic drugs, calcium-channel blockers, and vasodilators), medications likely to cause impairment of renal function (high doses of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers), or medications likely to accumulate with evolving renal failure (like digoxin). Oxygen should be administered as early as possible in hypoxemic patients to achieve an arterial oxygen saturation >95%. Administration of intravenous diuretics is recommended with caution in acute HF patients in the presence of symptoms secondary to congestion and volume overload. Inotropic agents should be considered in patients with low output states and low systolic blood pressure. When needed, inotropic agents should be administered as early as possible and withdrawn as soon as adequate organ perfusion is restored and/or the congestion is reduced. Vasopressors are only indicated in cases of cardiogenic shock when the combination of an inotropic agent and fluid challenge fails to restore systolic blood pressure >90 mmHg, with inadequate organ perfusion, despite an improvement in cardiac output.

As for the chronic HF and congestive hepatopathy, the main lines of treatment are angiotensin-converting enzyme (ACE) inhibitors and beta blockers. The addition of a low-dose aldosterone antagonist should be considered in all patients with an LV systolic dysfunction. ACE Inhibitors increase cardiac output and decrease LV filling pressure due to their vasodilatory effect. Some ACE inhibitors are prodrugs, which require transformation by the liver into active metabolites. These drugs include enalapril, ramipril, fosinopril, trandolapril, quinapril, benazepril, and moexipril. With liver dysfunction, decreases in the prodrug transformation and inactivation of the active drug may occur. For those patients who cannot tolerate ACE inhibitors due to cough, angiotensin receptor blockers (ARBs) are recommended instead. ARBs reduce morbidity and mortality in patients with systolic HF. Losartan is metabolized to the active metabolite via hepatic carboxylation. In patients with hepatic impairment, the bioavailability is doubled and the total plasma clearance is halved. Therefore, lower initial doses are recommended. Valsartan undergoes little metabolic conversion. Caution is recommended in patients with mild to moderate liver dysfunction but dosage adjustments are generally not needed. Similar to valsartan, irbesartan does not require biotransformation, thus dosage modification is not necessary.

The use of β-blockers is associated with a 30% reduction in total mortality in HF. Propranolol should be administered cautiously in patients with hepatic impairment. No dose adjustments are necessary for atenolol, nadolol, esmolol, sotalol, or acebutolol.

Diuretics: Loop diuretics, such as furosemide, bumetanide, and torsemide, are used for volume management in HF because of their superior natriuretic effects compared with other classes of diuretics. For unknown reasons, the pharmacologic response in patients with liver dysfunction and HF is diminished, and there is a net decreased in sodium excretion when compared with healthy individuals taking the same dose. No adjustments are necessary if renal function is normal.

In patients with severe HF, amiodarone has proven to be effective for suppressing ventricular arrhythmias, reducing sudden death and cardiac mortality, and improving exercise tolerance and ejection fraction. This drug undergoes an extensive hepatic metabolism to active metabolite, but no dosage reduction is indicated in hepatic impairment.

Statins undergo extensive hepatic metabolism. In patients with active liver disease or persistent unexplained elevations in serum transaminases to above 3 times the upper limit of normal, the use of statins is contraindicated.

For patients, who are refractory to medical therapy and who may be candidates for cardiac surgery, CH due to chronic HF can improve and reverse after temporary LV assistive device support or for selected patients or cardiac transplantation. The differences between acute and chronic hepatic impairment are summarized in Table 2.

Ventricular assist devices

Ventricular assist devices (LVADs) lead to volume shifts from the intrathoracic area to the systemic circulation, thus improving liver blood flow. Studies have shown improvement in the liver function in patients with mild abnormalities in pre-implant liver tests, and no deterioration in those with normal baseline values, up to 6 mo. However, pre-existing or post-LVAD severe liver dysfunction strikingly influences patients' prognosis and endangers their survival. Liver dysfunction can also occur or worsen after LVAD implantation. Pre-, peri-, and post-operative factors, such as large doses of vasopressors, prolonged cardiopulmonary bypass time, arterial hypotension, systemic inflammatory responses and, mainly, right ventricular failure predispose a patient to liver damage, often presenting with intrahepatic cholestasis. The model for end-stage liver disease (MELD), a scoring system assessing the severity of chronic liver disease based on serum bilirubin, creatinine and INR for prothrombin time that is widely used to determine prognosis and prioritize the receipt of a liver transplant, is able to predict mortality and morbidity following LVAD. The severity and course of post-ventricular assist devices liver damage can be monitored by sequential assessment of MELD-XI, a modified MELD score excluding INR to overcome the problem posed by concomitant anticoagulation.

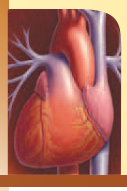
Heart transplantation

Chronic cardiac hepatopathy is common in patients evaluated for heart transplantation-x (HTx), and liver dysfunction predicts an adverse outcome following transplantation. At the same time, altered pre-HTx liver tests

Table 3: Diseases affecting both the liver and the heart concomitantly

	Hepatic manifestations	Cardiac manifestations
Congenital		
Allagile syndrome	Cholestasis	Congenital heart defects
Situs Inversus totalis	Concerns with liver or heart transplantation	
Infections		
Sepsis	Acute liver failure	Acute heart failure
Hepatitis C	Hepatitis	Myocarditis, cardiomyopathy
Cytomegalovirus	Hepatitis	Myopericarditis
HIV	Hepatitis, granuloma	Myocarditis , cardiomyopathy
Malaria	Hepatic necrosis	Cardiac failure
Dengue fever	Hepatic necrosis	Myocarditis
Amebiasis	Hepatitis, hepatic abscess	Pericarditis, effusion
Metabolic		
Wilson disease	Cirrhosis, hepatitis	Left ventricular remodeling
Hemochromatosis	Cirrhosis, hepatitis	Cardiomyopathy
Systemic		
SLE	Steatosis, hepatomegaly	Endocarditis, pericarditis`
Amyloidosis	Hepatomegaly, cholestasis	Cardiomyopathy
Sarcoidosis	Granuloma, cholestasis	Conduction defects, HF
Chronic alcoholism	Cirrhosis	Cariomyopathy
Autoimmune		
Grave's disease	Hepatitis, cholestasis	HF
Autoimmune hepatitis	Hepatitis, cirrhosis	Carditis

HF: Heart failure.



can significantly improve after surgery, suggesting that chronic cardiac hepatopathy is a potentially reversible disease. A careful assessment of liver function and detection of liver cirrhosis is required in all candidates for HTx. Higher MELD scores predict higher postoperative complication rates, including reoperation for bleeding, bacterial infections, and in-hospital death.

Patients with chronic hepatitis C or chronic hepatitis B should be treated before HTx to avoid antiviral drug intake after HTx which may be associated with graft rejection. Finally, patients with heart failure and irreversible cirrhosis could be offered combined heart and liver transplantation.

DISEASES AFFECTING BOTH THE HEART AND THE LIVER

There are many systemic diseases that affect both the liver and the heart. The spectrum of these diseases include congenital, autoimmune, metabolic and infectious causes (shown in Table 3).

Congenital causes

The famous example is Alagile syndrome (AS), which is a multisystemic disease that is autosomal dominant, with variable expression. The major clinical manifestations are as follows: chronic cholestasis, congenital heart disease, posterior embryotoxon in the eye, characteristic facial phenotype, and butterfly vertebrae. Cholestasis, pruritus and xanthomas have been successfully treated with choleretic agents (ursodeoxycholic acid) and other medications (cholestyramine, rifampin, naltrexone).

Infections

Cytomegalovirus (CMV) infection in inmunocompetent hosts generally is asymptomatic; whoever, it rarely can lead to severe organ complications. A rare, but serious complication of cytomegalovirus infection is the presence of myopericarditis concomitant with hepatitis with a possible role of oral valganciclovir in these patients.

Metabolic causes

Wilson disease: Wilson disease is an inherited autosomal recessive disorder of the copper metabolism resulting in the pathological accumulation of copper in the liver, brain and other tissues. One of the reported manifestations is cardiac involvement. Cardiac involvement in Wilson disease patients is characterized by LV parietal thickening with an increased prevalence of concentric LV remodelling. Children with Wilson diseases were asymptomatic upon cardiological examination, but had significantly lower mitral E velocities, mitral E/A ratios as estimated by pulsed wave Doppler echocardiography.

Hemochromatosis: Hemochromatosis is an autosomal recessive disorder affecting the white population. In this disorder, the inappropriate absorption and deposition of dietary iron may result in the development of hepatic and non-hepatic end-organ injury, leading to liver cirrhosis, hepatocellular carcinoma, diabetes, arthritis, skin pigmentation and cardiac diseases. Cardiac involvement in hemochromatosis affects mainly the myocardium: iron overload of the myocytes reduces left ventricular distensibility. Heart failure is the most frequent manifestation of cardiac involvement. Diagnosis of cardiac involvement depends essentially on Doppler echocardiography showing abnormal left ventricular filling and, later, ventricular dilatation with left ventricular systolic dysfunction. Magnetic resonance imaging can quantify intrahepatic and intramyocardial iron levels. The two principal means of treatment by iron depletion are phlebotomy in primary hemochromatosis and excretion of iron by chemical chelation in secondary hemochromatosis. Early diagnosis and iron depletion improve survival by reducing the organ iron overload, especially in the liver and myocardium.

Autoimmune diseases: The atypical clinical presentations of Graves' disease (GD) include anemia, vomiting, jaundice, and right heart failure. Hyperthyroidism may present with jaundice, and on the other hand, deep jaundice may develop with the onset of overt hyperthyroidism in previously compensated chronic liver disease patients. Pulmonary hypertension is reported to be associated with GD and to respond to its treatment. GD-related pulmonary hypertension may be so severe that it produce isolated right-sided heart failure, which is occasionally identified as the presenting manifestation of GD.

Chronic alcoholism: Patients with chronic alcoholism can be presented with both hepatic and cardiac complications. Actively drinking alcoholics with cirrhosis have significantly lower mean ejection fraction and shortening fraction, as well as a greater mean end-diastolic diameter and left ventricular mass than abstaining alcoholics with cirrhosis. Alcoholics admitted solely for cardiomyopathy have a higher prevalence of cirrhosis than unselected alcoholics without heart disease. Patients with alcoholic cirrhosis should be screened for cardiomyopathy.

CONCLUSION

Chronic liver diseases may induce systolic and diastolic dysfunctions in addition to electrophysiological changes, and the prolongation of QT interval in conditions of cirrhotic cardiomyopathy; all of these may improve completely after liver transplantations. Recent studies have found cardiac changes in patients with NAFLD, hepatitis C and primary biliary cirrhosis. On the contrary, acute and chronic heart failure have been shown to lead to acute hepatic injury and chronic congestive hepatopathy with manifestations of liver failure and laboratory data specific to ischemic hepatitis or congestive hepatopathy. There are systemic diseases that affect both the heart and the liver, thus necessitating good cardiac and hepatic evaluation.

Edited from: Hepato-cardiac disorders. Yasser Mahrous Fouad, Reem Yehia. World J Hepatol 2014 January 27; 6(1): 41-54

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Cardiology News

Hospitalization for Pneumonia Is a CVD Risk Factor

Healthy middle-aged and older adults who are hospitalized for pneumonia have an increased risk for cardiovascular disease (MI, stroke, or death from CVD) years later, a new study suggests. Researchers found that participants in the Cardiovascular Health Study (CHS), who had a mean baseline age of 73, had a fourfold higher risk of CVD in the 30 days following hospitalization for pneumonia and a 1.86-fold increased risk of CVD 10 years later, after adjustment for multiple confounders. Even the participants in the Atherosclerosis Risk in Communities (ARIC) study, who were younger (a mean baseline age of 56) and had fewer CVD risk factors, had a 2.38-fold higher risk of CVD within 30 days of hospitalization for pneumonia and a 1.88-fold greater risk of CVD 2 years later, compared with their peers. The findings suggest that clinicians need to take [hospitalization for pneumonia] into account when stratifying patients for future risk for CV events.

JAMA 2015; 313:264-274.

Inactivity More Deadly Than Obesity

Fresh evidence that just a little bit of exercise, such as 20 minutes walking a day, is extremely beneficial — regardless of whether people are overweight/obese or not — has emerged from a large European study. The study — in more than 330,000 men and women — showed that twice as many premature deaths may be attributable to lack of physical activity compared with the number of deaths attributable to obesity. Over the 12 years of follow-up, 21,438 participants died. The greatest reduction in risk for premature death occurred in the comparison between inactive and moderately inactive groups. All-cause mortality was reduced by 16% to 30% in the moderately inactive group compared with those categorized as inactive, across all strata of BMI and waist circumference. Emerging evidence is accumulating indicating that substantial health benefits may be achieved by fairly small increases in physical activity.

Am J Clin Nutr. Published online January 24, 2015

High Mortality After Carotid Stenting Raises Concern

A mortality rate of 32% at 2 years after carotid artery stenting (CAS) in a new study has raised concerns about the risk-benefit of this procedure, especially in older patients. The researchers analyzed data from 22,516 US Medicare beneficiaries (average age, 76 years) who underwent CAS between 2005 and 2009. At 30 days, 1.7% of patients had died, 3.3% had had a stroke or transient ischemic attack (TIA), and 2.5% had experienced a myocardial infarction. Older age, symptomatic carotid stenosis, and nonelective hospital admission were associated with increased risk for death and stroke or TIA during and after the periprocedural period. Mortality at a mean follow-up duration of 2 years was 32.0% in the whole population. This rose to 37.3% in symptomatic patients; asymptomatic patients had a mortality rate at 2 years of 27.7%. The authors point out that two randomized trials (SAPPHIRE [Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy] and CREST [Carotid Revascularization Endarterectomy vs Stenting Trial]) have suggested similar outcomes for carotid stenting compared with carotid endarterectomy, but the situation in real-world patients may be different, especially because they are generally older, with more comorbidities, and are treated by less skilled operators.

JAMA Neurol. Published online January 12.

Editorial Note

Dear Doctor,

We are happy to present the 36th issue of "Insight Heart". It is a small endeavor to provide you compiled & updated information on cardiovascular diseases and its management. This issue is focused on ***"the relation between heart and liver"***. We will appreciate your thoughtful comments.

Thanks and regards.