

Gastrointestinal and Liver Issues in Heart Failure

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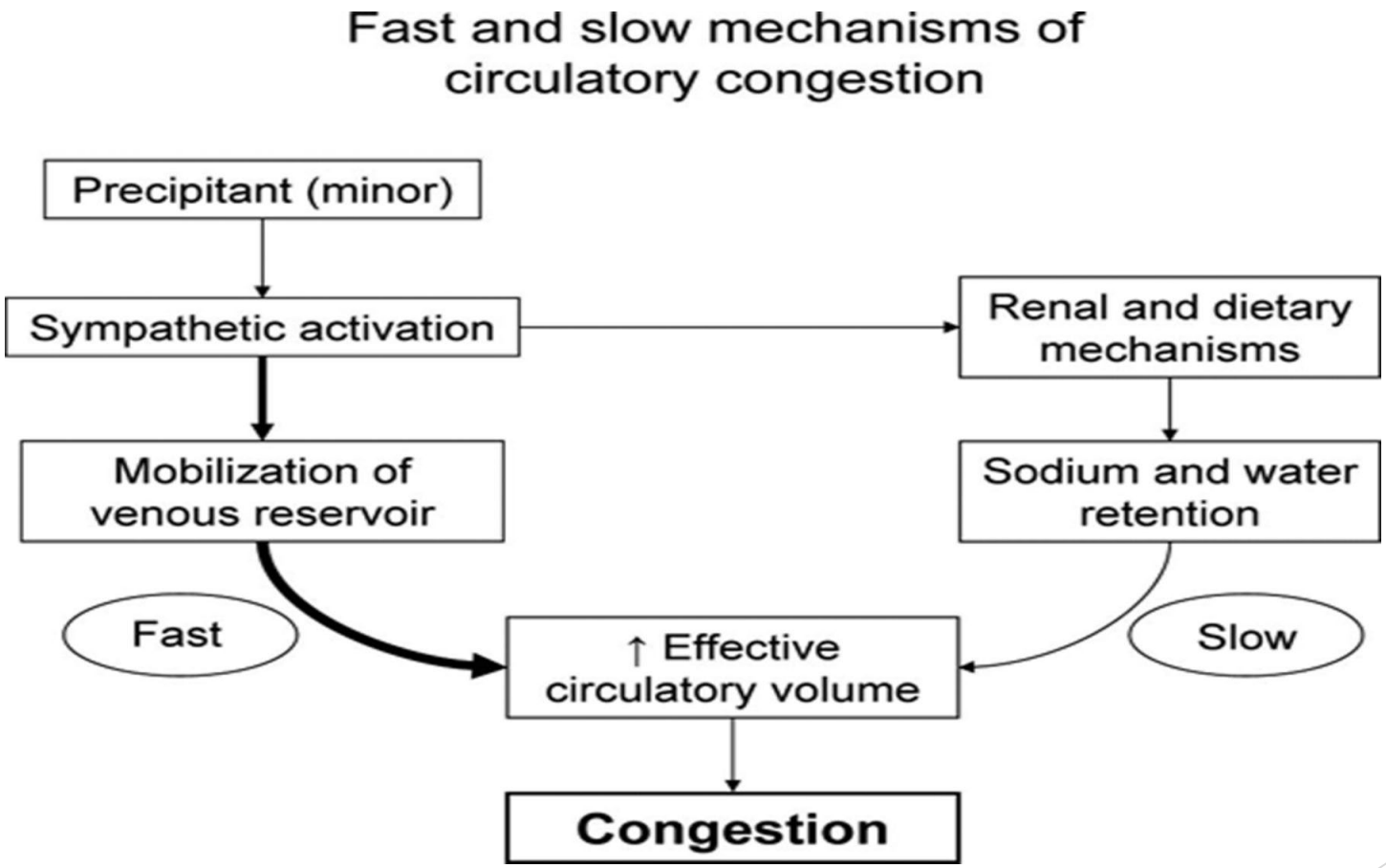
The Gut in HF

- Heart failure (HF) is a systemic disorder caused by the inability of the heart to accommodate the venous return and to maintain sufficient cardiac output to meet the body's metabolic needs
- the systemic volume overload characteristic of HF is generally accompanied by concomitant gut edema, which can lead to bacterial translocation into the systemic circulation. Consequent monocyte activation and excessive cytokine release result in systemic inflammation
- weight gain in 33% to 46% of patients
- This shift increases the preload without increasing total body volume and exaggerates the hemodynamic effects of sodium and water retention
- abdominal discomfort, nausea, constipation, and diarrhea common in advanced HF.

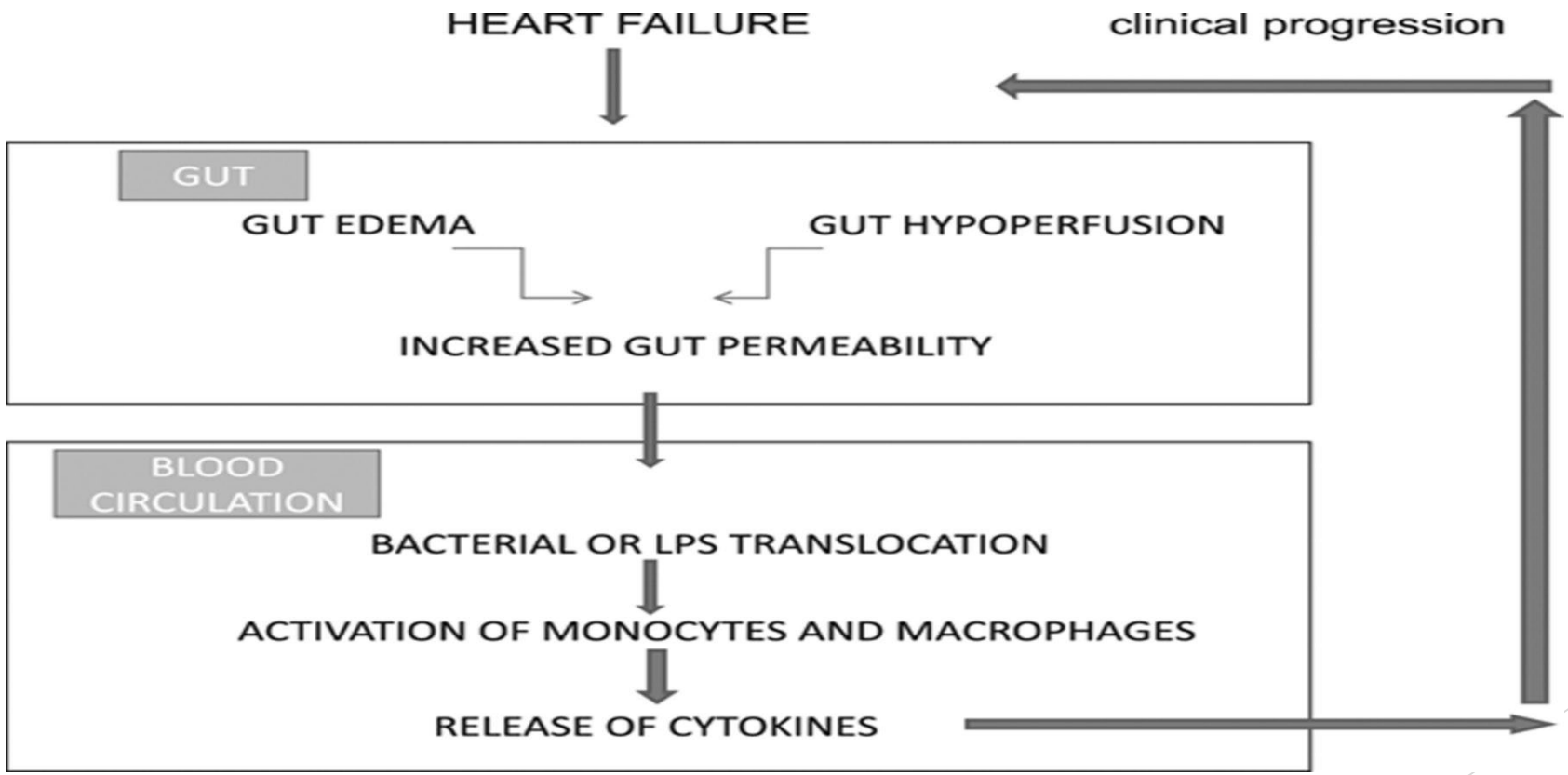
Gastrointestinal system as a venous reservoir



Cardiointestinal Syndrome

- Common gastrointestinal manifestations of HF include anorexia, early satiety, and abdominal pain;
- in patients with advanced HF, ascites, protein-losing enteropathy (PLE), and cachexia may be present
- increased gut permeability in HF appears to be a consequence of gut edema and gastrointestinal hypoperfusion
- patients with edematous HF had significantly higher plasma concentrations of C-reactive protein, tumor necrosis factor (TNF)-α, soluble TNF receptor-1 and -2, interleukin-6, and soluble CD14
- Intestinal mucosal ischemia also may lead to increased gut permeability and bacterial translocation.

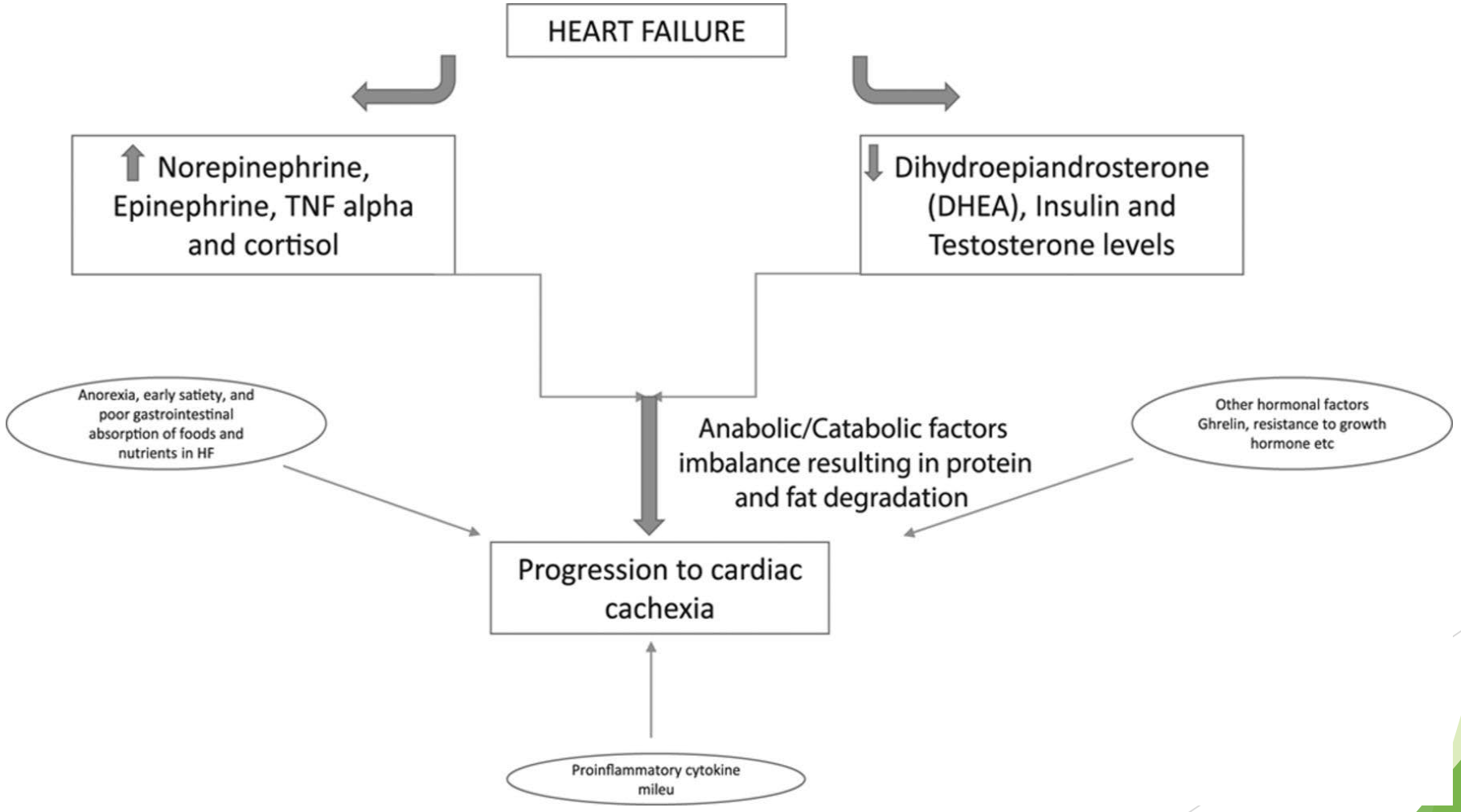
Pathophysiology of cardiointestinal syndrome



Cardiac Cachexia

- Cardiac cachexia has been described as a catabolic state characterized by unintentional and nonedematous weight loss of >7.5% of premorbid body weight over 6 months
- has been reported to be as high as 45%
- The annual mortality in cachectic HF patients may be as high as 20% to 30%.
- upregulation of hormonal factors (norepinephrine, epinephrine, TNFα and cortisol levels) that promote catabolism
- an inadequate anabolic response (eg, reduced dehydroepiandrosterone, insulin, and testosterone levels), signifying an anabolic/catabolic imbalance in cachectic HF patients.
- Anorexia, early satiety, and poor gastrointestinal absorption of foods and nutrients in HF may further exacerbate this anabolic/catabolic imbalance

Pathophysiology of cardiac cachexia.



Protein-Losing Enteropathy

- Hypoalbuminemia/hypoproteinemia is a common condition in patients with HF and is an independent predictor of poor prognosis
- malnutrition, inflammation, and cachexia, but other causal factors include hemodilution, liver dysfunction, proteinuria, and PLE.
- related to gut edema and rupture of intestinal lacteals from elevated central venous pressures.
- elevated right-sided filling pressures, including constrictive pericarditis, tricuspid regurgitation, and congenital heart disease
- albumin with diuretics in refractory diuretic-resistant edema confers modest clinical benefit
- clearance of α-1 antitrypsin (A1AT) from plasma
- Elevated A1AT clearance suggests excessive gastrointestinal protein loss distal to pylorus. Patients with PLE generally have A1AT clearance values >50 mL/24 h (normal, <27 mL/24 h).

Alteration in the Pharmacokinetics and Pharmacodynamics of HF Drugs as a Result of Gastrointestinal Issues

- decreasing intestinal absorption of HF drugs
- mechanisms include edematous changes in the intestinal wall, increased thickness of the bowel tissues as a result of collagen deposition, and intestinal damage from chronic hypoperfusion.
- Gut edema may also alter the rate of absorption of certain drugs such as loop diuretics
- oral furosemide is delayed in the presence of gut edema

Involvement of the Liver in HF

- Congestive hepatopathy is the most common cause of liver dysfunction in HF, more common than reduced cardiac output
- sinusoidal congestion, resulting in peri-sinusoidal edema, which decreases oxygen diffusion to the hepatocytes
- high-protein-concentration ascites (typically >2.5 g/dL) and distinguishes cardiac ascites from other types

Table 1. Patterns of Liver Involvement in HF

Condition	Pathophysiology	LFTs	Other Testing	Reversible?
Congestive hepatopathy	Right-sided heart volume overload	Modest increase	Rarely required	Yes
Hepatic fibrosis	Prolonged congestion (usually years) with wound-healing response	Modest increase	HVPGLiver biopsyLiver-spleen scan	Maybe
Hepatic cirrhosis	End-stage fibrosis with liver synthetic dysfunction and portal hypertension	Modest increase	HVPGLiver biopsyLiver- spleen scan	No
Ischemic hepatitis	Acute hypotension and more likely with decrease in cardiac output and concomitant congestion	Dramatic elevation	Rarely required	Usually

HF indicates heart failure; HVPG, hepatic venous pressure gradient; and LFT, liver function test.

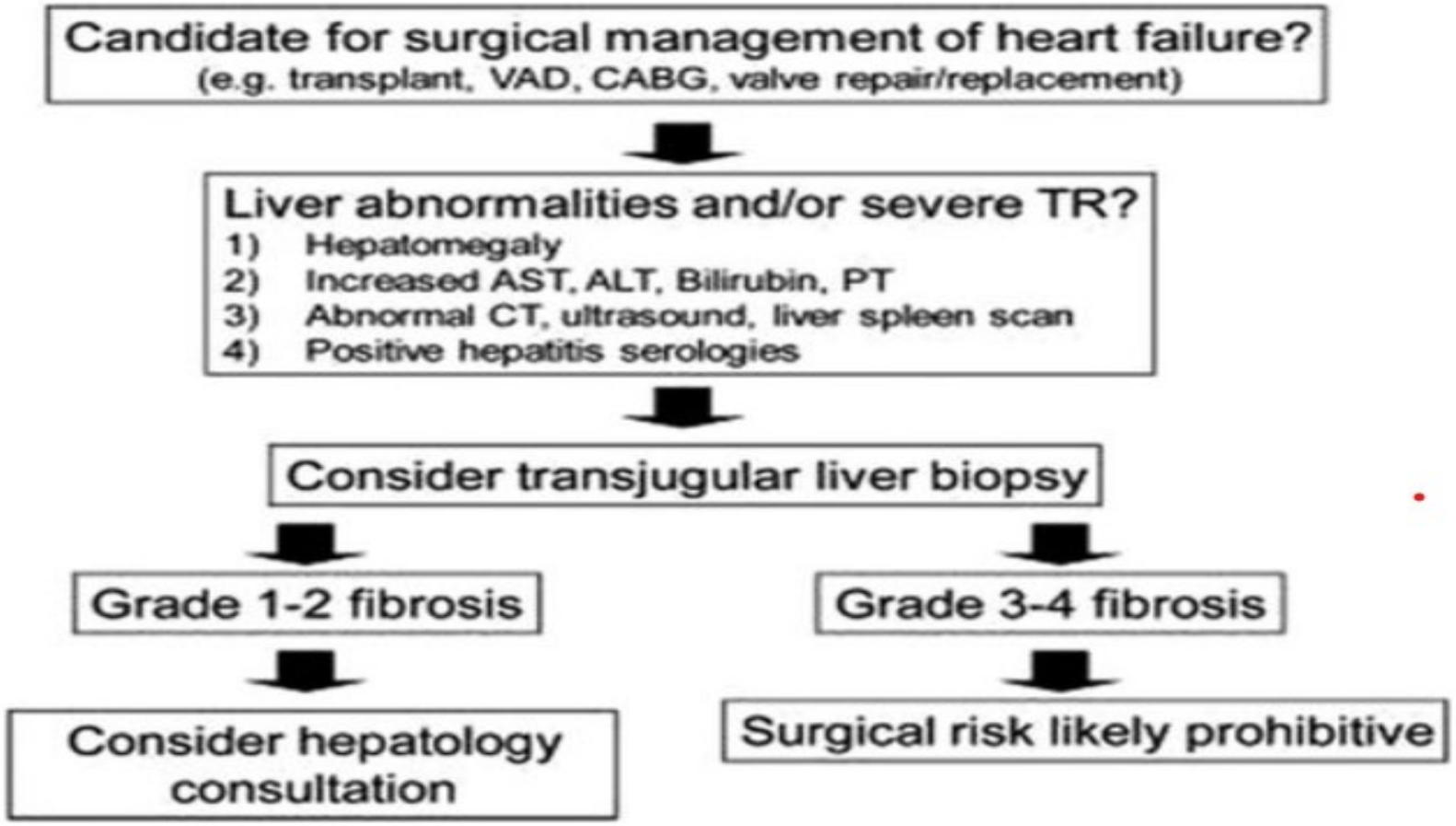
Clinical Manifestations

- Nausea, early satiety, and weight loss may also be present.
- Physical examination findings include hepatic enlargement, ascites, jaundice, and signs of portal hypertension.
- usually asymptomatic
- Chronic passive congestion can also impair hepatic synthetic function, leading to prolonged prothrombin time and hypoalbuminemia low albumin (18.3%), elevated alkaline phosphatase (14.0%), and elevated total bilirubin (13.0%).
- Alanine aminotransferase and aspartate aminotransferase were less commonly abnormal in these patients.

Clinical Manifestations

- Ischemic hepatitis is characterized by rapid increases in serum aminotransferases and lactate dehydrogenase, often to dramatic levels.
- The aminotransferases peak ≈1 to 3 days after the hemodynamic insult and can rise to 250 times the upper limit of normal.
- These laboratory values usually return to normal within 7 to 10 days in the absence of any further hemodynamic insult.
- Serum bilirubin levels rarely rise to >4 times the upper limit of normal, and serum alkaline phosphatase is usually within 2 times the upper limit of normal.
- Ischemic hepatitis generally has a benign and self-limited course, but under rare circumstances, fulminant hepatic failure can occur

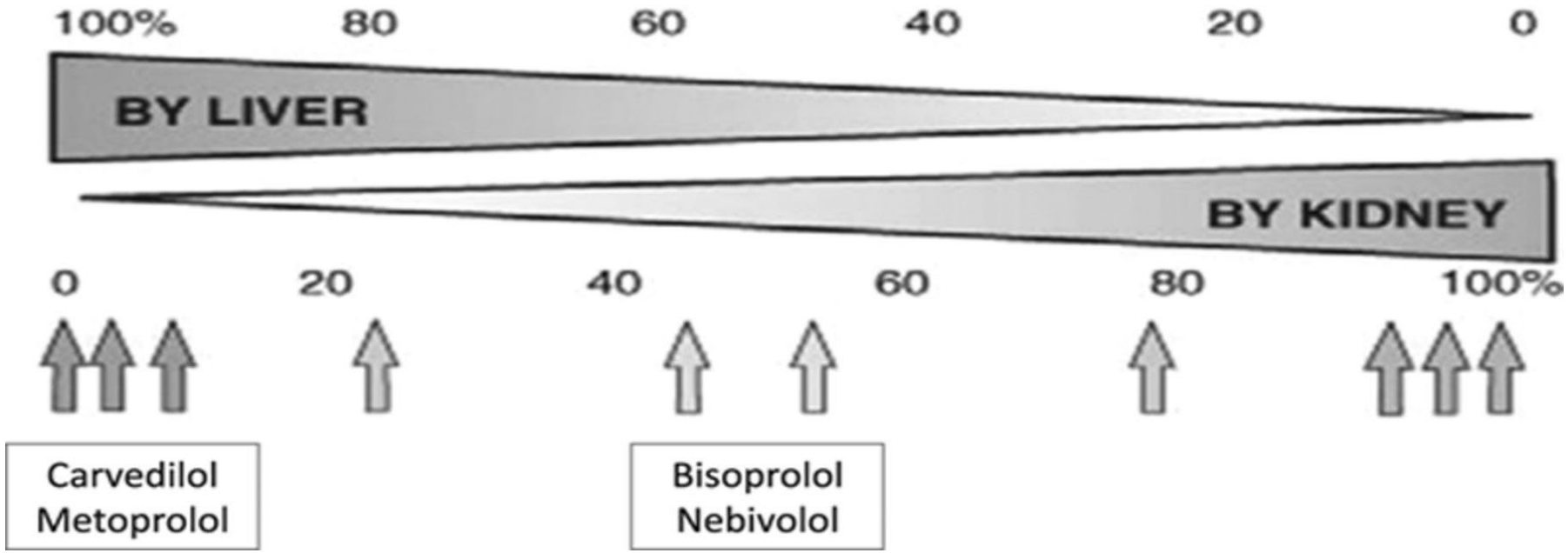
cardiac cirrhosis being considered for advanced heart failure therapies



. Commonly Used HF Drugs That Are Eliminated via the Liver

Drugs	Clearance
β-Blockers	
Carvedilol	Liver
Metoprolol succinate	Liver
Bisoprolol	Liver, kidney
Nebivolol	Liver, kidney
Angiotensin-converting enzyme inhibitors	
Trandolapril	Liver, kidney
Fosinopril	Liver, kidney
Angiotensin receptor blockers	
Losartan	Predominantly liver (90%)
Candesartan	Liver, kidney
Heart failure (HF) drugs (aldosterone antagonists, hydralazine, isosorbide dinitrate, other angiotensin-converting enzyme inhibitors) not mentioned above predominantly have nonhepatic clearance.	

Route of elimination of β-blockers used in heart failure



HF Drugs and Complication

- Calcium blocker
- B blocker
- Vasodilator
- ASA
- anticoagulant

Liver congestion in Liver Fibroscan

Aortic stenosis

- A common valvular disease affecting mainly individuals older than 60 y.
- AS is associated with increased incidence of GI bleeding from angiodysplasia.
- Mechanism of GI bleeding in AS:
- An acquired type 2A Von Willebrand syndrome (reduced levels of high molecular-weight multimers of von Willebrand factor
- Aortic valve replacement lead to increased lever of multimers→ improvement in shear-induced platelet aggregation and adhesion.
- Angiodysplasia treatment: Endoscopic cautery, angiographic embolization, Intestinal resection but they have not been proven as a long term alternative to aortic valve replacement.

