Renal Failure in Cirrhosis

Review Article

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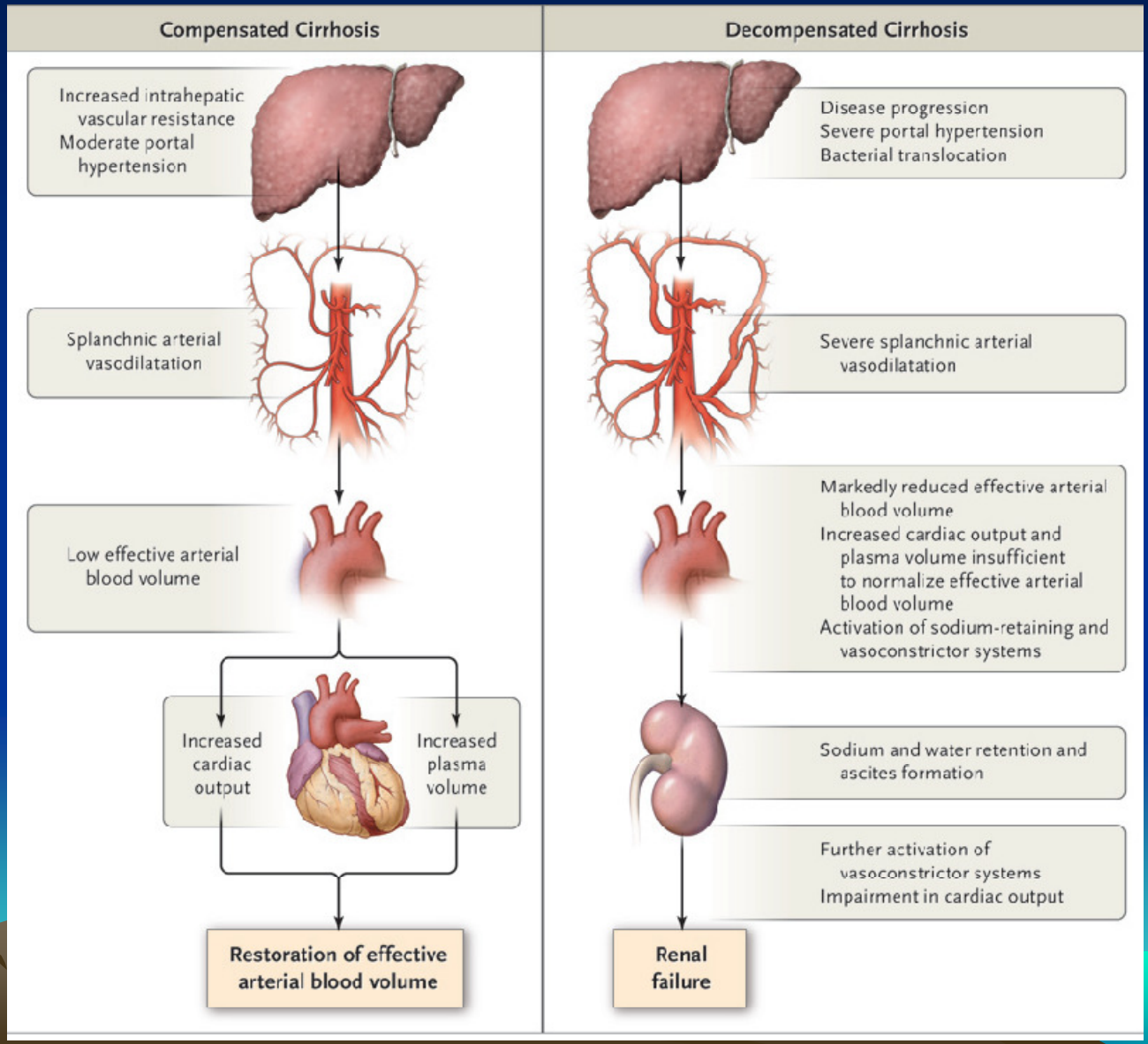
Introduction-1

- Renal failure is a challenging complication of cirrhosis.
- One of the most important risk factors when liver transplantation.
- Patients with cirrhosis and renal failure:
  - ↑risk for death while awaiting transplantation
  - ↑complications and ↓survival rate after transplantation

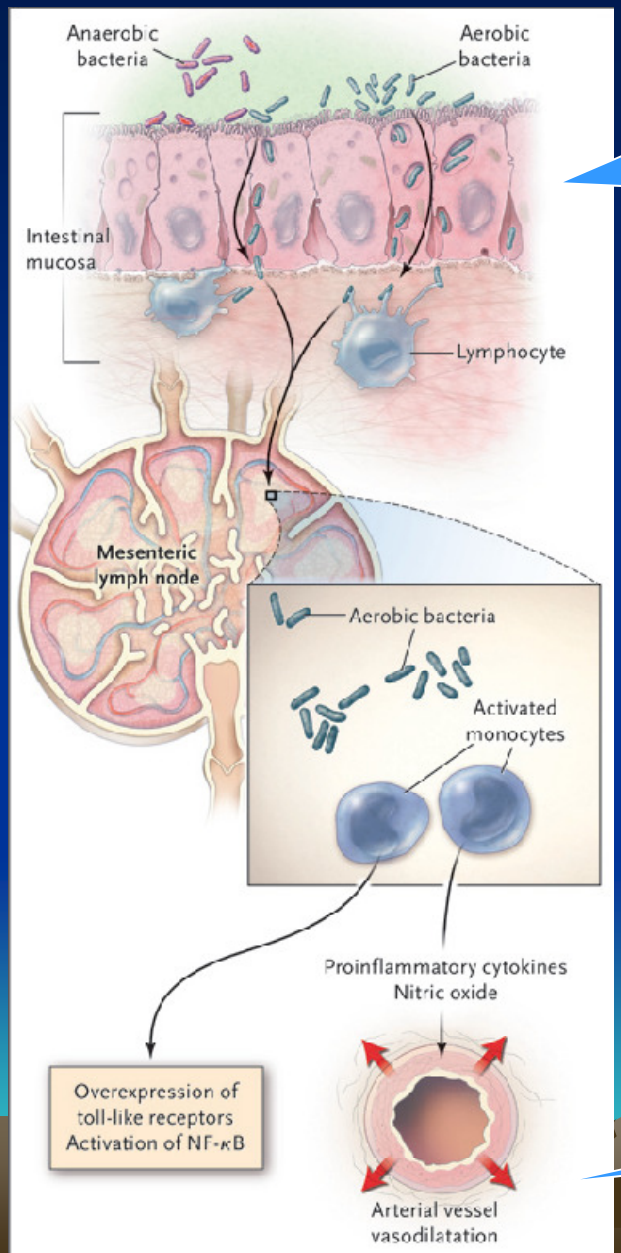
Introduction-2

- In 2002, the Model for End-Stage Liver Disease (MELD) score:
- MELD Score = 0.957 × Loge(creatinine mg/dL) + 0.378 × Loge(bilirubin mg/dL) + 1.120 × Loge (INR) + 0.643。
- ↑No. of patient with renal failure receive a liver transplantation→ ↓mortality
- Pathogenesis and natural history of renal failure in cirrhosis→ prevention and management of this complication

Pathophysiology of Renal Failure



Role of Bacterial Translocation



Risk Factors:
- Intestinal bacterial overgrowth
- Impaired intestinal motility
- Alterations in gut permeability
- Disturbances in local immune systems

In general, anaerobic bacteria do not translocate.

Proinflammatory cytokine: TNF-α, Interlukin-6
Vasodilator factor: nitric oxide (NO)

What event will induce renal failure ?

- Hypovolemia:
  - GI fluid loss: GI bleeding, Diarrhea(lactulose)
  - Excessive diurectics
- Bacterial infection: SBP(GNB translocation)
- Drugs: NSAID
- Intrinsic renal disease: glomerulonephritis
  - Hepatitis B or hepatitis C infection
  - Alcoholic cirrhosis

Evaluation of Patient with Cirrhosis and Renal Failure

Evaluation of renal function

Serum creatinine should be measured daily in patients with acute impairment of renal function; increases of 0.3 to 0.5 mg/dl (27 to 44 μmol/liter) may indicate marked reductions in glomerular filtration rate.

Serum sodium and potassium concentrations should be monitored daily in patients with acute renal failure and monthly or every other month in patients with chronic renal failure; hyponatremia is common; potassium-sparing diuretics should be discontinued to prevent hyperkalemia.

Electrolytes and protein should be measured (preferably in 24-hr urine samples) in all patients with renal failure; significant proteinuria (>500 mg of protein/day) and urine-sediment abnormalities usually indicate parenchymal renal disease.

Renal ultrasonography rules out urinary tract obstruction, but the ultrasonographic appearance of the kidney is normal in most cases of cirrhosis with renal failure; abnormal renal ultrasonograms indicate chronic parenchymal renal disease.

A renal biopsy is helpful when parenchymal renal disease is suspected because of proteinuria, hematuria, or both and is also helpful in deciding on simultaneous kidney transplantation in candidates for liver transplantation; renal biopsy is contraindicated if severe coagulation abnormalities are present; there is little information on the use of transvenous renal biopsy.

Evaluation of Patient with Cirrhosis and Renal Failure

Evaluation of liver function

Liver disease should be evaluated by means of standard liver-function tests and abdominal ultrasonography.

Liver biopsy should be performed if the diagnosis of liver disease is not clear and if biopsy is not contraindicated by the results of clotting studies.

Upper gastrointestinal endoscopy is helpful for detecting gastroesophageal varices; if large varices are present, prophylactic measures should be taken (i.e., beta-blocker therapy, variceal ligation, or both).

Assessment of bacterial infection

Bacterial infection should be ruled out in all patients with acute renal failure or worsening of renal function.

Leukocytosis may be absent owing to hypersplenism in patients with cirrhosis and infection.

In patients with ascites, cell count and culture should be performed to rule out infection of ascitic fluid.

Blood and urine cultures should be carried out even in the absence of obvious signs of infection.

Chest radiography should be performed to rule out lung infection.

GI blood loss: clinical examination, Hb level
Medication: such as diuretics

Differential Diagnosis of Renal Failure in Cirrhosis

Table 2. Main Types of Renal Failure in Patients with Cirrhosis.

Disorder	Comments
Hepatorenal syndrome*	The hepatorenal syndrome is diagnosed on the basis of a serum creatinine concentration of more than 1.5 mg/dl (133 μmol/liter), which is not reduced (to <1.5 mg/dl) with the administration of albumin (1 g/kg of body weight) and after a minimum of 2 days off diuretics, along with the absence of current or recent treatment with potentially nephrotoxic drugs, the absence of shock, and the absence of findings suggestive of parenchymal renal disease (urinary excretion of >500 mg of protein/day, >50 red cells/high-power field, or abnormal kidneys on ultrasonography). The syndrome is classified into two types: type 1 is characterized by a doubling of the serum creatinine level to more than 2.5 mg/dl (221 μmol/liter) in less than 2 weeks; type 2 is characterized by a stable or less rapidly progressive course than in type 1.
Hypovolemia-induced renal failure	Hypovolemia is usually due to hemorrhage (in most cases gastrointestinal bleeding) or to fluid losses — either renal losses because of excessive diuretic therapy or gastrointestinal losses as a result of diarrhea from excessive lactulose administration or gastrointestinal infection. Renal failure occurs soon after the onset of hypovolemia.
Parenchymal renal disease	Parenchymal renal disease should be suspected as a cause of renal failure when proteinuria (>500 mg of protein/day), hematuria (>50 red cells/high-power field), or both are present and ideally should be confirmed by renal biopsy, if this procedure is not contraindicated. The differential diagnosis between acute tubular necrosis and the hepatorenal syndrome remains a difficult issue; the presence of renal tubular epithelial cells in the urine sediment favors the diagnosis of acute tubular necrosis.
Drug-induced renal failure	Current or recent treatment with nonsteroidal antiinflammatory drugs or aminoglycosides suggests drug-induced renal failure.

Management of Renal Failure in Cirrhosis

- Severity and complication of the renal failure.
- Awaiting liver transplantation:
  - Intensive care setting
  - Third-generation cephalosporins for bacterial infection
  - Hydrocortisone for relative adrenal insufficiency
  - Avoid excessive IVF
  - Potassium-sparing diuretics are contraindicated.
  - Repeated large-volume paracenteses and albumin support (8 g/L of ascites removed)

Management of Renal Failure in Cirrhosis

- Treatment of Renal Failure:
  - Early identification and treatment of the cause of the renal failure.
- Management of the Hepatorenal Syndrome:
  - Vasoconstrictor drugs
  - Albumin
  - Other therapies

Specific therapy for Hepatorenal Syndrome

Table 3. Specific Therapies for the Hepatorenal Syndrome in Patients with Cirrhosis.

Therapy	Regimen and Comments
Vasoconstrictor drugs	
Terlipressin*	0.5–1 mg every 4–6 hr intravenously, with an increase up to 2 mg every 4–6 hr until serum creatinine decreases to 1–1.2 mg/dl (88–106 μmol/liter); usual duration of therapy, 5 to 15 days.
Norepinephrine†	0.5–3 mg/hr given as continuous intravenous infusion with the aim of increasing mean arterial pressure by 10 mm Hg; treatment is maintained until serum creatinine decreases to 1–1.2 mg/dl (88–106 μmol/liter).
Midodrine‡	7.5 mg given orally 3 times daily, with an increase to 12.5 mg 3 times daily if needed, in association with octreotide (100 μg given subcutaneously 3 times daily, with an increase to 200 μg 3 times daily if needed).
Albumin§	Intravenous administration of albumin together with vasoconstrictor drugs (1 g of albumin/kg of body weight on day 1, followed by 20–40 g/day).
Other therapies	Transjugular intrahepatic portosystemic shunts may be effective in selected patients, but available data are very limited. Renal-replacement therapy should be considered in patients who do not have a response to vasoconstrictor drugs.

Prognosis for Patient with Cirrhosis and Renal Failure

- Poor prognosis.
- Overall survival rate:
  - ~50% at 1 month
  - ~20% at 6 months
- Survival rates:
  - Differ according to the type of renal failure
  - Hepatorenal Syndrome: the worst prognosis
- Type1 vs. Type 2 Hepatorenal Syndrome:
  - Median survival: 1 month vs. 6 months

Prevention

- Risk of Hepatorenal Syndrome:
  - Cirrhosis with SBP
  - Albumin IV (1.5 g/kg of BW at diagnosis and 1.0 g/kg of BW 48 hours later)
  - Oral Norfloxacin (400 mg/day)
  - Adequate diuretics
  - Correct hypovolemia (ex: GI bleeding)
  - Avoid NSAID and Aminoglycosides

What time Norfloxacin will be prescribed?

- Ascitic Fluid TP<15g/L
- Impairment of liver function, renal function, or both:
  - Bilirubin>3 mg/dL
  - Child–Pugh score>10
  - Serum Na<130 mmol/L
  - Serum Cr> 1.2 mg/dL

Renal Failure and Liver Transplantation

- High mortality in cirrhosis and renal failure, particularly with Type 1 HRS
- Liver Transplantation: ASAP
- Severe renal failure: poor outcome after transplantation
- MELD score give higher priority to liver-transplant.

Effects of MELD score

- Patient survival:
  - MELD vs. Pre-MELD period:
  - 3-year Survival Rate: 74.7% vs. 73.1%
- Renal function:
  - No increased incidence of acute or chronic kidney dysfunction after LT.
  - No increased need for HD after LT

Effects of MELD score

- Combined Liver & Kidney transplantation:
  - MELD non-available vs. MELD available:
  - Incidence: 2.6% vs. **4.4%↑**
- Indication: reversible renal failure
- Predictive factor:
  - Presence of sustained renal failure before transplant
  - Duration of renal–replacement therapy (>8~12weeks)
- 1-year Survival Rate of combined L-KT vs. LT: 82% vs. 81.8%

Summary

- Renal failure:
  - Very common and severe complication in patients with decompensated cirrhosis.
  - A risk factor for a poor outcome of liver transplantation.
- Prevention and Management of the Hepatorenal Syndrome
- Use of these therapies in patients awaiting liver transplantation may help improve the outcome after transplantation.

Thanks for your attention