TREATMENT OF ASCITES

DESIRED OUTCOME

- Clinical improvement or resolution of acute complications, such as variceal bleeding, and resolution of hemodynamic instability for an episode of acute variceal hemorrhage.

- Prevention of complications, achieving adequate lowering of portal pressure with medical therapy using β-adrenergic blocker therapy, or supporting abstinence from alcohol.

- Identify and eliminate the causes of cirrhosis (e.g., alcohol abuse).

- Assess the risk for variceal bleeding and begin pharmacologic prophylaxis where indicated, reserving endoscopic therapy for high-risk patients or acute bleeding episodes.

- The patient should be evaluated for clinical signs of ascites and managed with pharmacologic treatment (e.g., diuretics) and paracentesis.

- HE is a common complication of cirrhosis and requires clinical vigilance and treatment with dietary restriction, elimination of CNS depressants, and therapy to lower ammonia levels.

- Frequent monitoring for signs of hepatorenal syndrome, pulmonary insufficiency, and endocrine dysfunction is necessary.

Criteria and Scoring for the Child-Pugh Grading of Chronic Liver Disease

Score	1	2	3
Bilirubin (mg/dL)	1–2	2–3	>3
Albumin (mg/dL)	>3.5	2.8–3.5	<2.8
Ascites	None	Mild	Moderate
Encephalopathy (grade)	None	1 and 2	3 and 4
Prothrombin time (sec prolonged)	1–4	4–6	>6

MANAGEMENT OF PORTAL HYPERTENSION AND VARICEAL BLEEDING:

- The management of varices involves three strategies:
- (1) primary prophylaxis to prevent rebleeding,
- (2) treatment of variceal hemorrhage, and
- (3) secondary prophylaxis to prevent rebleeding in patients who have already bled.

Primary Prophylaxis

- The mainstay of primary prophylaxis is the use of nonselective β –adrenergic blocking agents such as propranolol or nadolol.

- These agents reduce portal pressure by reducing portal venous inflow.

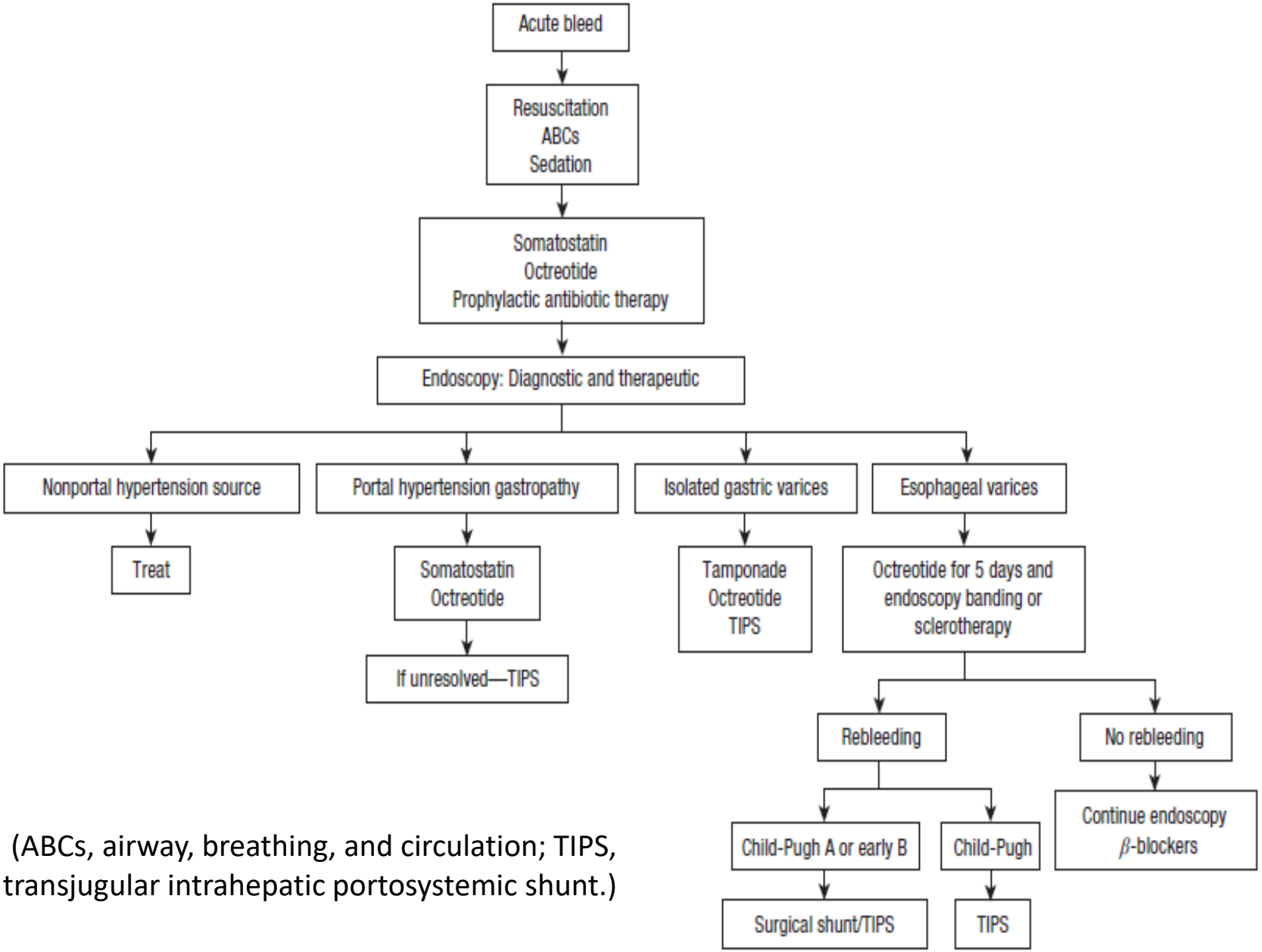
- B -Adrenergic blocker therapy should be continued for life, unless it is not tolerated, because bleeding can occur when therapy is abruptly discontinued.

- All patients with cirrhosis and portal hypertension should be considered for endoscopic screening, and patients with large varices should receive primary prophylaxis with β -adrenergic blockers.

- Therapy should be initiated with propranolol, 10 mg three times daily, or nadolol, 20 mg once daily, and titrated to a reduction in resting heart rate of 20% to 25%, an absolute heart rate of 55 to 60 beats/min, or the development of adverse effects.

- There is insufficient evidence to recommend nitrates in addition to β - adrenergic blockers to further lower portal pressure.

Management of acute variceal hemorrhage



(ABCs, airway, breathing, and circulation; TIPS, transjugular intrahepatic portosystemic shunt.)

Prevention of Rebleeding:

- In patients without contraindications, β-adrenergic blocking agents should be the initial step in prevention of rebleeding, along with endoscopic band ligation (EBL).

- Use of a long-acting β-adrenergic blocker (such as nadolol) is usually recommended to improve compliance, and gradual, individualized dose escalation may help to minimize side effects.

- Propranolol may be given at 20 mg three times daily (or nadolol, 20 to 40 mg once daily) and titrated weekly to achieve a goal of heart rate 55 to 60 beats/min or a heart rate that is 25% lower than the baseline heart rate.

- For patients who fail to achieve sufficient reductions in portal pressure with β-blocker therapy alone, combination therapy with isosorbide mononitrate may more effectively lower portal pressures.

ASCITES:

- The treatment of ascites secondary to portal hypertension includes abstinence from alcohol, sodium restriction, and diuretics. Sodium chloride should be restricted to 2 g/day.

- Diuretic therapy should be initiated with single morning doses of spironolactone, 100 mg, and furosemide, 40 mg, with a goal of 0.5-kg maximum daily weight loss.

- The dose of each can be increased together, maintaining the 100:40 mg ratio, to a maximum daily dose of 400 mg spironolactone and 160 mg furosemide.

- If tense ascites is present, a 4- to 6-L paracentesis should be performed prior to institution of diuretic therapy and salt restriction.

- Patients who experience encephalopathy, severe hyponatremia despite fluid restriction, or renal insufficiency should have diuretic therapy discontinued.

- Liver transplantation should be considered in patients with refractory ascites.

SPONTANEOUS BACTERIAL PERITONITIS:

- Antibiotic therapy for prevention of SBP should be considered in all patients who are at high risk for this complication (those who experience a prior episode of SBP or variceal hemorrhage, and those with low-protein ascites).

- Patients with documented or suspected SBP should receive broad-spectrum antibiotic therapy to cover Escherichia coli, Klebsiella pneumoniae, and Streptococcus pneumoniae.

- Cefotaxime, 2 g every 8 hours, or a similar third-generation cephalosporin is considered the drug of choice.

- Oral ofloxacin , 400 mg every 12 hours, is equivalent to IV cefotaxime.

Hepatic Encephalopathy:

✓ Treatment approaches include:

(1) reduction of blood ammonia concentrations by dietary restrictions, and drug therapy aimed at inhibiting ammonia production or enhancing its removal (lactulose and antibiotics) and

(2) Inhibition of γ -aminobutyric acid–benzodiazepine receptors by flumazenil.

✓ Approaches to reducing blood ammonia concentrations include: In patients with acute HE, limit protein intake to 10 to 20 g/day while maintaining the total caloric intake.

✓ Protein intake can be titrated by increasing 10 to 20 g/day every 3 to 5 days to a total of 0.8 to 1 g/kg/day. With chronic HE, restrict protein intake to 40 g/day.

- In episodic HE, lactulose is initiated at 45 mL every hour (or 300 mL lactulose syrup with 700 mL water given as a retention enema) until catharsis begins.

- The dose is then decreased to 15 to 30 mL orally every 8 to 12 hours and titrated to produce two to three soft, acidic stools per day.

- Antibiotic therapy with metronidazole or neomycin is reserved for patients who have not responded to diet and lactulose.

- Zinc acetate supplementation (220 mg twice daily) is recommended for long-term management in patients with cirrhosis who are zinc deficient.

Management Approach and Outcome Assessments

Complication	Treatment Approach	Monitoring Parameter	Outcome Assessment
Ascites	Diet, diuretics, paracentesis, TIPS	Daily assessment of weight	Prevent or eliminate ascites and its secondary complications
Spontaneous bacterial peritonitis	Antibiotic therapy, prophylaxis if undergoing paracentesis	Evidence of clinical deterioration (e.g., abdominal pain, fever, anorexia, malaise, fatigue)	Prevent/treat infection to decrease mortality
Variceal bleeding	Pharmacologic prophylaxis	Child-Pugh score, endoscopy, CBC	Appropriate reduction in heart rate and portal pressure
	Endoscopy, vasoactive drug therapy (octreotide), sclerotherapy, volume resuscitation, pharmacologic prophylaxis	CBC, evidence of overt bleeding	Acute: control acute bleed. Chronic: variceal obliteration, reduce portal pressures
Coagulation disorders	Blood products (PPF, platelets), vitamin K	CBC, prothrombin time, platelet count	Normalize PT, maintain/improve hemostasis
Hepatic encephalopathy	Ammonia reduction (lactulose, cathartics), elimination of drugs causing CNS depression, limit excess protein in diet	Grade of encephalopathy, EEG, psychological testing, mental status changes, concurrent drug therapy	Maintain functional capacity, prevent hospitalization for encephalopathy, decrease ammonia levels, provide adequate nutrition
Hepatorenal syndrome	Eliminate concurrent nephrotoxins (NSAIDs), decrease or discontinue diuretics, volume resuscitation, liver transplantation	Serum and urine electrolytes, concurrent drug therapy	Prevent progressive renal injury by preventing dehydration and avoiding other nephrotoxins Liver transplantation for refractory hepatorenal syndrome
Hepatopulmonary syndrome	Paracentesis, O_2 therapy	Dyspnea, presence of ascites	Acute: relief of dyspnea and hypoxia. Chronic: manage ascites as above

PPF, plasma protein fraction