Anesthesia for Liver Disease & Transplantation

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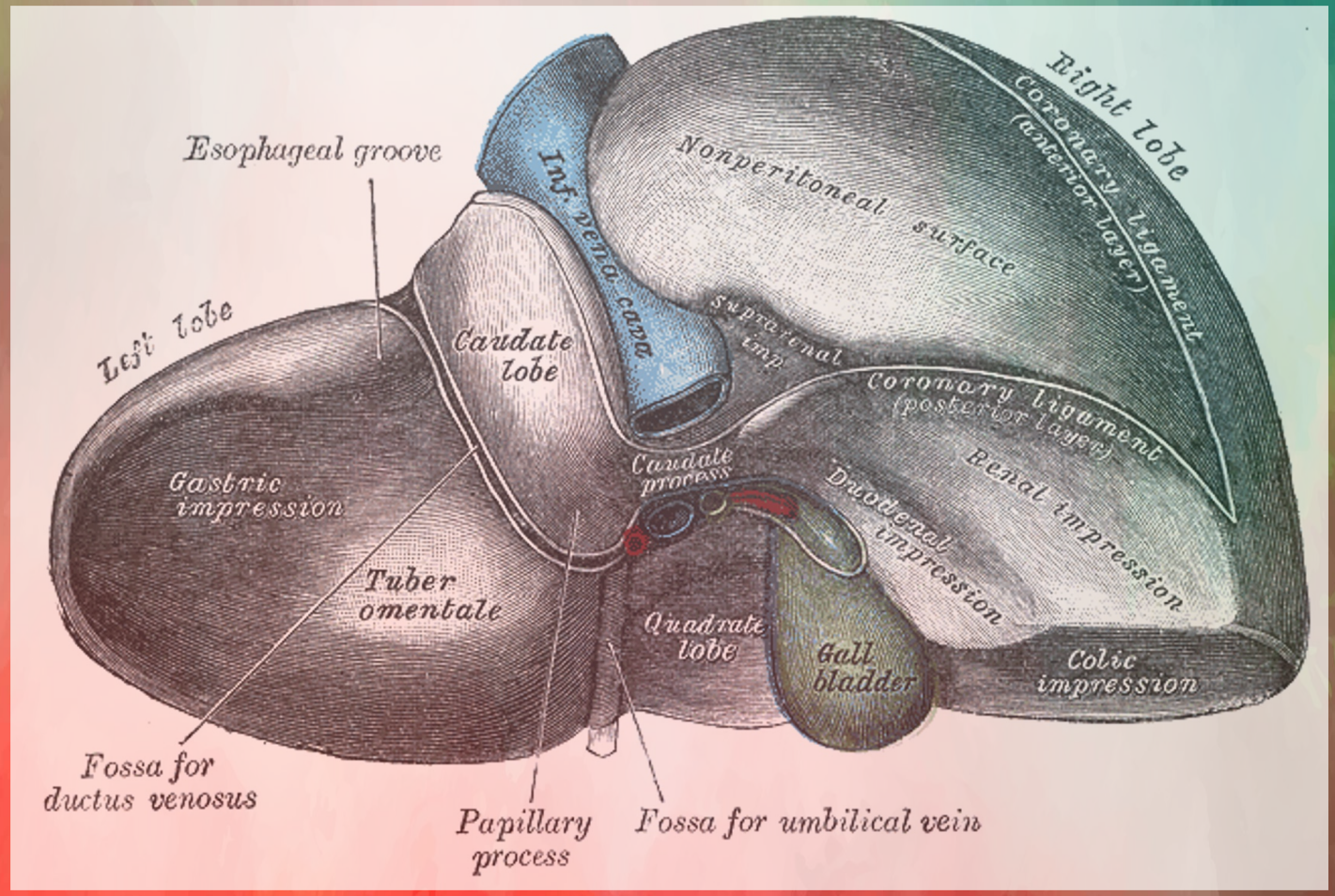
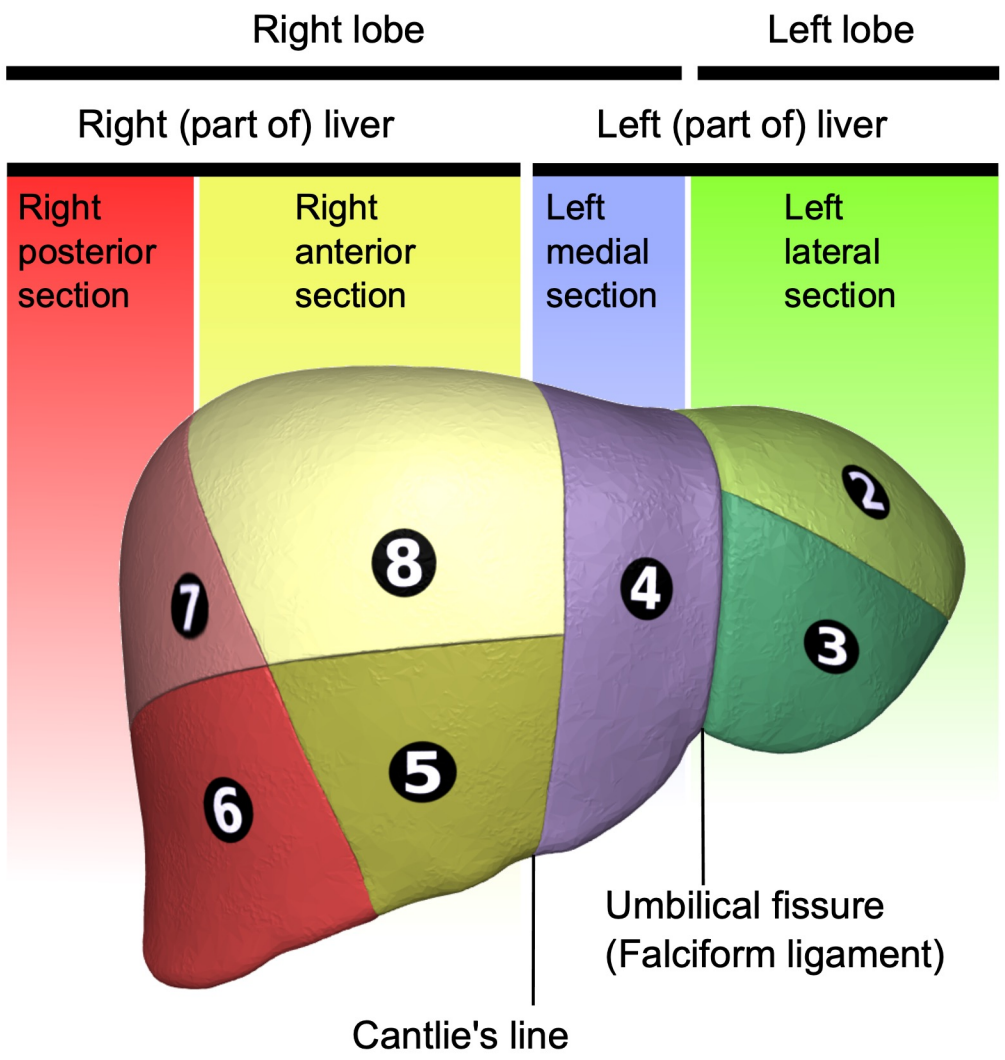
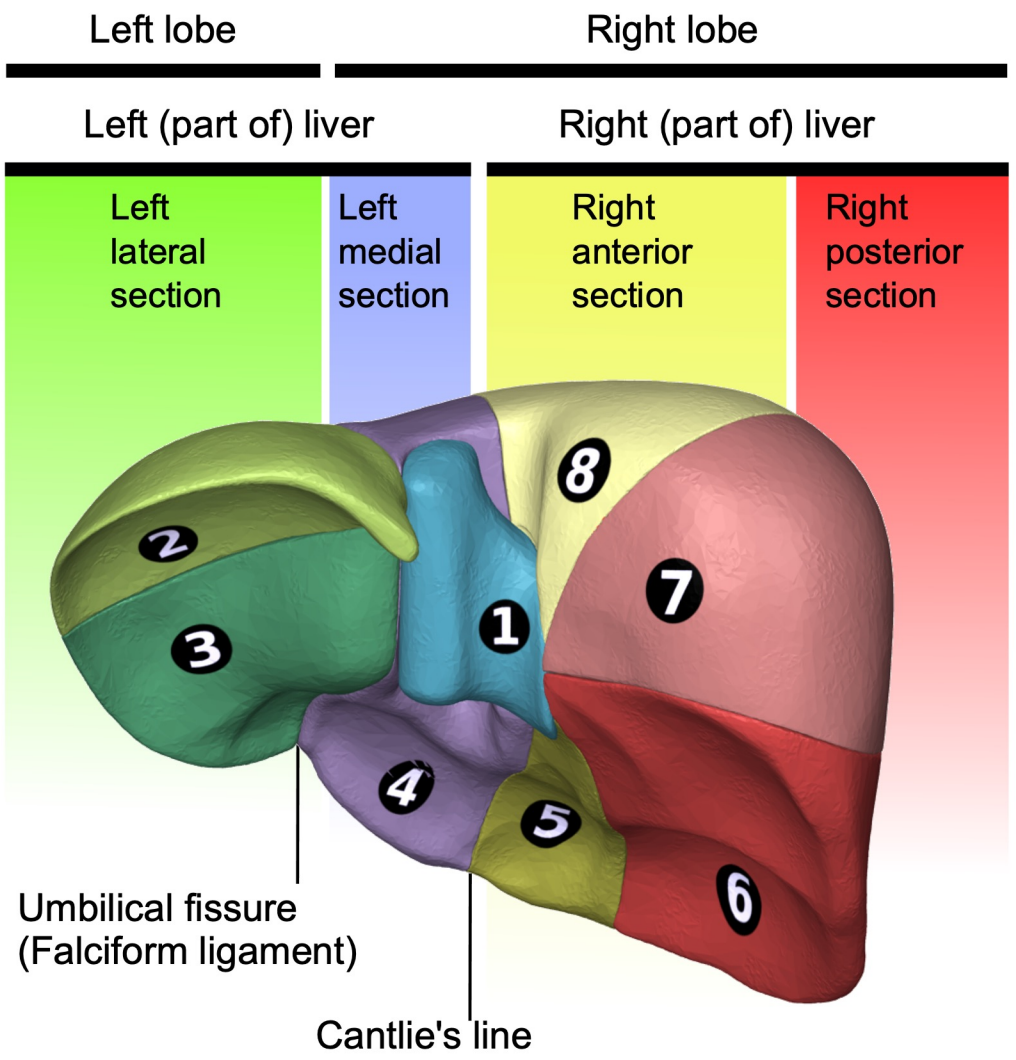


Objectives

- **Anatomy & Physiology**
- Liver Disease
- High Yield Concepts
- Anesthetic Considerations
- Liver Transplant



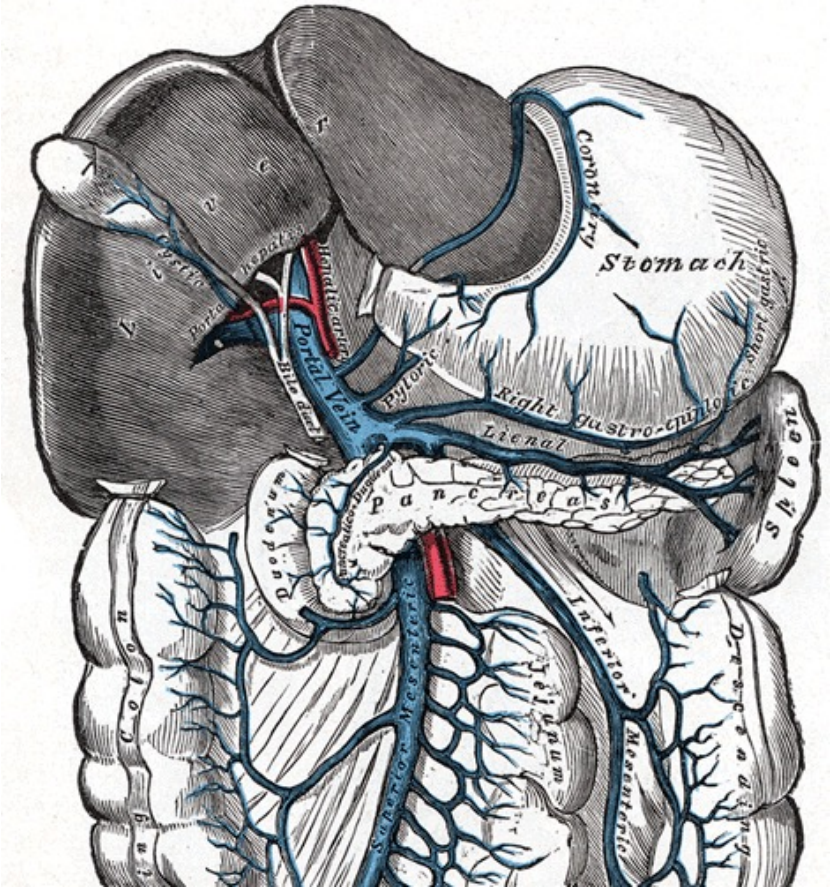
Anterior view



Posterior view

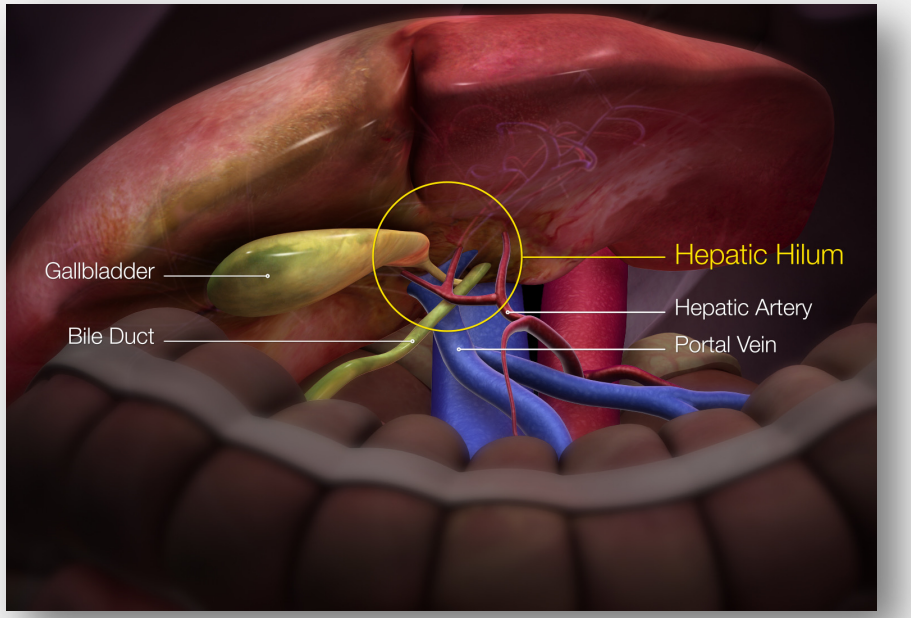
Blood Supply & Regulation

- 25% of resting cardiac output
  - Hepatic artery:
    - 25% of total hepatic blood flow | 50% oxygen supply
    - Arises from celiac trunk (80%) or SMA (20%)
  - Portal vein:
    - 75% of total hepatic blood flow | 50% oxygen supply
    - Confluence of SMA, IMV, splenic vein
- Hepatic Veins
  - Right, middle, and left – drain into IVC



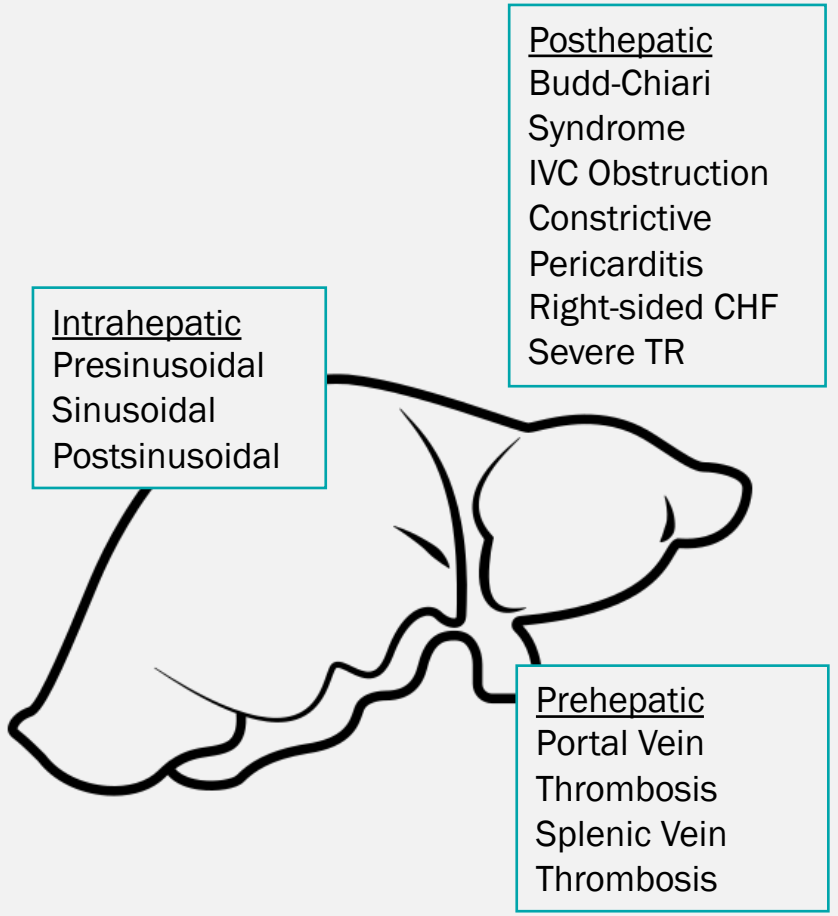
Hepatic Blood Flow Regulation

- Hepatic Arterial Buffer Response
  - Modulates blood flow through the hepatic artery in response to reduction in portal flow
  - Mediated by ADENOSINE
  - Affected by acidosis, hypoxemia, and hypercarbia
- Attenuated by volatile anesthetics and cirrhosis
  - Increased ischemic vulnerability



Hepatic Blood Flow Regulation

- Hepatic Perfusion Pressure (HPP)
  - MAP or Portal Vein Pressure – Hepatic Vein Pressure
- Splanchnic Vascular Resistance (innervated by SNS)
  - Increased by pain, hypoxemia, surgical stress, operative proximity
- Hepatic Vein Pressure is increased by increased CVP
  - PPV, CHF, Fluid Overload = decreased HPP



Hepatic Synthetic Function

- Normal adult liver produces 12 – 15g of protein a day
  - Albumin:
    - drug binding | oncotic pressure
  - Alpha$_1$-acid glycoprotein:
    - binds basic drugs | acute phase reactant
  - Pseudocholinesterase:
    - degrades succinylcholine, mivacurium, and ester local anesthetics
  - All proteinaceous clotting factors except FVIII
- Additional:
  - glucose regulation | cholesterol formation hematopoiesis | bile formation | protein degradation steroid hormone degradation | drug metabolism

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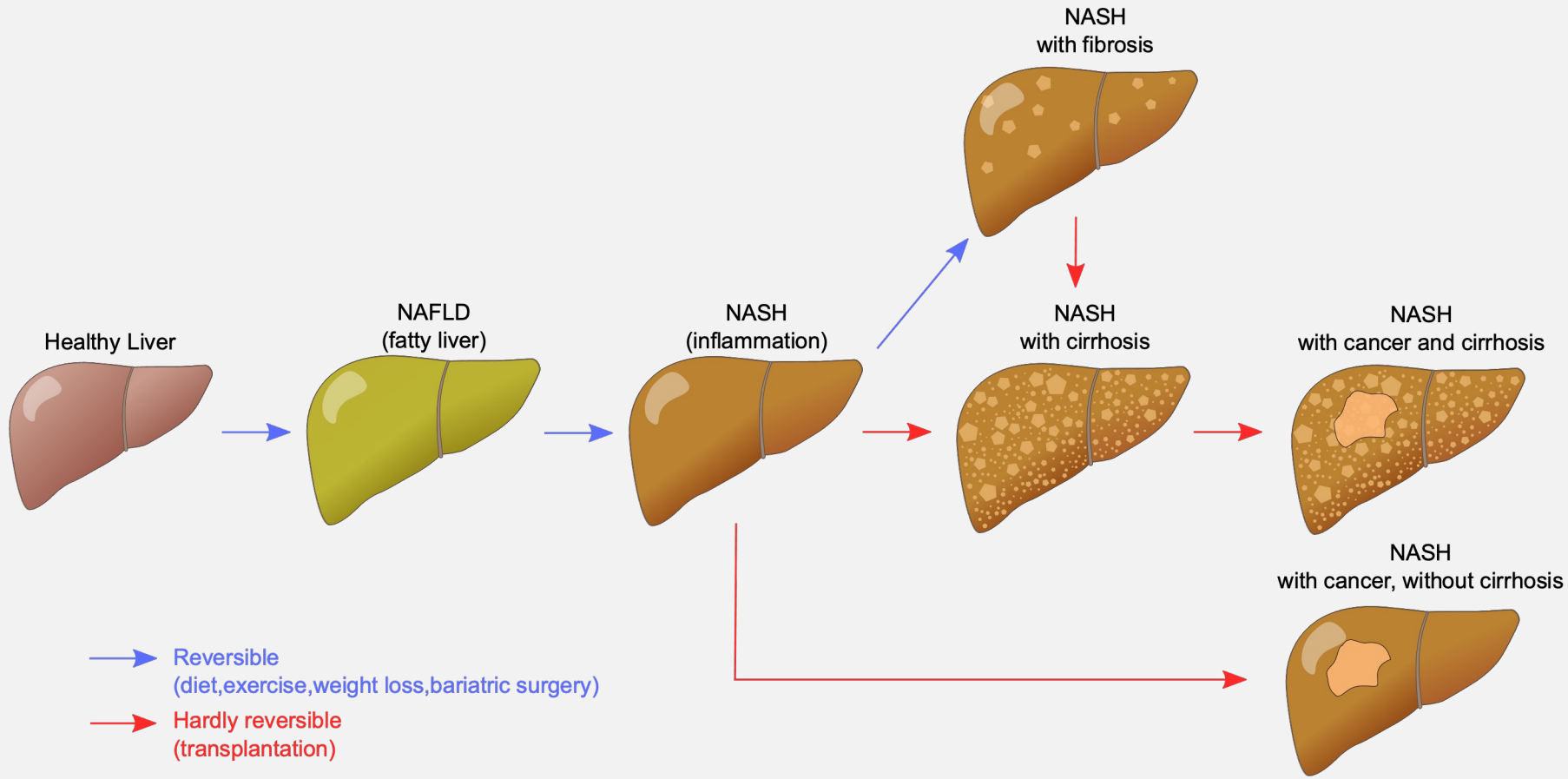
Preoperative Assessment



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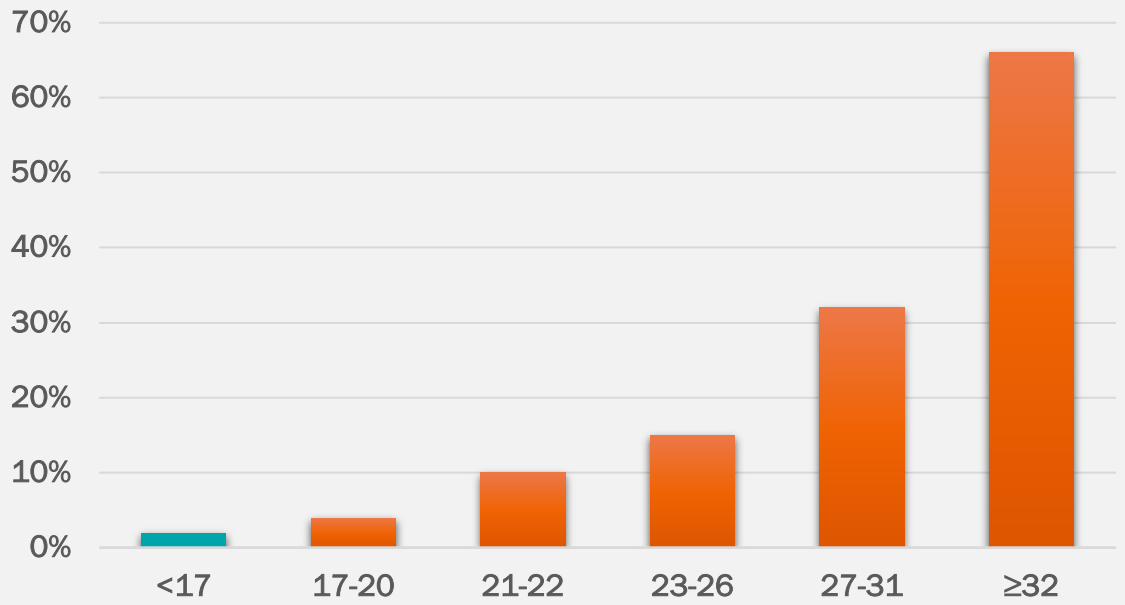
Prognostication

Modified Child-Pugh Score

	1	2	3
Albumin (g/dL)	>3.5	2.8 – 3.5	<2.8
Bilirubin (mg/dL)	<2.0	2.0 – 3.0	>3.0
Ascites	Absent	Slight	Moderate
Encephalopathy	Absent	Grades I & II	Grades III & IV
PT prolongation (s)	<4.0	4.0 – 6.0	>6.0
Class A: 5 – 6 points			
Class B: 7 – 9 points			
Class C: 10 – 15 points			

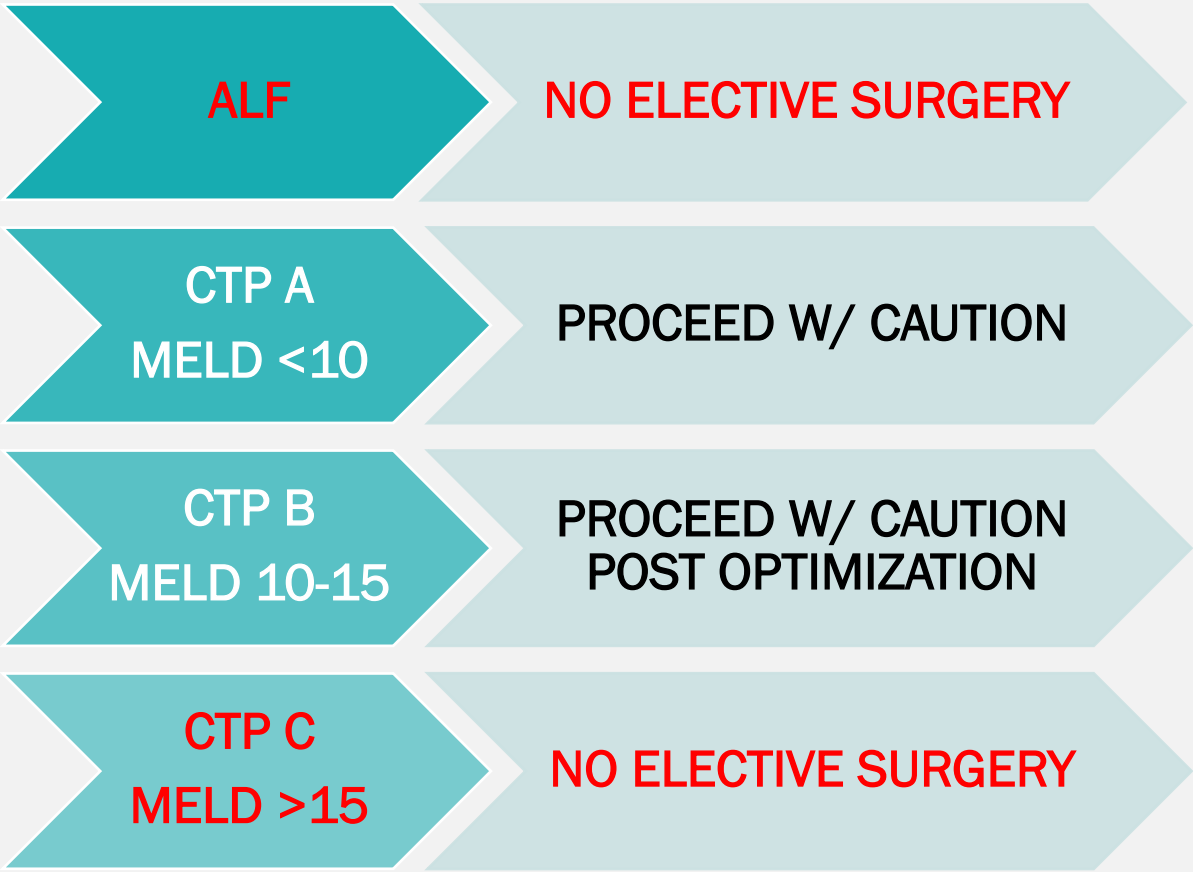
MELD-Na 3-month mortality



MELD = 3.78[Ln Serum Bilirubin (mg/dL)] + 11.2[Ln INR] + 9.57[Ln Serum Creatinine (mg/dL)] + 6.43
MELD-Na = MELD − Na − (0.025 × MELD × (140 − Na)) + 140

Elective Surgery

- Contraindications
  - Acute alcoholic hepatitis
  - Acute liver failure
  - Child-Pugh class C cirrhosis
  - Severe chronic hepatitis
  - Severe coagulopathy
  - Severe extrahepatic complications
    - Acute renal failure
    - Cardiomyopathy, heart failure
    - Hypoxemia



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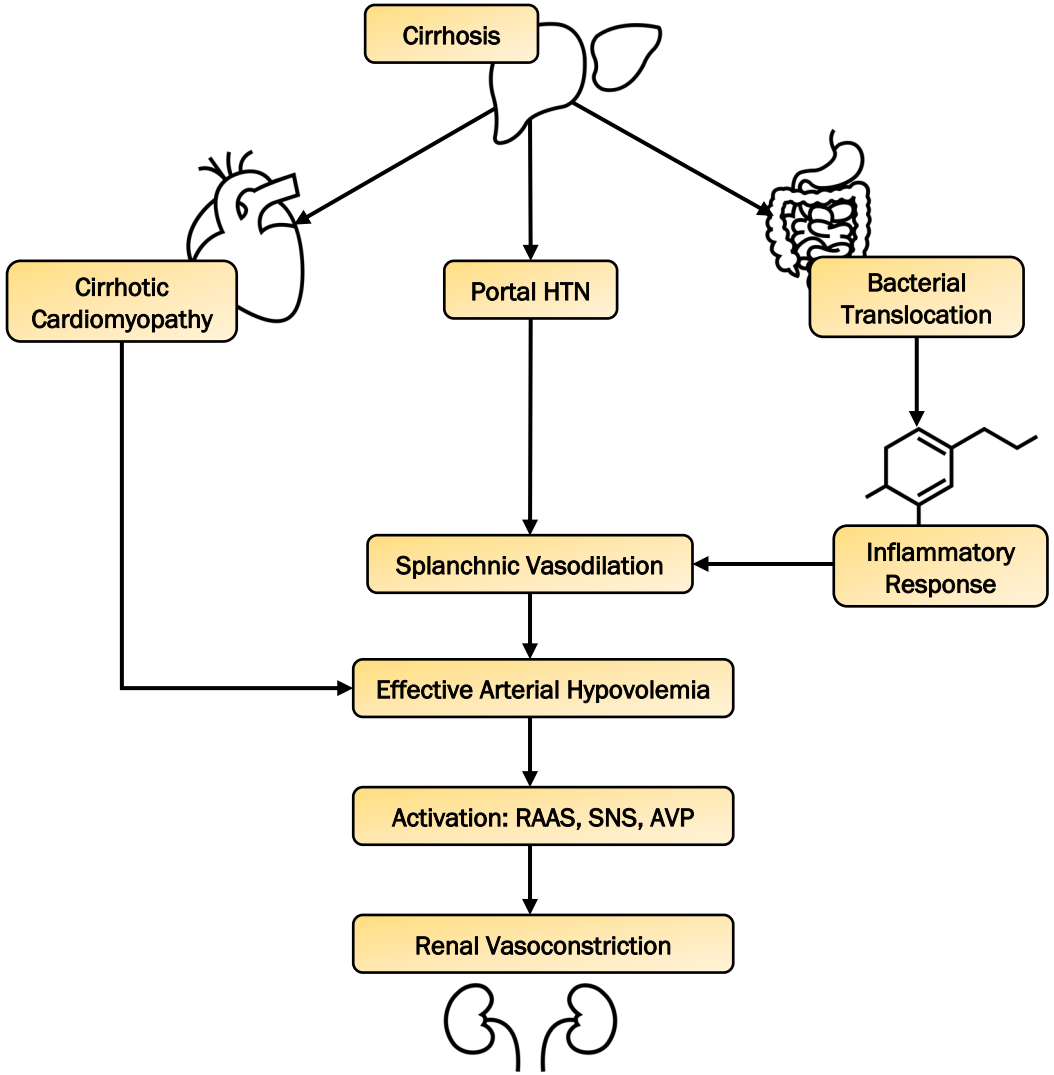
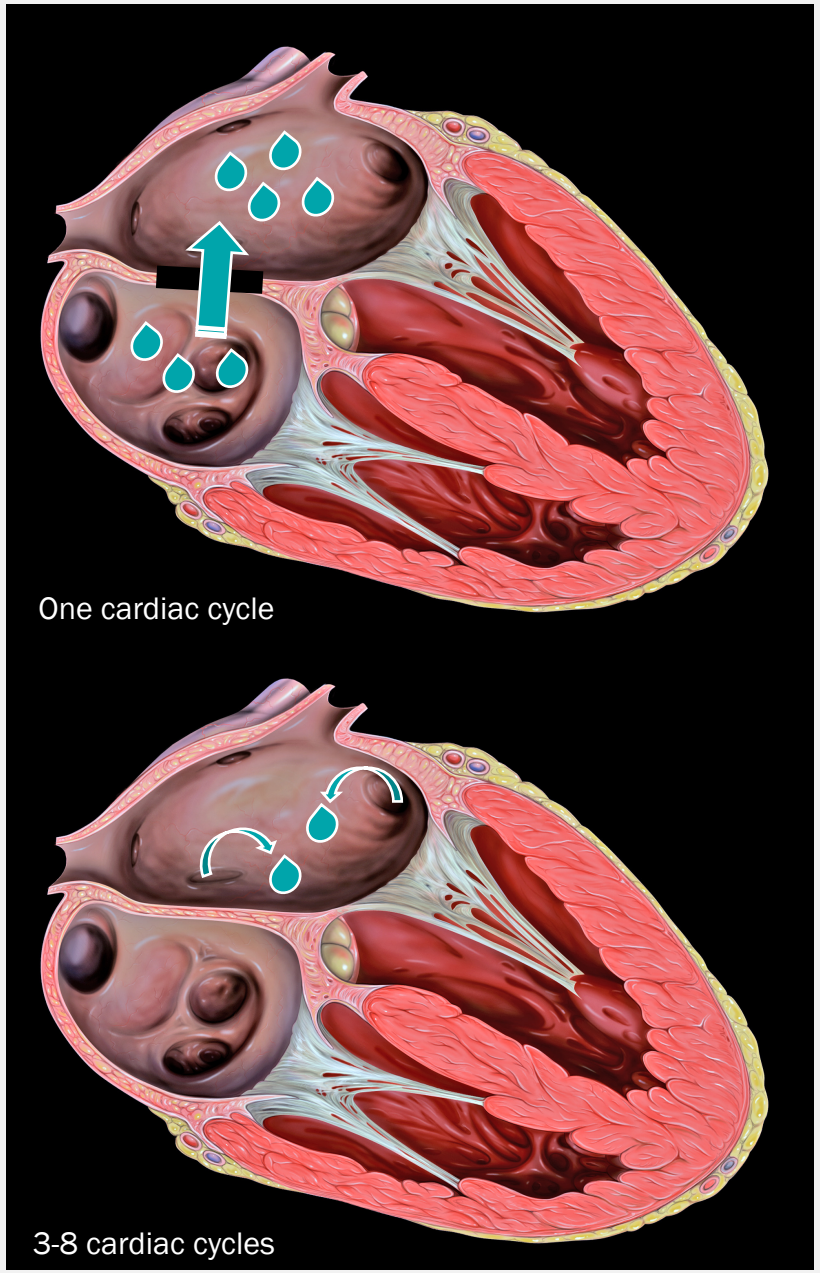
Hepatorenal Syndrome

- Diagnosis of exclusion
- Poor prognosis
- Type 1 HRS aka HRS-AKI
- Type 2 HRS aka HRS-CKD
- ICU: norepinephrine + albumin +/- vasopressin
- Non-ICU: albumin + terlipressin or midodrine + octreotide
- TIPS, RRT as bridge



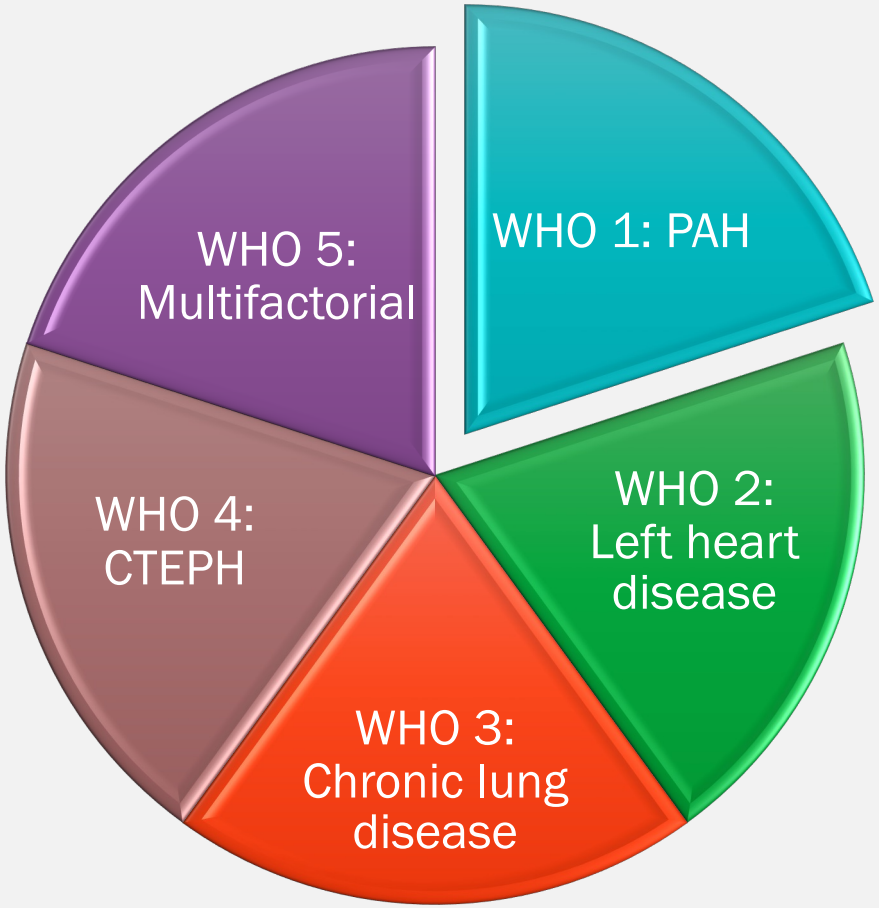


Hepatopulmonary Syndrome

- Triad
  - Liver disease and/or portal hypertension
  - A-a gradient ≥ 15 mmHg on room air with PaO2 < 80 mmHg
  - Intrapulmonary vascular dilatations (IPVD) | Intrapulmonary shunt
- Platypnea
  - Upright: increase in dyspnea
  - Recumbent: decrease in dyspnea
- Orthodeoxia:
  - Upright: decrease in PaO2
  - Recumbent: increase in PaO2

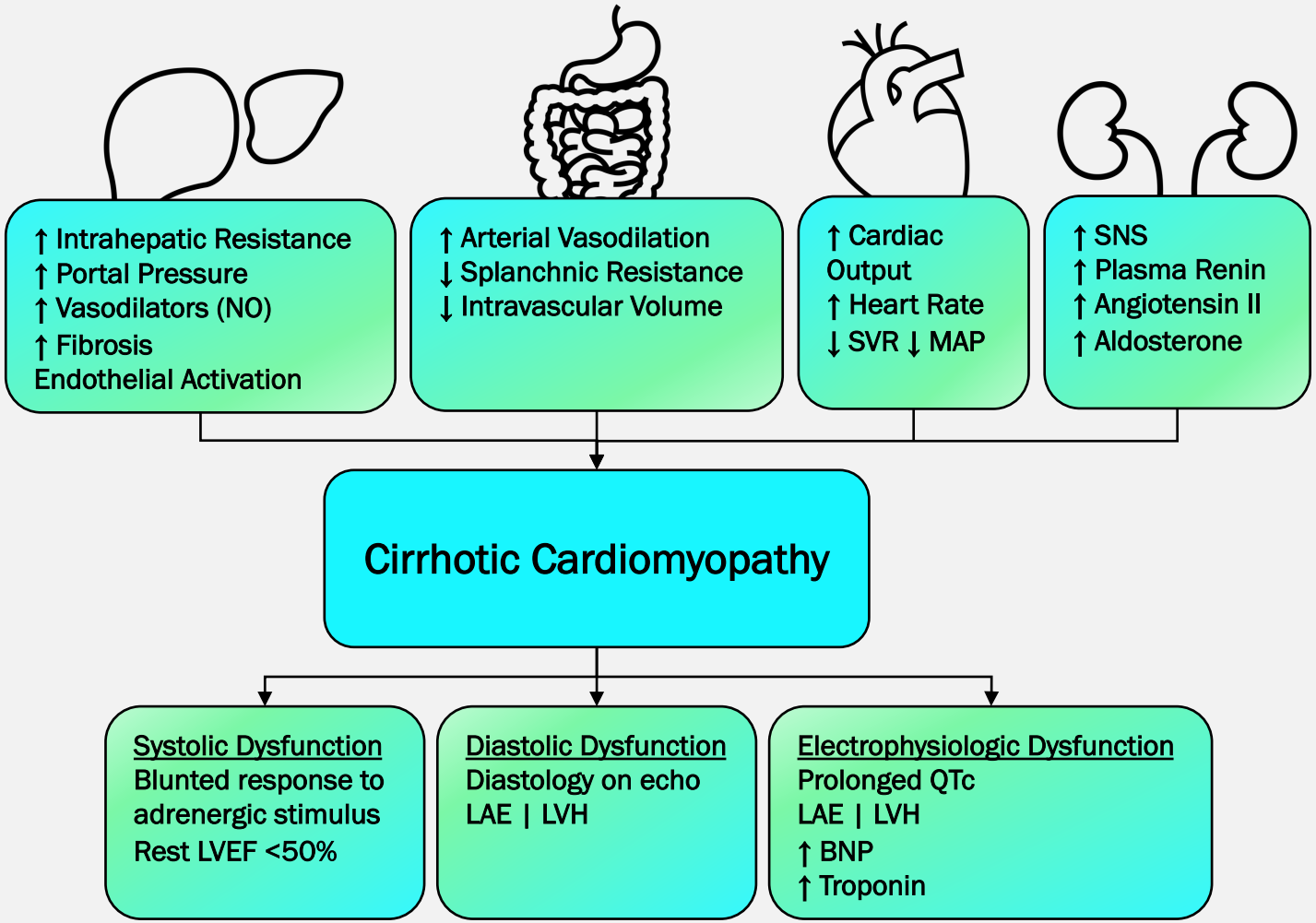
Portopulmonary Hypertension

- mPAP ≥ 25 mmHg + portal hypertension = portopulmonary hypertension (POPH)
- mPAP ≥ 35 mmHg is a predictor of increased mortality following LT
- Screening: TTE, RVSP good estimate in diagnosing mod-severe PPHTN in absence of pulmonary stenosis
- Confirmation: RHC is the gold standard
  - Indicated if RVSP ≥ 45 mmHg per AASLD
- RHC: confirm PVR ≥ 240-dynes sec cm^{-5} m^2 and PCWP ≤ 15 mmHg
- Exclude other causes of pulmonary hypertension



Cirrhotic Cardiomyopathy

- Mimics hyperdynamic changes in sepsis
  - Tachycardia
  - Increased cardiac output
  - Hypotension
  - Low SVR
- Decreased clearance of NO, CO, and endogenous cannabinoids
- Splanchnic dilation from bacterial translocation
- Portosystemic shunt: increased venous capacitance
- Impaired systolic & diastolic dysfunction
- Resistance to B-adrenergic stimulation
- QTc prolongation



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Anesthetics: Liver Disease

- ✅ Propofol
  - Metabolism: ~50% hepatic
  - Elimination: 88% renal
  - Termination: redistribution
  - Protein binding: 97 – 99%
- ✅ Etomidate
  - Metabolism: hepatic | plasma esterases
  - Elimination: ~75% renal
  - Termination: redistribution
  - Protein binding: 76%
  - Helpful in ALI to maintain CPP
- ⚠️ Ketamine
  - Metabolism: hepatic
  - Norketamine: 30% activity of parent drug
  - Elimination: renal 91%
  - Protein binding: 27%
- ⚠️ Barbiturates
  - Metabolism: hepatic
  - Hypoalbuminemia: ↑ free fraction = ↑ potency
- ⚠️ Dexmedetomidine
  - Metabolism: hepatic
  - Elimination: renal
  - Protein binding: 94%

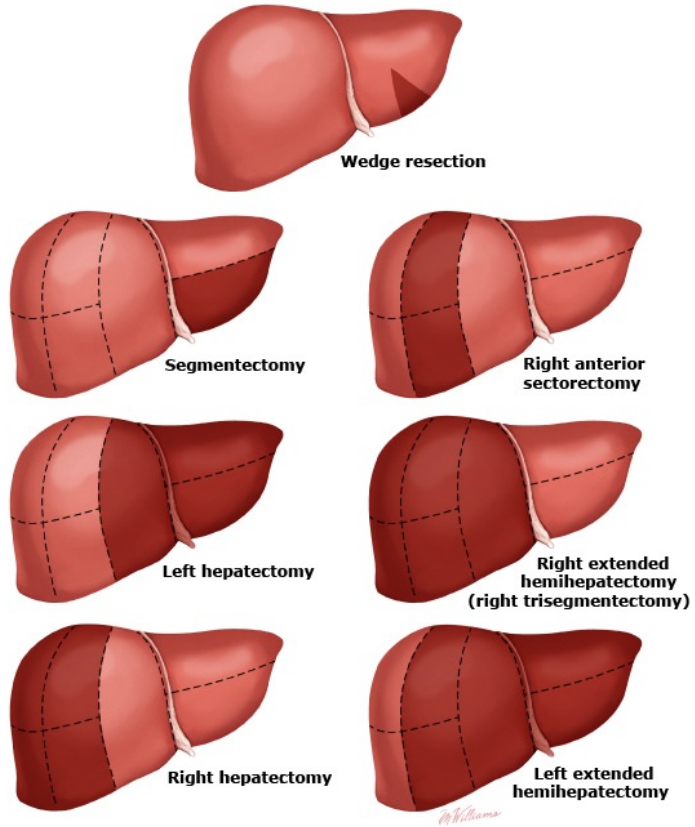
Anesthetics: Liver Disease

- ⚠️ Benzodiazepines & Opioids
  - Metabolism: hepatic
  - Hypoalbuminemia: ↑ free fraction = ↑ potency
  - 🌟 Remifentanil cleared by nonspecific plasma esterases
  - ❌ Morphine | ⚠️ Fentanyl | ⚠️ Hydromorphone
- ✅ Volatiles
  - Preferred: eliminated primarily through respiratory system
- ⚠️ Regional anesthesia:
  - Coagulopathy | Thrombocytopenia
- ⚠️ Acetaminophen: max dose 2g in 24 hours
- ❌ NSAIDS

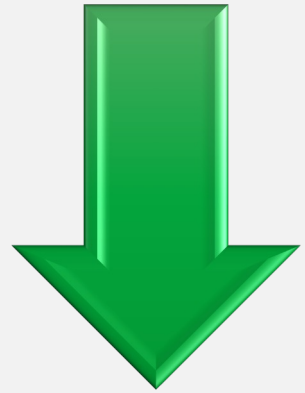
- Neuromuscular blocking agents
  - ↑ resistance due to ↑ volume of distribution
  - ↓ elimination
  - ⚠️ Vecuronium:
    - Metabolism: 30-40% hepatic
    - Elimination: 40% renal
  - ⚠️ Rocuronium:
    - Metabolism: minimal hepatic
    - Elimination: 30 – 40% renal
  - ✅ ⚠️ Succinylcholine: pseudocholinesterase
  - ✅ Cisatracurium/Atracurium:
    - Metabolism: 70 – 90% Hofmann elimination
    - Elimination: 10 – 30% renal

Hemodynamic Management

- Balance hepatic perfusion and blood loss reduction
- Decrease portal pressure with restrictive fluid therapy to minimize bleeding
- Volume expansion with albumin
- May require higher doses of vasopressors to maintain BP
- Surgical techniques to decrease blood loss
    - Total hepatic vascular exclusion | Pringle maneuver
      low CVP anesthesia | venovenous bypass
- Consider thoracic epidural if liver resection ≤20-30%
    - Risk for epidural hematoma and delayed removal due to postoperative coagulopathy



Hemostasis

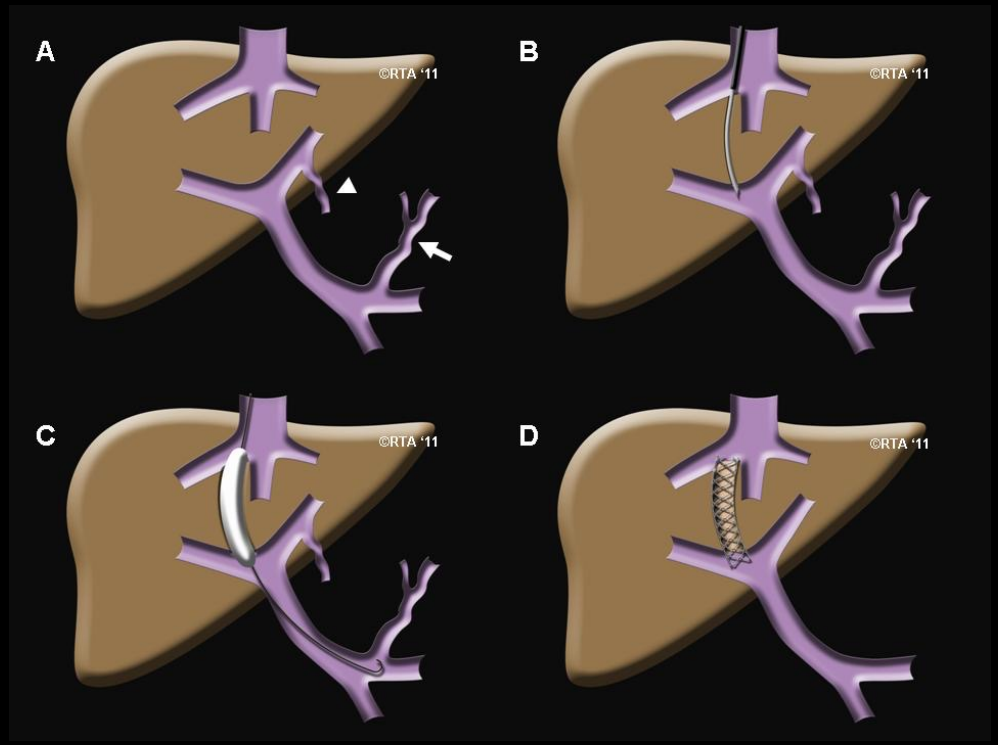


Thrombocytopenia
Decreased thrombopoietin synthesis
Decreased FII, V, VII, IX, X, and XI
Vitamin K deficiency
Dysfibrinogenemia
Increased tPA

Increased VWF
Decreased ADAMTS13
Increased FVIII
Decreased Protein C&S
Decreased ATIII
Inherited thrombophilia
Decreased plasminogen

TIPS

- Decompress portal system in patients with decompensated portal HTN
- Target portosystemic gradient <12 mmHg
- LVP prior to tips: albumin 6 – 8 g/L if >5L drain
- GETA or MAC (usually need RSI)
- Massive ascites – increased risk for aspiration and/or inability to lie flat
- Variceal bleeding may necessitate resuscitation
- Large volume paracentesis may necessitate albumin
- Intraprocedure complications
    - Vascular injury, hemorrhage, pneumothorax, and dysrhythmias
- Delayed complications: encephalopathy and/or heart failure
    - Increased preload may unmask cardiac dysfunction or pulmonary hypertension



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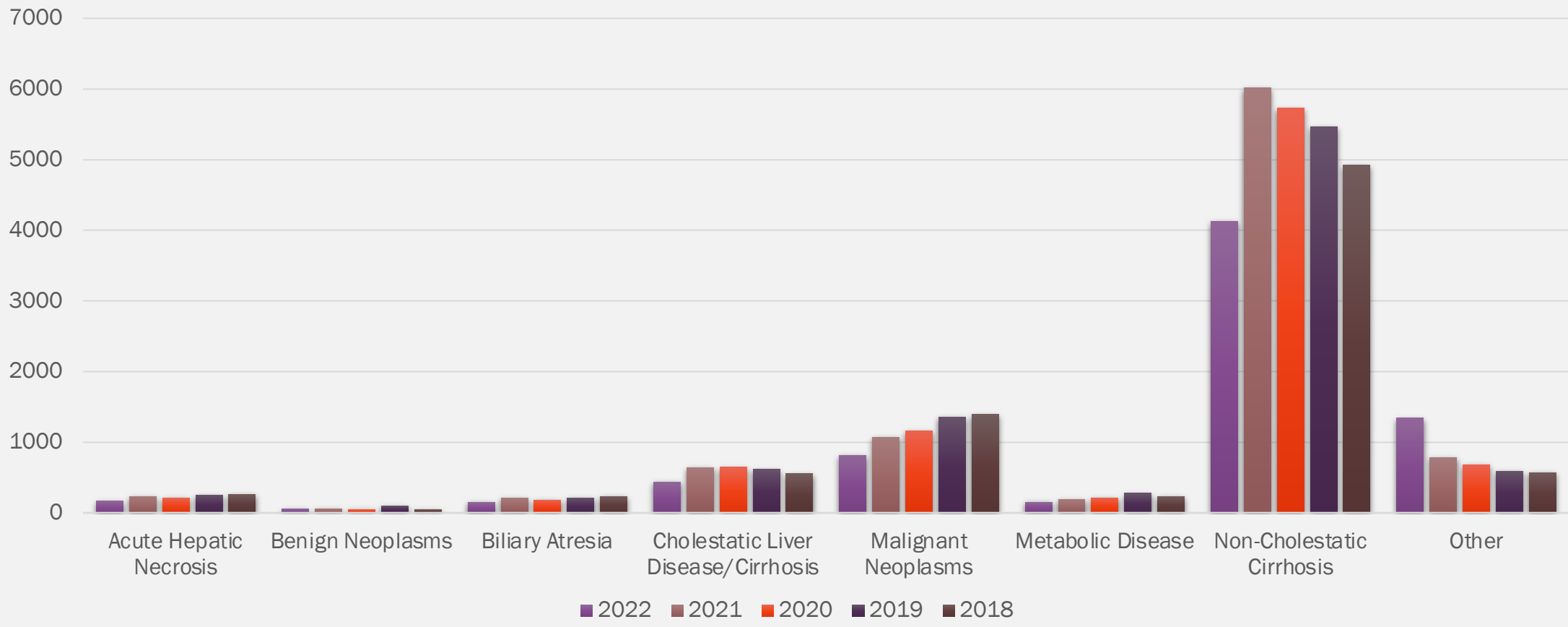
Liver Transplant Indications



Liver Transplant Contraindications

- Uncorrectable cardiopulmonary disease
- Severe pulmonary HTN, mPAP > 35 unresponsive to vasodilator therapy
- Acquired immunodeficiency syndrome (AIDS)
- Malignancy outside of the liver not meeting oncologic criteria for cure
- Hepatocellular carcinoma with metastatic spread
- Intrahepatic cholangiocarcinoma
- Hemangiosarcoma
- Uncontrolled sepsis
- Anatomic abnormalities that preclude liver transplantation
- Acute liver failure with a sustained ICP >50 mmHg or a CPP <40 mmHg
- Persistent nonadherence with medical care / lack of adequate social support
- **Relative:** >65 (comorbidity dependent)
- **Relative:** HIV +/- HCV co-infection
- **Relative:** High BMI with metabolic syndrome
    - Gastric sleeve with liver transplant

Preoperative Evaluation

- Extensive workup
  - Labs | cardiopulmonary evaluation |cancer screening | infectious disease | psychosocial evaluation
- LT presents a major challenge to the cardiovascular system
- Perioperative MI, HF and arrhythmias are leading causes of mortality after LT
- Increase in NAFLD/NASH as etiology for cirrhosis, even higher risk for CAD
- Cardiac evaluation needs to include assessment of cardiac risk factors with stress echocardiography as an initial screening test with cardiac catheterization as clinically indicated (1-B)
- Cardiac revascularization should be considered in LT candidates with significant coronary artery stenosis prior to transplant (2-C)

Graft Options

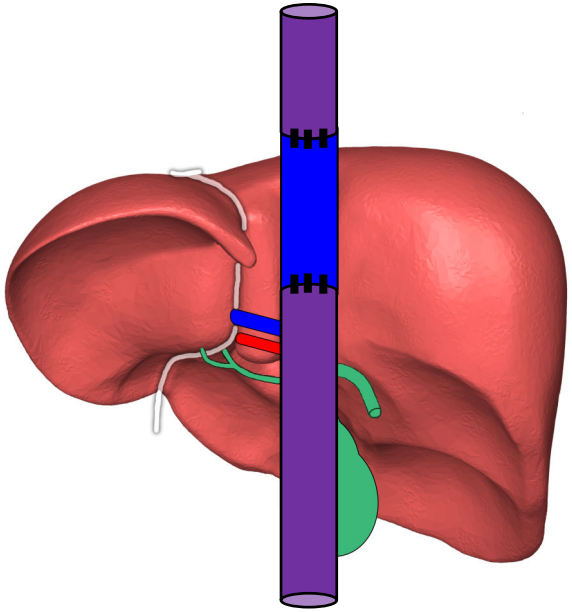
Deceased Donor

- DCD or brain death
- DCD fastest growing source of transplant organs
- Generally classified as emergent or urgent
- Recipients are older, sicker, and have multiple co-morbidities
- Expanded donor pool with marginal donors and increasing donor age

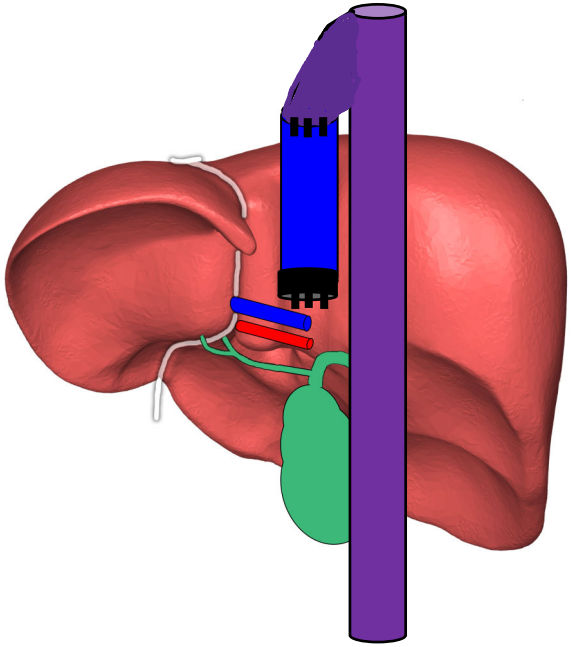
Living Donor

- Donor liver can regenerate in 2-3 weeks
    - 84-92% of original volume by 6 months
- Elective operations for chronic liver disease, occasionally performed emergently in ALF
- Adult-to-Adult LDLT: usually right hepatectomy
    - Technically more challenging, higher perioperative risk
- Donor hepatectomy can be any combination of open, laparoscopic, or robotic
- Hepatic vein reconstruction to maximize venous outflow

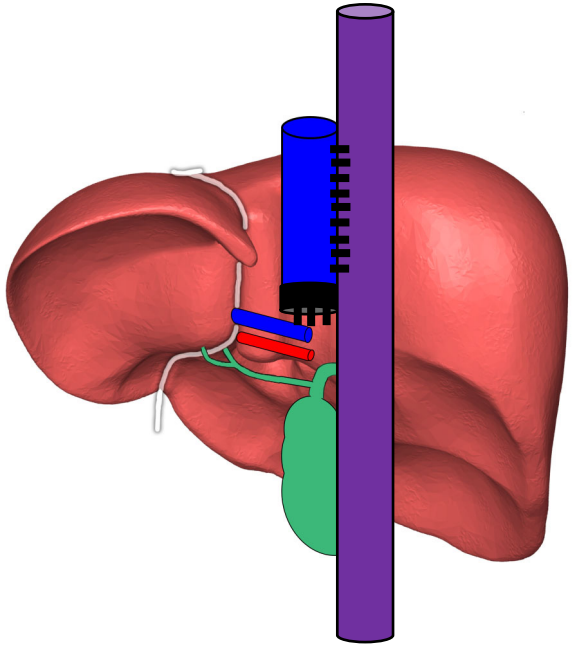
Surgical Technique



Intercaval Connection



Piggyback Technique



Cavo-Caval Anastomosis

Recipient IVC

Donor IVC

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Surgical Stages

- Pre-anhepatic phase
  - Skin incision to clamping of IVC, PV, and HA
  - Significant bleeding can occur
- Anhepatic phase
  - Hepatic inflow clamped until graft reperfusion
  - IVC clamped: decreased cardiac output
- Neo-hepatic phase
  - Moment of liver reperfusion
  - Resumption of flow in PV and IVC
  - Complicated by post-reperfusion syndrome (PRS) and bleeding from vascular anastomoses

Pre-Anhepatic Phase

- Can have massive bleeding
  - Portal hypertension and portosystemic venous shunts, previous surgeries, SBP, redo LT
- Drainage of ascites can cause hemodynamic instability
- Colloid resuscitation is needed to avoid hypovolemia during anhepatic phase
- Early octreotide infusion reduces portal venous pressures, improves renal function and decreases total RBCs transfused
- Concern for dilutional coagulopathy, thrombocytopenia – viscoelastic testing recommended
- Correct hypothermia, acidosis, hypocalcemia, keep K < 4 mEq/L
- Treat hyperfibrinolysis – consider fibrinogen, platelets and recombinant activated Factor 7
- Goal: optimize volume status – balance between fluid perfusion and vasopressors to prepare for IVC clamping
- Veno-venous bypass if clinically warranted

Anhepatic Phase

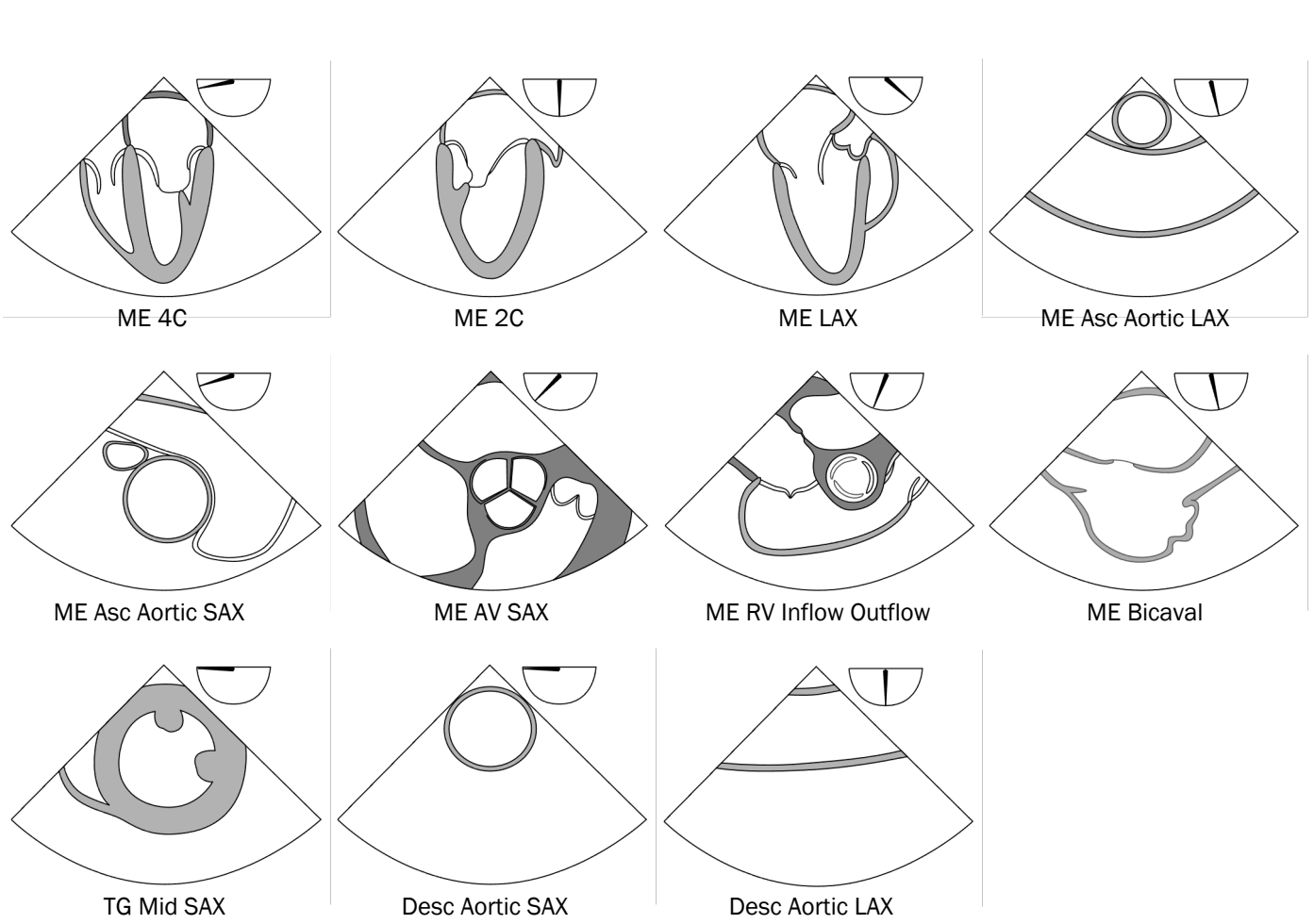
- Most challenging part – hepatic outflow obstructed and IVC may be clamped - decrease in preload, CO, and arterial pressures
- Extensive collaterals may contribute to cardiovascular stability
- Some may require surgical portosystemic shunt or portosystemic veno-venous bypass
- Total loss of liver function: acidotic, hypocalcemia (no lactate or citrate metabolism), hyperkalemia
- Methylprednisolone 500 – 1000 mg IV
- Normalize potassium and calcium
- Judicious fluid resuscitation – will lead to RV failure and graft congestion during reperfusion
- Minimal bleeding during this phase
- Coagulopathy severity correlates with duration of anhepatic phase – viscoelastic testing
- Accumulation of tPA and other anticoagulant factors – will be metabolized with reperfusion

Neohepatic Phase

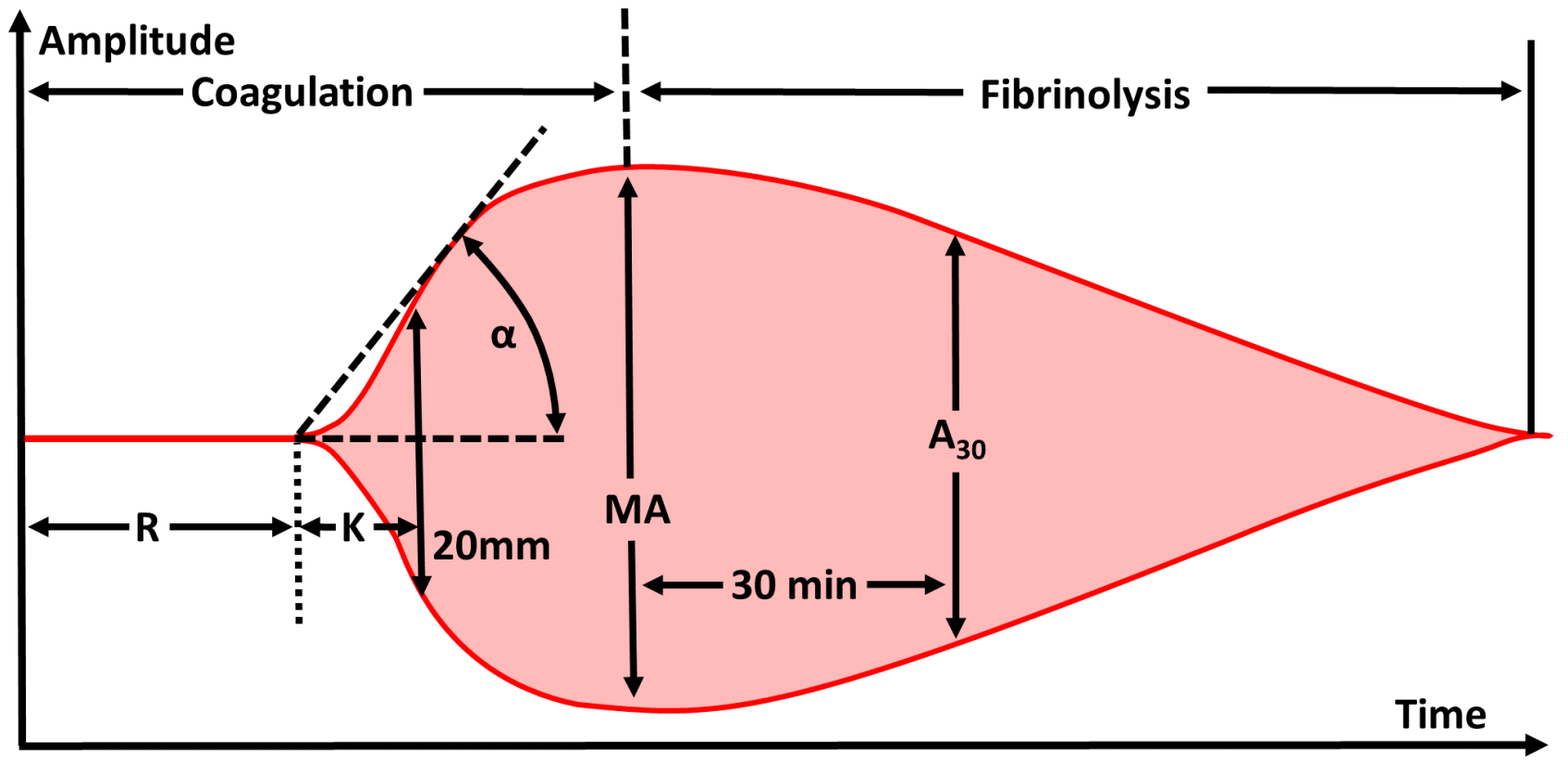
- Reperfusion: significant hemodynamic perturbations – sudden decrease in BP, HR, SVR and CO
- Can result in worsening pHTN and RV failure
- Rapid increase in K+ can lead to sinus arrest
- Sequestered blood from the portal and lower body venous system return to heart (no VVB)
- High K preservative solutions and endogenous metabolites are released from the graft
- Post Reperfusion Syndrome (PRS): 30% decrease in MAP for at least one minute and appears within first 5 minutes of graft reperfusion
    - Can have fatal consequences such a severe arrhythmias or asystole
    - Increased risk of postoperative renal dysfunction and 15 days mortality prediction
- Pre-emptive management with calcium chloride, inotropes, vasopressors, bicarbonate or THAM
- Cell saver can wash blood and lower K+ concentration
- TEE for RV failure, intra-cardiac clots (heparin), and pulmonary thromboembolism (tPA)
- Viscoelastic testing for surgical bleeding and hemostatic abnormalities – good hemostasis should be achieved before biliary duct anastomosis

TEE

- Direct visualization of heart in real time
  - Optimize euvolemia – avoid organ perfusion impairment and ischemia
- Intraoperative diagnosis
  - Portopulmonary hypertension
  - Air embolism
  - Thromboembolism
  - LVOTO
- Esophageal varices not a contraindication in the hands of experienced operators



Thromboelastography



R-time (R) [Time to clot formation] ⇧ = FFP	K-time (K) [Time to clot strength] ⇧ = CRYO	Alpha angle (α) [Rate of clot formation] ⇧ = CRYO
Max Amplitude (MA) [Greatest clot strength] ⇩ = PLT		Lysis @ 30 min (A30) [Rate of clot breakdown] ⇩ = TXA

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