Anesthesia for Liver Disease & Transplantation

December 9, 2023

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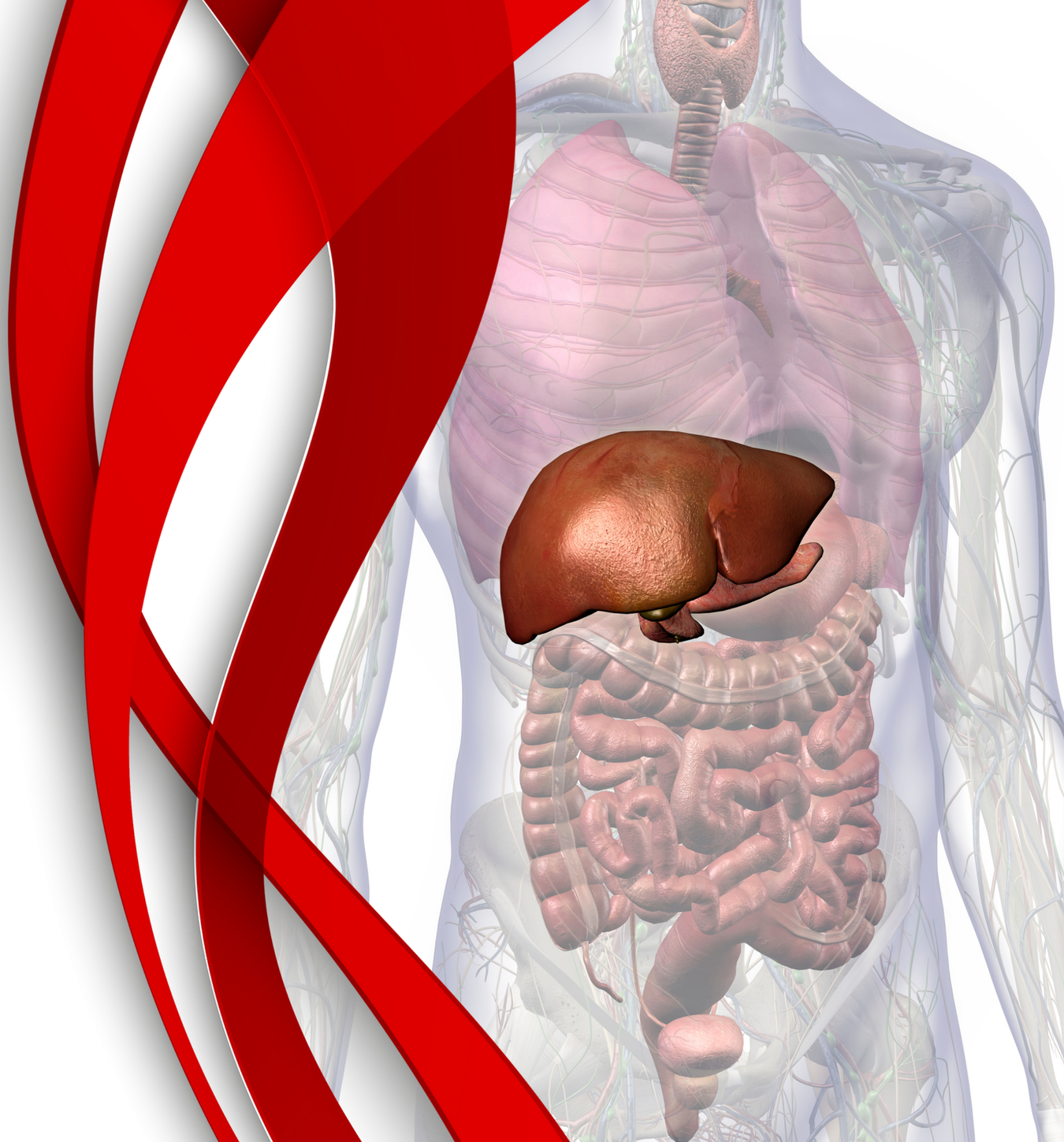
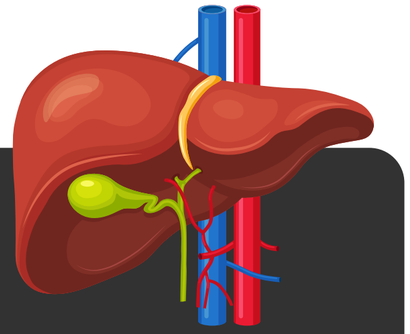


Objectives



Anatomy & Physiology

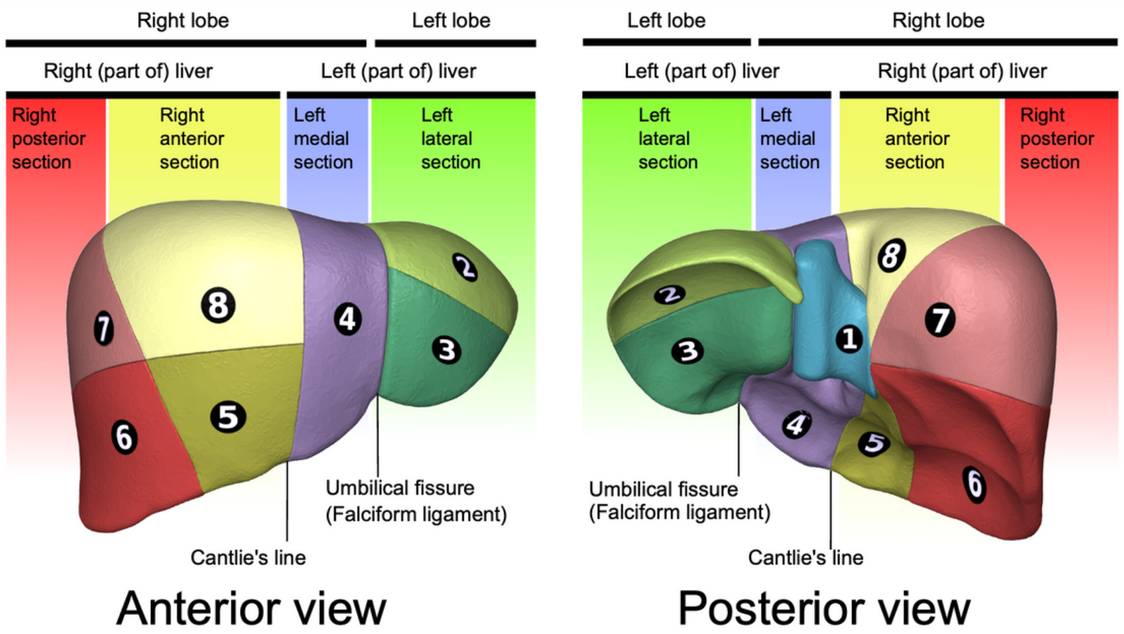
Liver Disease

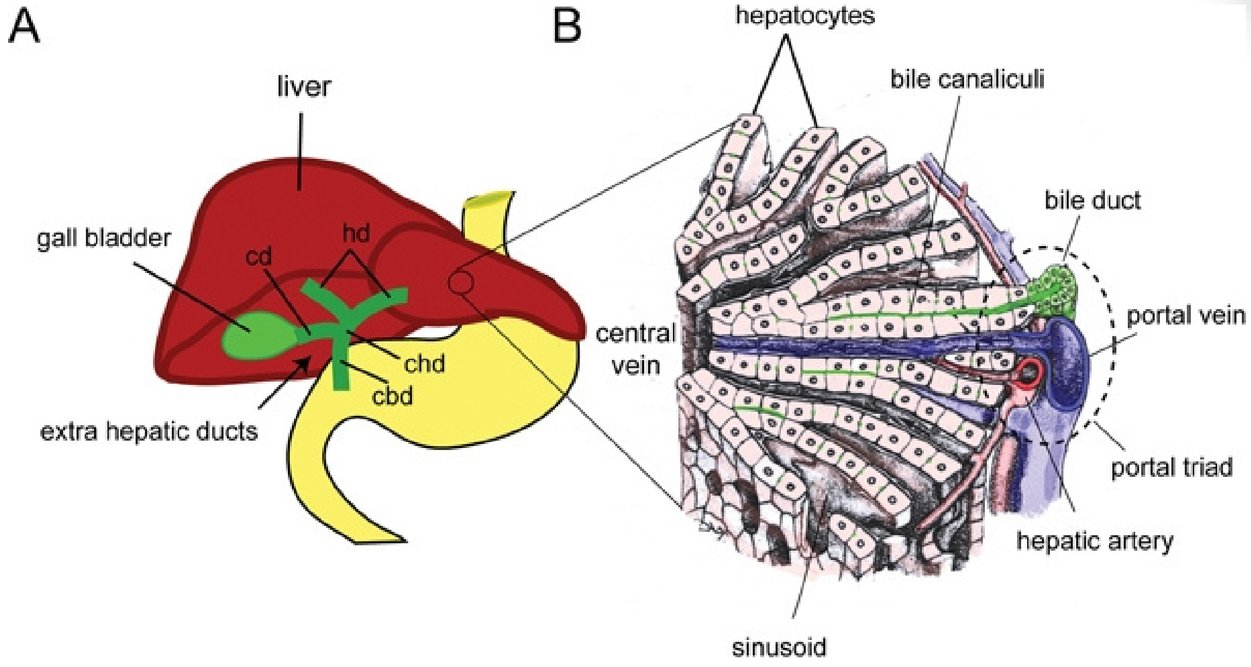
High Yield Concepts

Anesthesia

Liver Transplant

Liver Anatomy





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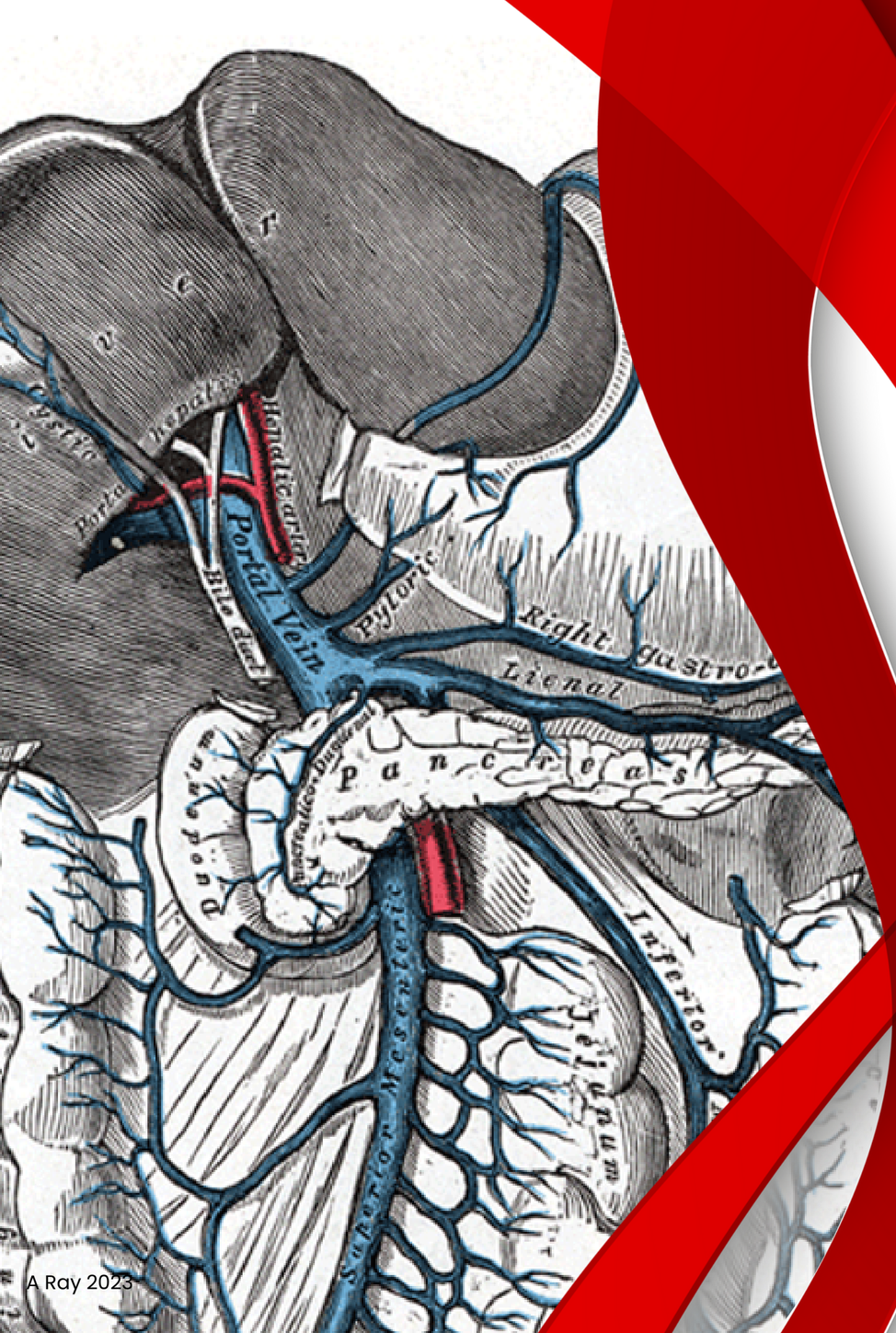
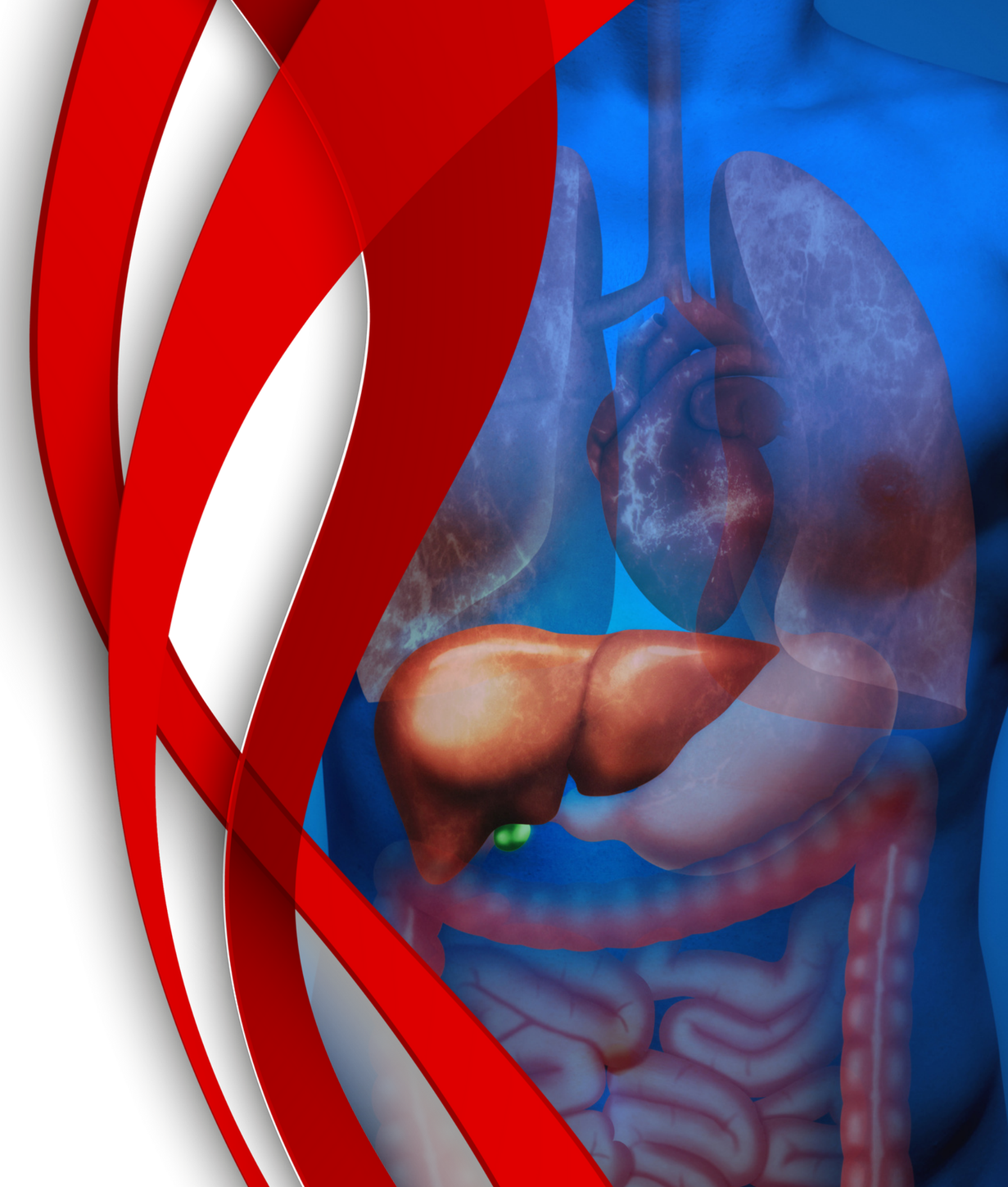


Blood Supply and Regulation

- 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
  - Increased by pain, hypoxemia, surgical stress, operative proximity
- Hepatic Vein Pressure is increased by increased CVP
  - PPV, CHF, Fluid Overload = decreased HPP

POSTHEPATIC

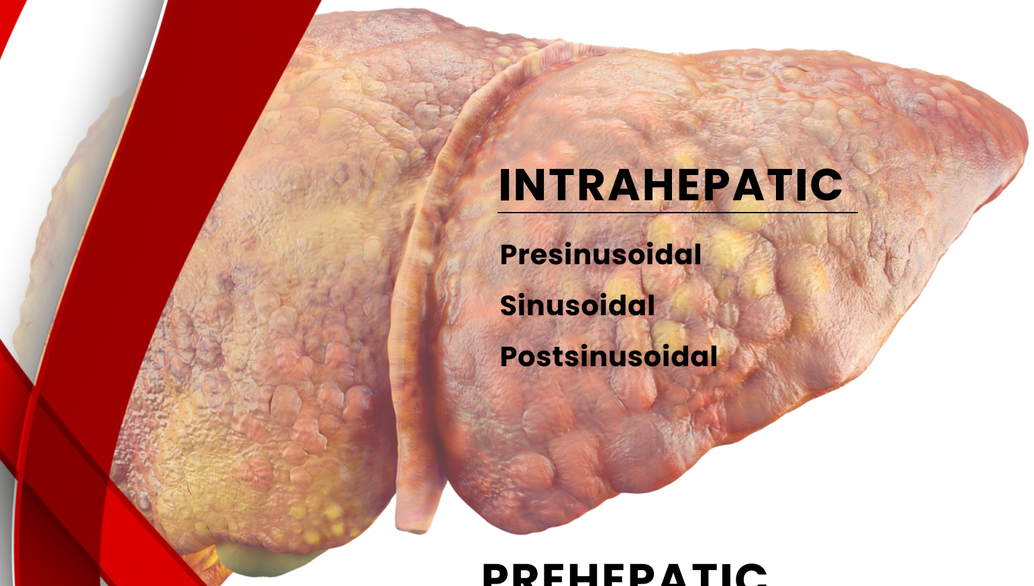
Budd-Chiari Syndrome

IVC Obstruction

Constrictive Pericarditis

Right-Sided CHF

Severe TR



INTRAHEPATIC

Presinusoidal

Sinusoidal

Postsinusoidal

PREHEPATIC

Portal Vein Thrombosis

Splenic Vein Thrombosis

Hepatic Synthetic Function

Normal adult liver produces 12 – 15g of protein a day

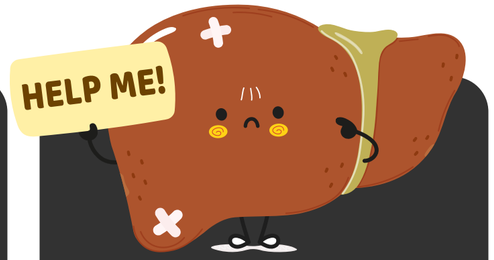
- Albumin:
  - drug binding and oncotic pressure
- Alpha-1 glycoprotein:
  - binds basic drugs & acute phase reactant
- Pseudocholinesterase:
  - degrades succinylcholine, mivacurium, and ester local anesthetics
- All proteinaceous clotting factors **except FVIII**

Additional:

- glucose regulation, cholesterol formation, hematopoiesis, bile formation, protein degradation, steroid hormone degradation, drug metabolism

Objectives

Anatomy & Physiology



Liver Disease

High Yield Concepts

Anesthesia

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Preoperative Assessment

- History
  - Jaundice, pruritis, malaise, anorexia
  - Exposure to drugs, alcohol, and toxins
  - Paracentesis
  - Admissions
  - History of TIPS and/or GIB
- Comorbidities
  - Cardiac, CKD, diabetes
- Physical exam
  - Stigmata of liver disesase

- Preoperative optimization
  - Coagulopathy, ascites, volume status, electrolytes, renal dysfunction, encephalopathy, thrombocytopenia, inadequate nutrition

Prognostication

Modified Child-Pugh Score

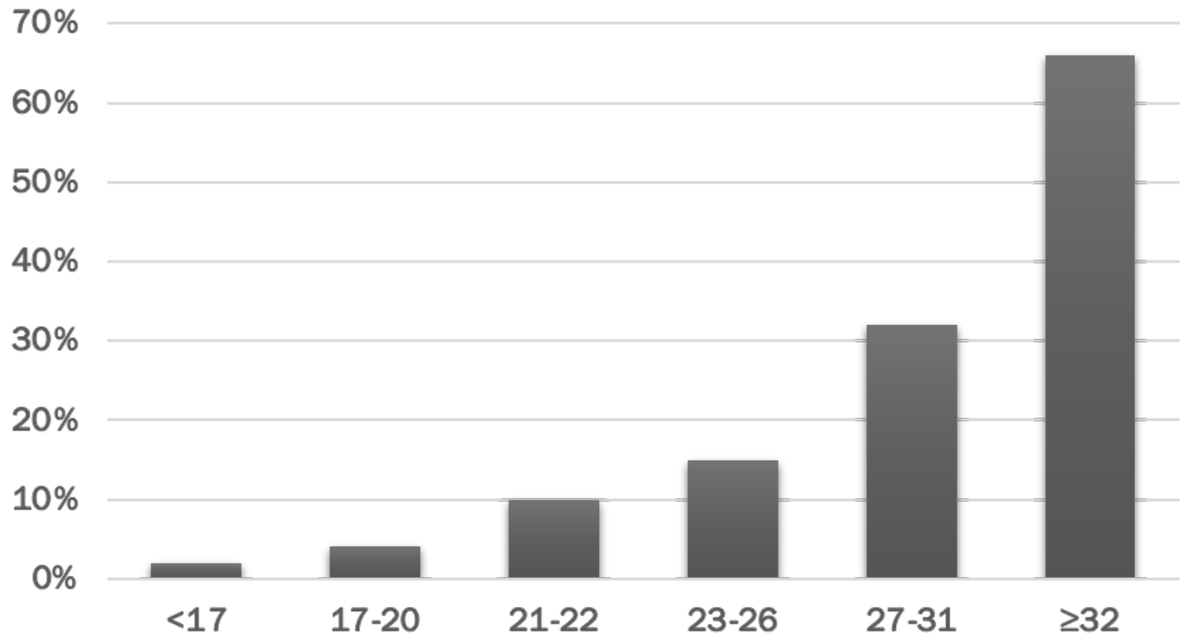
	1	2	3
Albumin (g/dL)	>3.5	2.8 – 3.5	<2.8
Bilirubin (mg/dL)	<2.0	2.0 – 3.0	>3.0
Ascites	Absent	Slight	Moderate
Encephalopathy	Absent	Grades I & II	Grades III & IV
PT prolongation (s)	<4.0	4.0 – 6.0	>6.0

Class A: 5 – 6 points

Class B: 7 – 9 points

Class C: 10 – 15 points

MELD-Na 3-month mortality

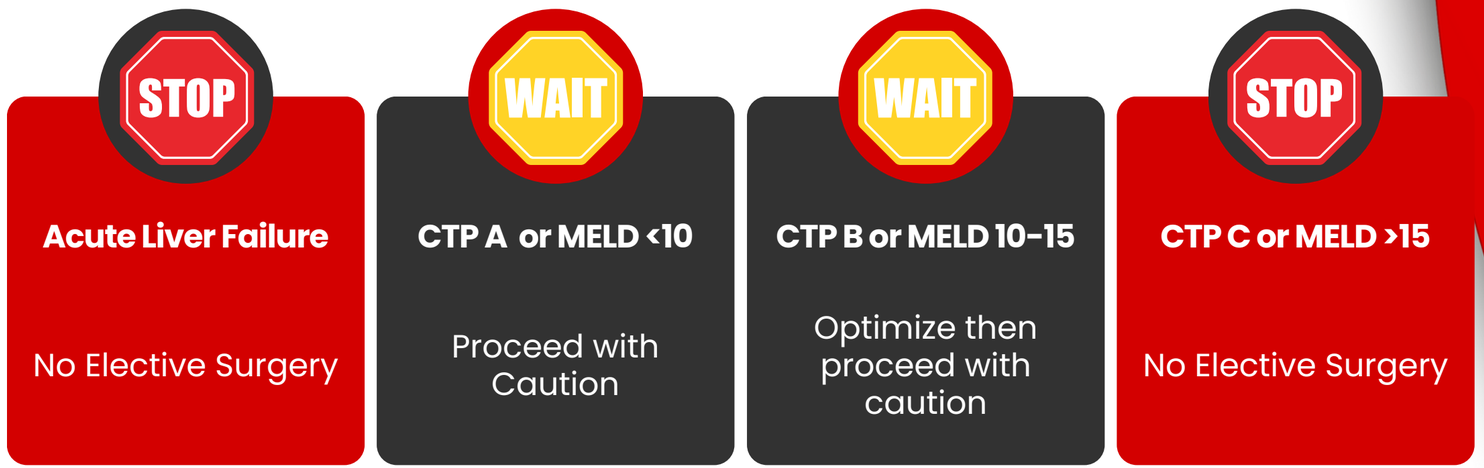


MELD = 3.78[Ln Serum Bilirubin (mg/dL)] + 11.2[Ln INR] + 9.57[Ln Serum Creatinine (mg/dL)] + 6.43

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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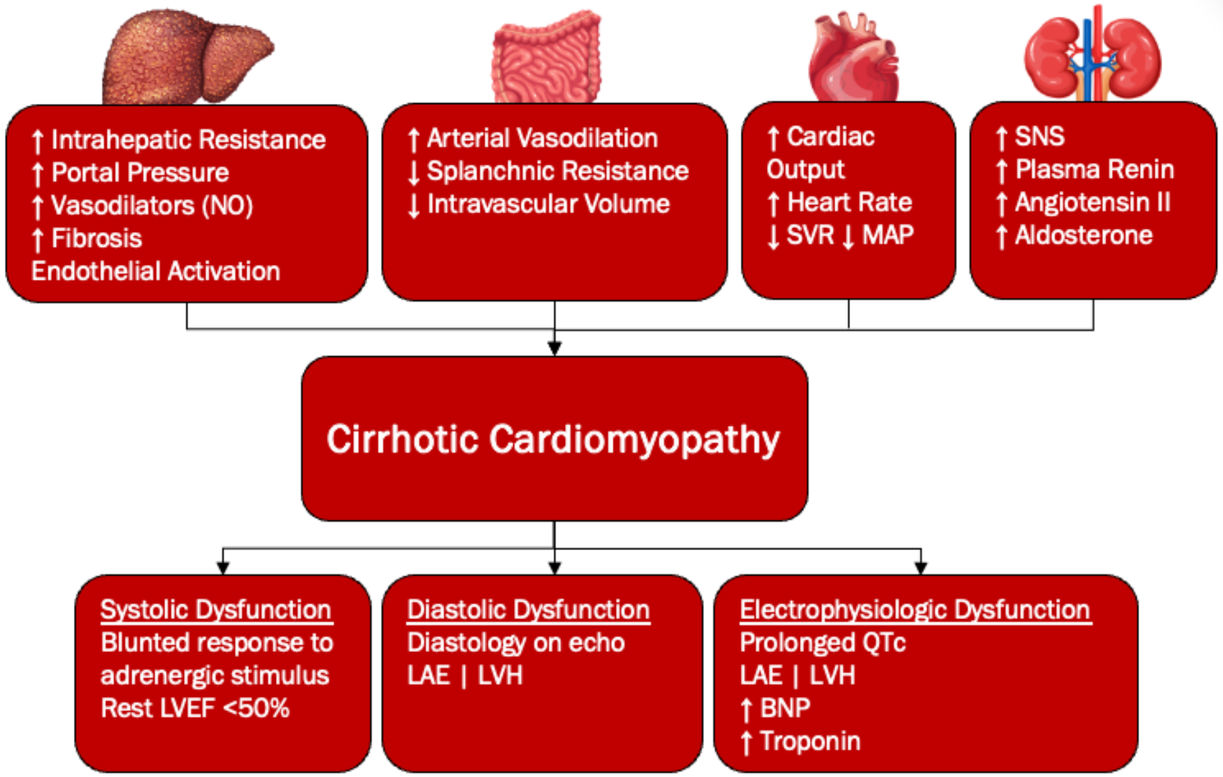
Cirrhotic Cardiomyopathy

- 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



Portopulmonary Hypertension

- mPAP ≥ 25 mmHg + portal hypertension = portopulmonary hypertension (POPH)
- mPAP ≥ 35 mmHg is a predictor of increased mortality following liver transplant
- Screening: TTE, RVSP good estimate in diagnosing mod-severe PHTN 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 m2 and PCWP ≤ 15 mmHg
- Exclude other causes of pulmonary hypertension

WHO 1

PAH

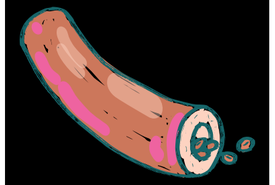
WHO 2

Left Heart Disease

WHO 3

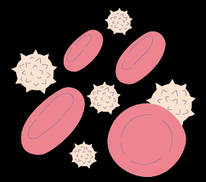
Chronic Lung Disease

WHO 4

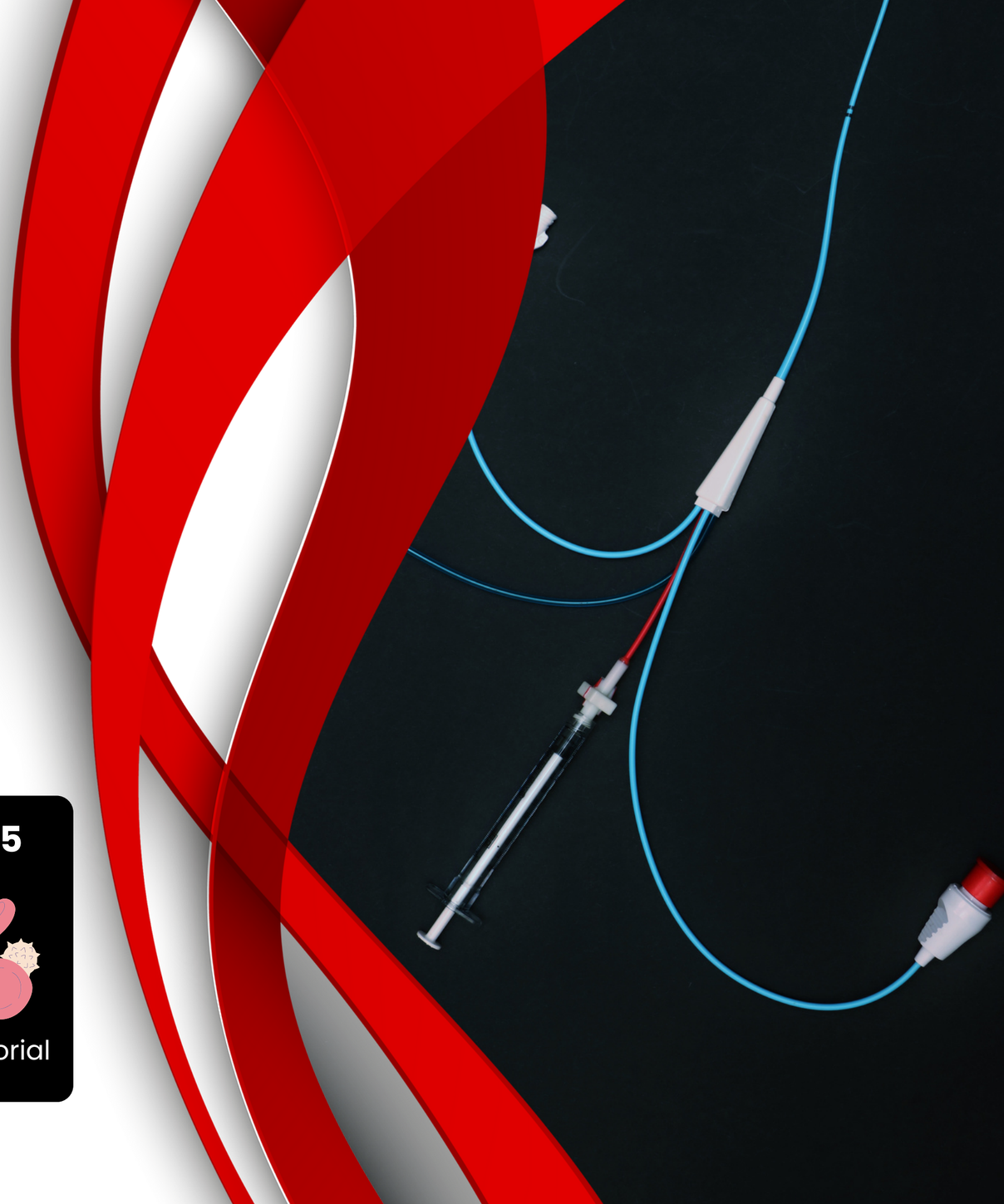


CTEPH

WHO 5



Multifactorial



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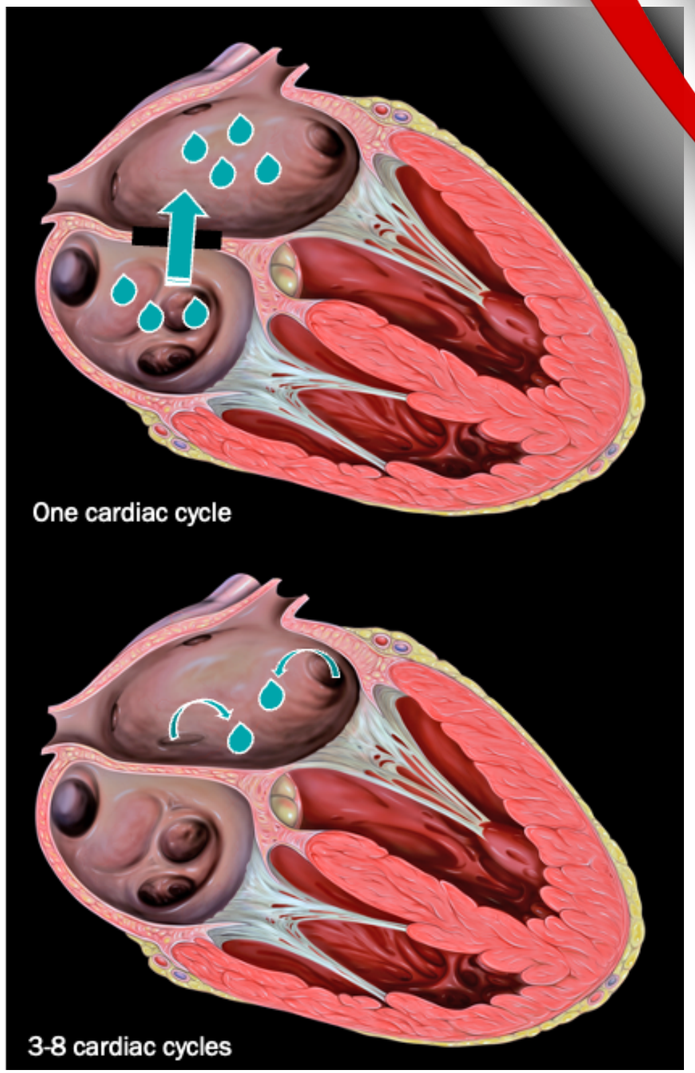
Hepatopulmonary Syndrome

- **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
- **Orthodeoxia:**
  - Upright: decrease in PaO2
  - Supine: increase in PaO2
- **Platypnea**
  - Upright: increase in dyspnea
  - Recumbent: decrease in dyspnea



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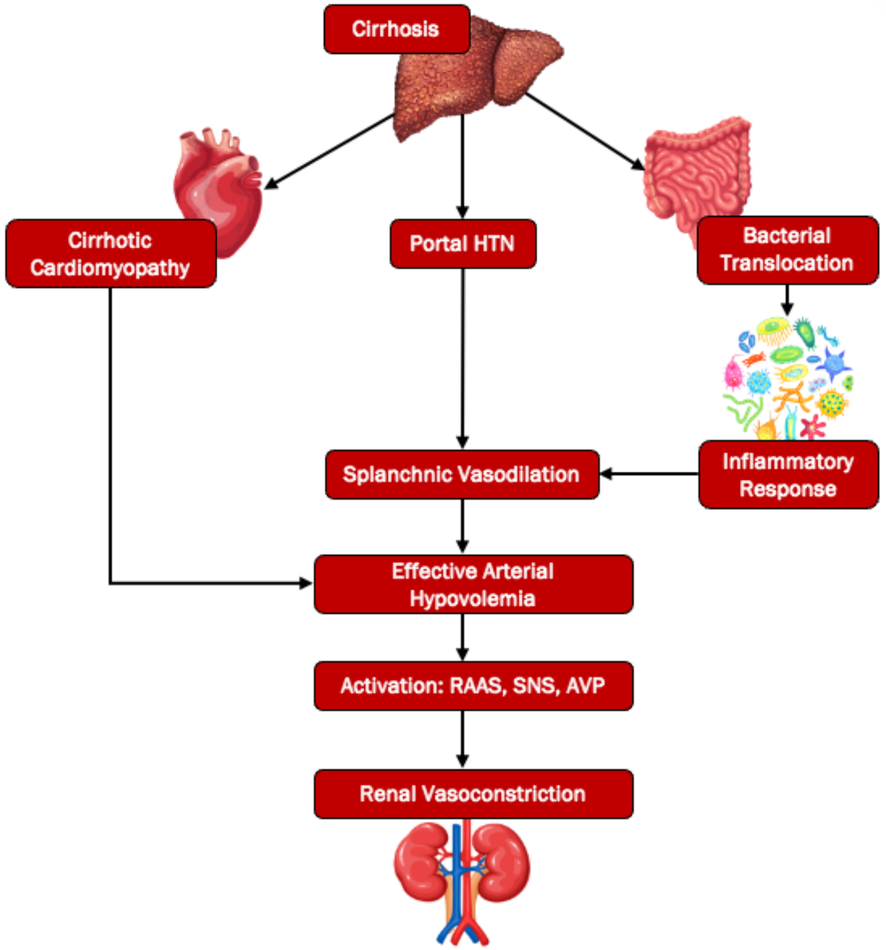
Hepatorenal Syndrome

- 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



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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

Anesthetics: Liver Disease

- **Ketamine** CAUTION
  - Metabolism: hepatic
  - Norketamine: 30% activity of parent drug
  - Elimination: renal 91%
  - Protein binding: 27%
- **Barbiturates** CAUTION
  - Metabolism: hepatic
  - Hypoalbuminemia: ↑ free fraction = ↑ potency
- **Dexmedetomidine** CAUTION
  - Metabolism: hepatic
  - Elimination: renal
  - Protein binding: 94%

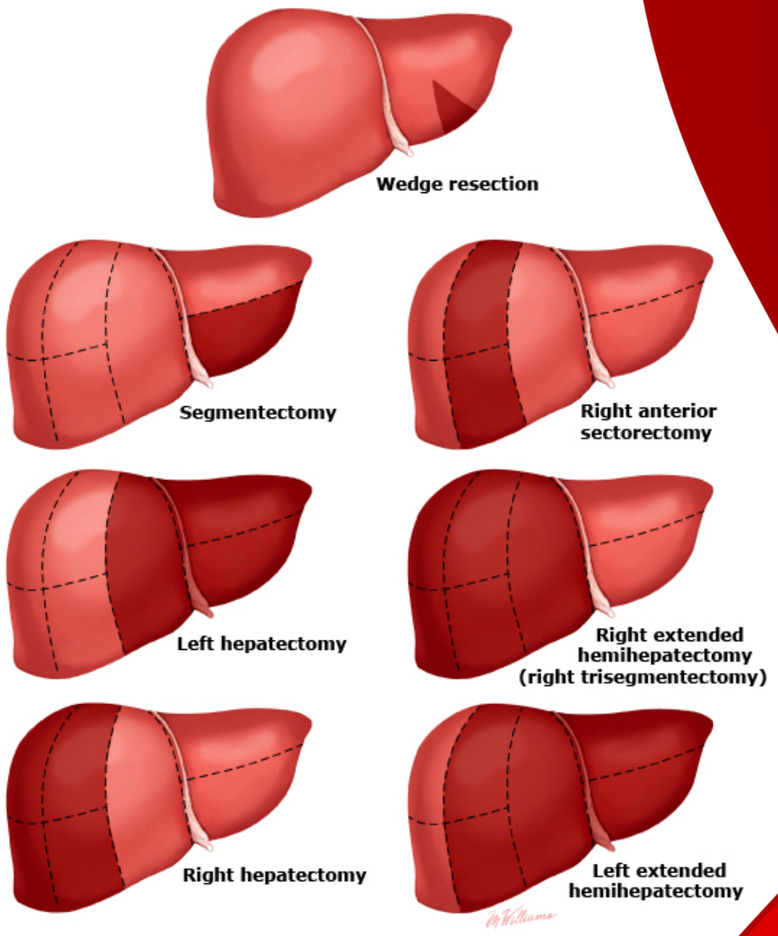
Anesthetics: Liver Disease

- **Benzodiazepines & Opioids**
  - Metabolism: hepatic
  - Hypoalbuminemia: ↑ free fraction = ↑ potency
  - **Remifentanil** YES nonspecific plasma esterases
  - **Fentanyl** CAUTION
  - **Hydromorphone** CAUTION
  - **Morphine** NO
- **Volatiles** YES
  - Preferred: eliminated primarily through the lungs
- **Regional anesthesia:** CAUTION
  - Coagulopathy | Thrombocytopenia
- **Acetaminophen:** max dose 2g in 24 hours CAUTION
- **NSAIDS** NO

Anesthetics: Liver Disease

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

Hemodynamic Management



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- 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

Increased Bleeding

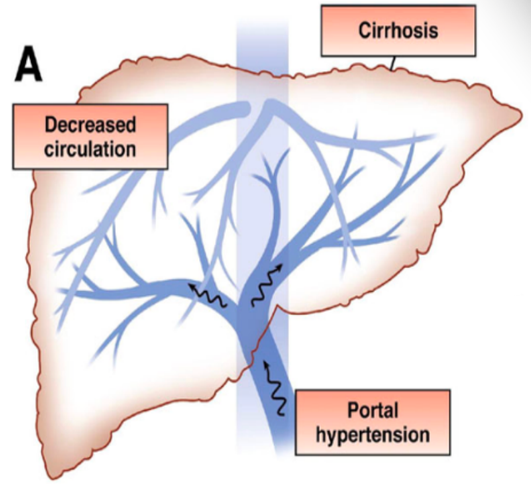
- Thrombocytopenia
- Decreased thrombopoietin synthesis
- Decreased FII, V, VII, IX, X, and XI
- Vitamin K deficiency
- Dysfibrinogenemia
- Increased tPA

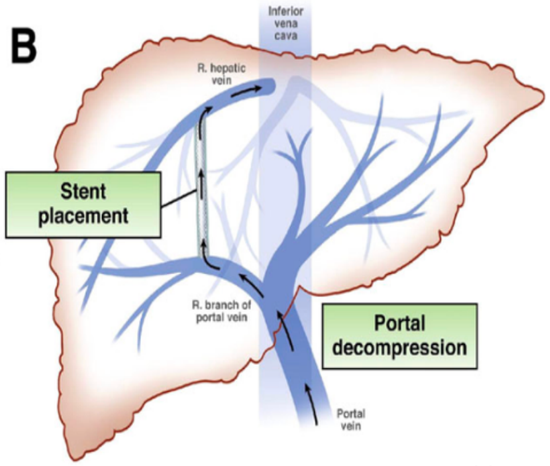
Increased Clotting

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

TIPS Procedure

- 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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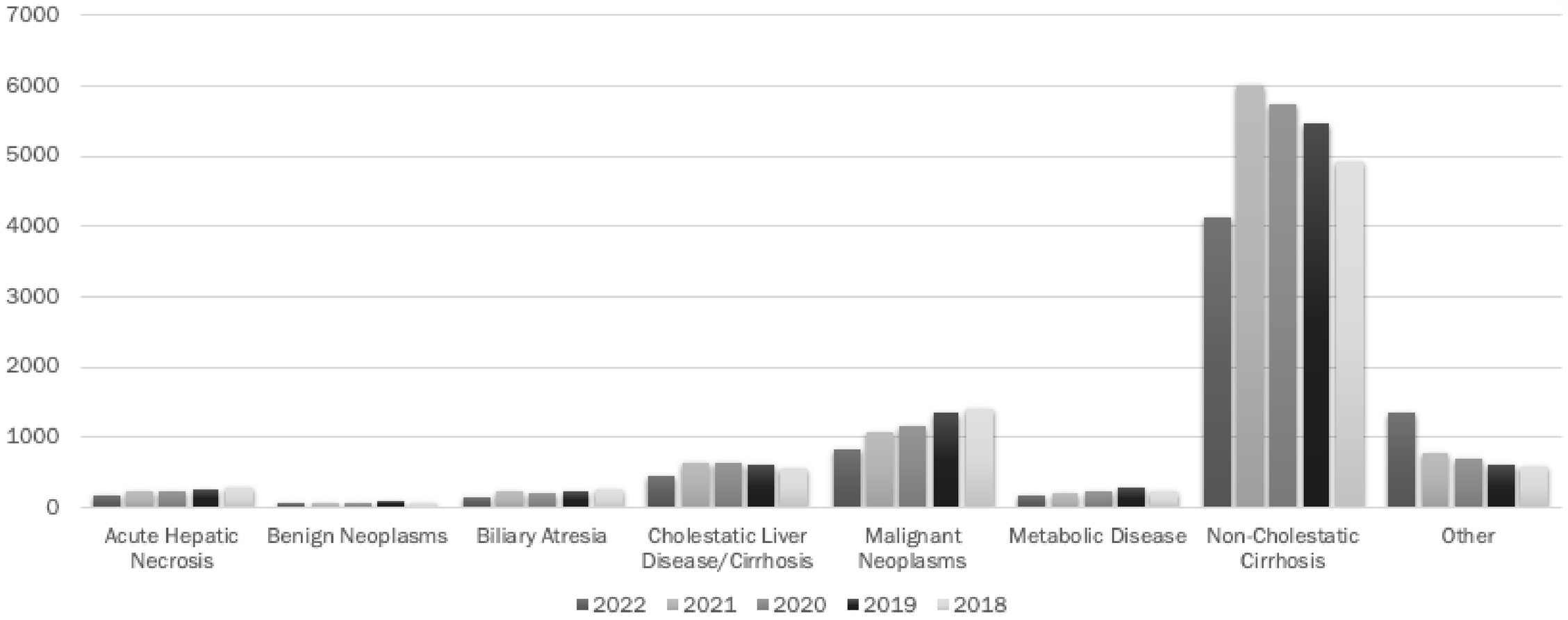
Liver Transplant Indications



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 coinfection
- 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)

AASLD
PRACTICE GUIDELINE

Evaluation for Liver Transplantation in Adults:
2013 Practice Guideline by AASLD and AST

Graft Options

Deceased Donor

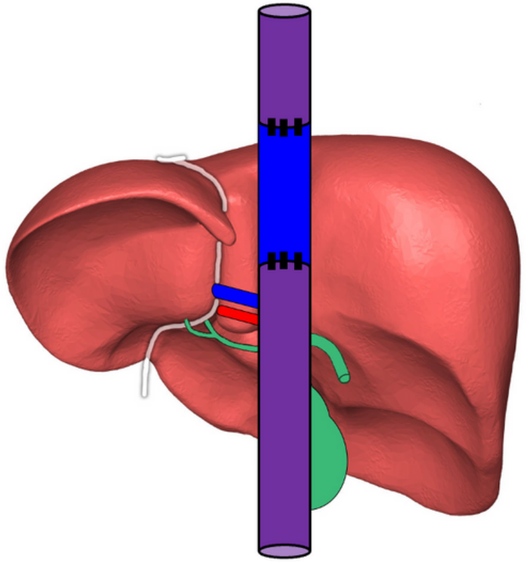
- DCD or brain death
- DCD fastest growing source of transplant organs
- Generally classified as emergent or urgent
- Recipients are older, sicker, and have multiple co-morbidities
- Expanded donor pool with marginal donors and increasing donor age

Graft Options

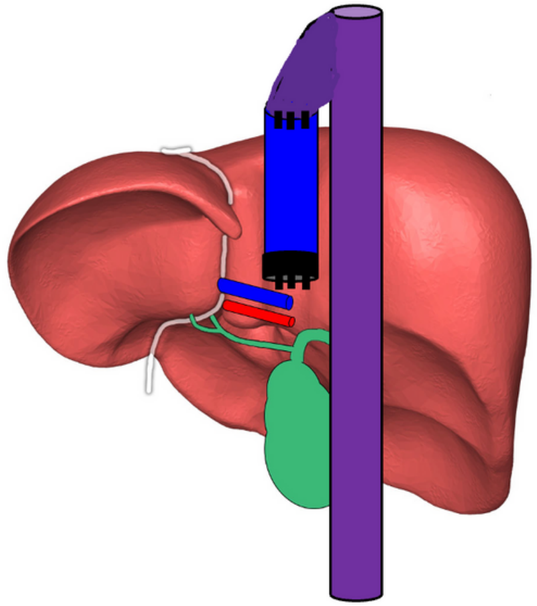
Living Donor

- 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

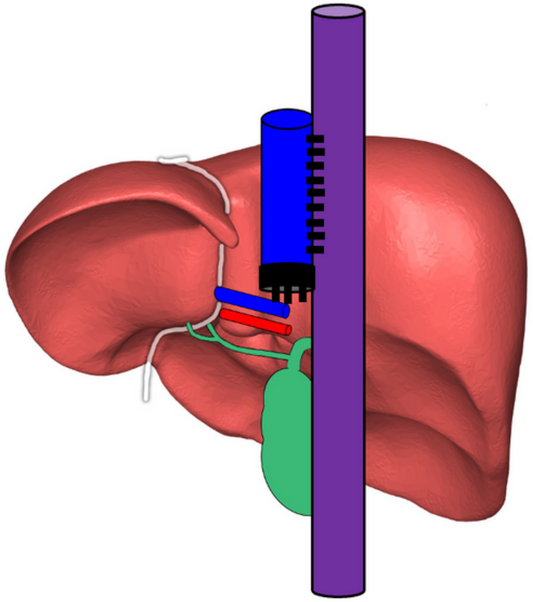
Surgical Technique



Intercaval Connection



Piggyback Technique



Cavo-Caval Anastomosis

Recipient IVC

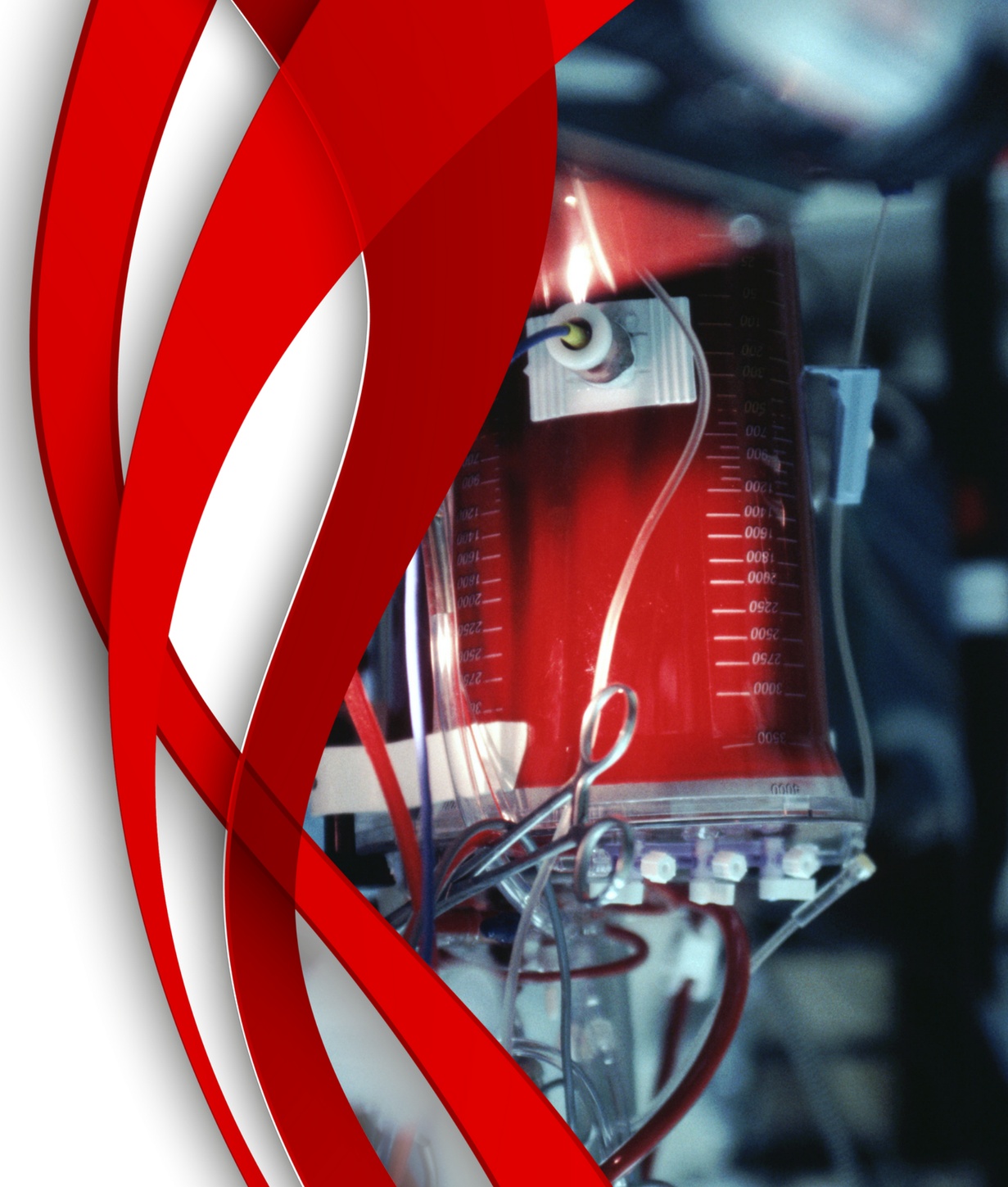
Donor IVC

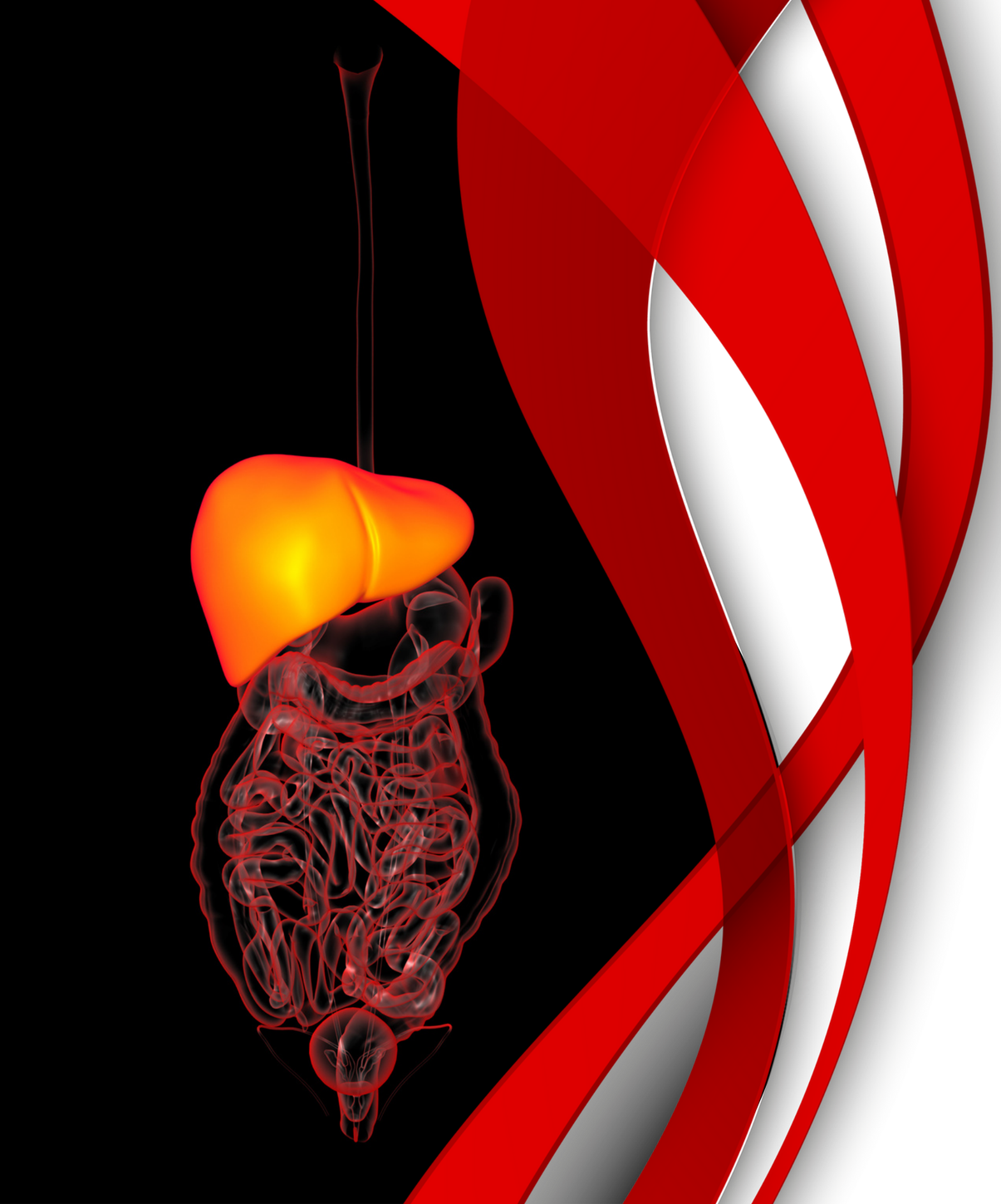
Surgical Stages

- **Preanhepatic 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
- **Neohepatic phase**
  - Moment of liver reperfusion
  - Resumption of flow in PV and IVC
  - Complicated by post-reperfusion syndrome (PRS) and bleeding from vascular anastomoses

Preanhepatic 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



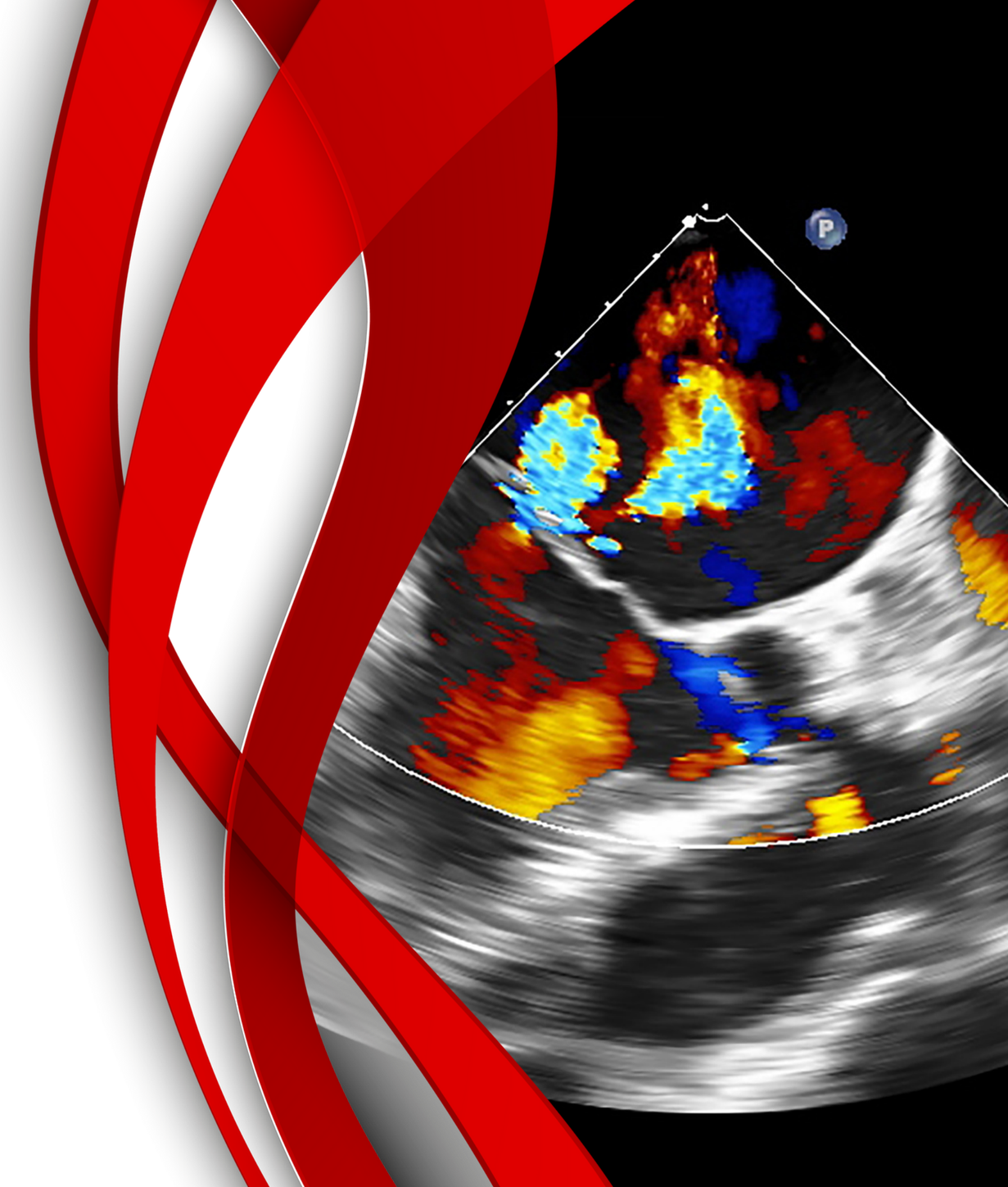


Anhepatic Phase

- 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

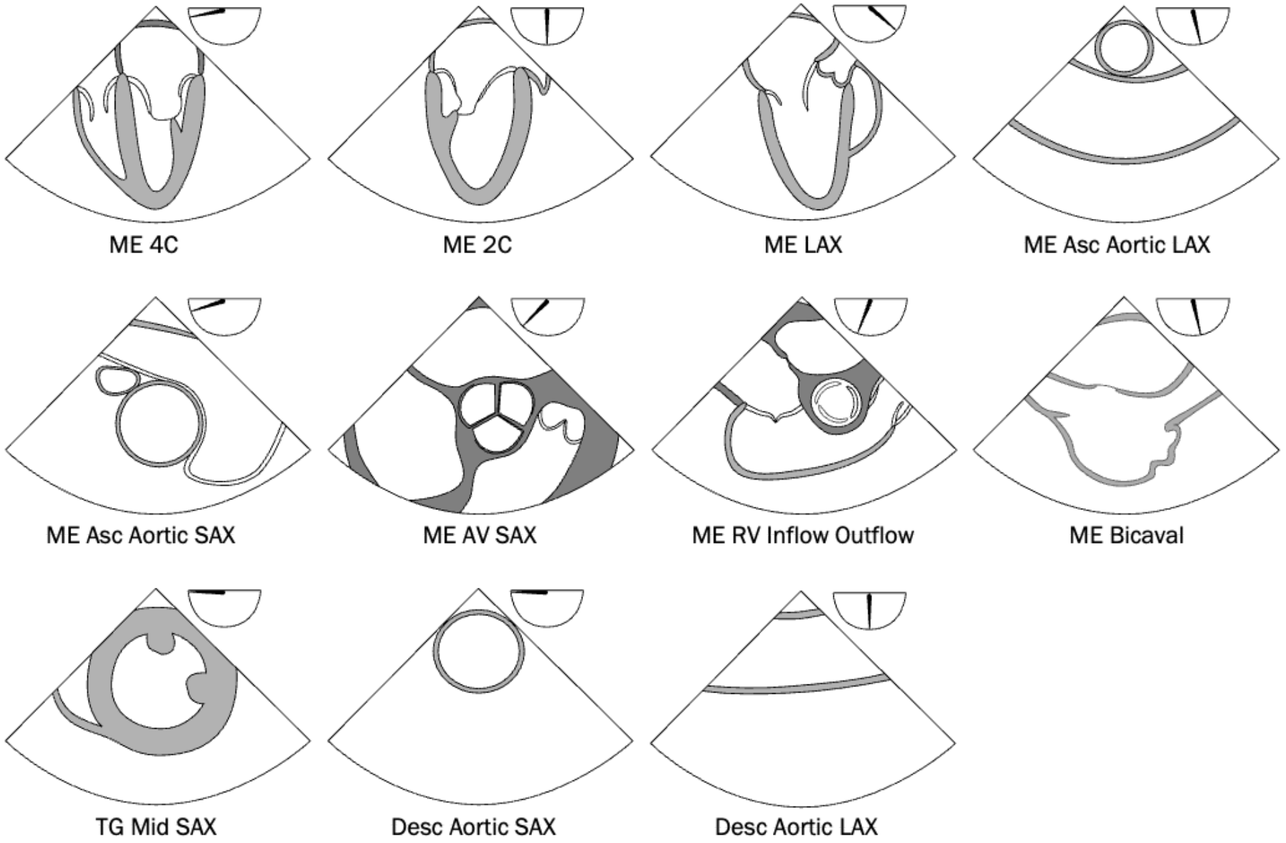
Neohepatic Phase

- Reperfusion: significant hemodynamic perturbations – sudden decrease in BP, HR, SVR and CO
- Can result in worsening pHTN and RV failure
- 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
- Rapid increase in K+ can lead to sinus arrest
- 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, intracardiac clots (heparin), and pulmonary thromboembolism (tPA)
- Viscoelastic testing for surgical bleeding and hemostatic abnormalities – good hemostasis should be achieved before biliary duct anastomosis



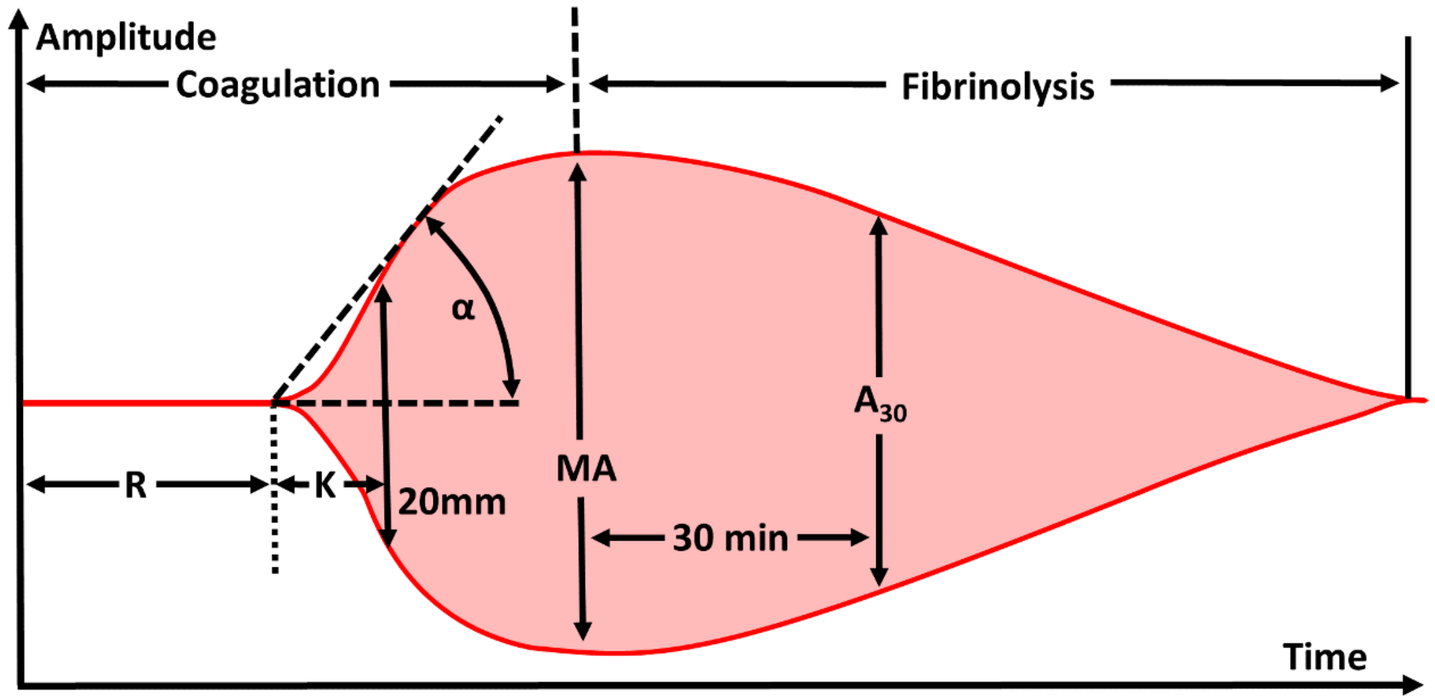
TEE Evaluation

- 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

- **Reaction Time (R)**
  - Coagulation Time
    - Time to 2 mm amplitude
    - Prolonged = FFP or PCC
- **Kinetics (K)**
  - Clot Kinetics
    - time from 2 - 20 mm amplitude
- **Alpha angle**
  - Slope between R and K
- **Maximum Amplitude (MA)**
  - Maximum Clot Strength
  - Decreased: Platelets (+/- cryo)*
- **Amplitude**
  - At fixed time intervals in mins (A30, A60)
- **Clot Lysis (LY)**
  - At fixed time intervals in mins (LY30, LY60)
  - LY30 >7.5%: TXA or Amicar



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