

Anesthesia for Liver Disease & Transplantation

Anna Ray, MD

December 15, 2024

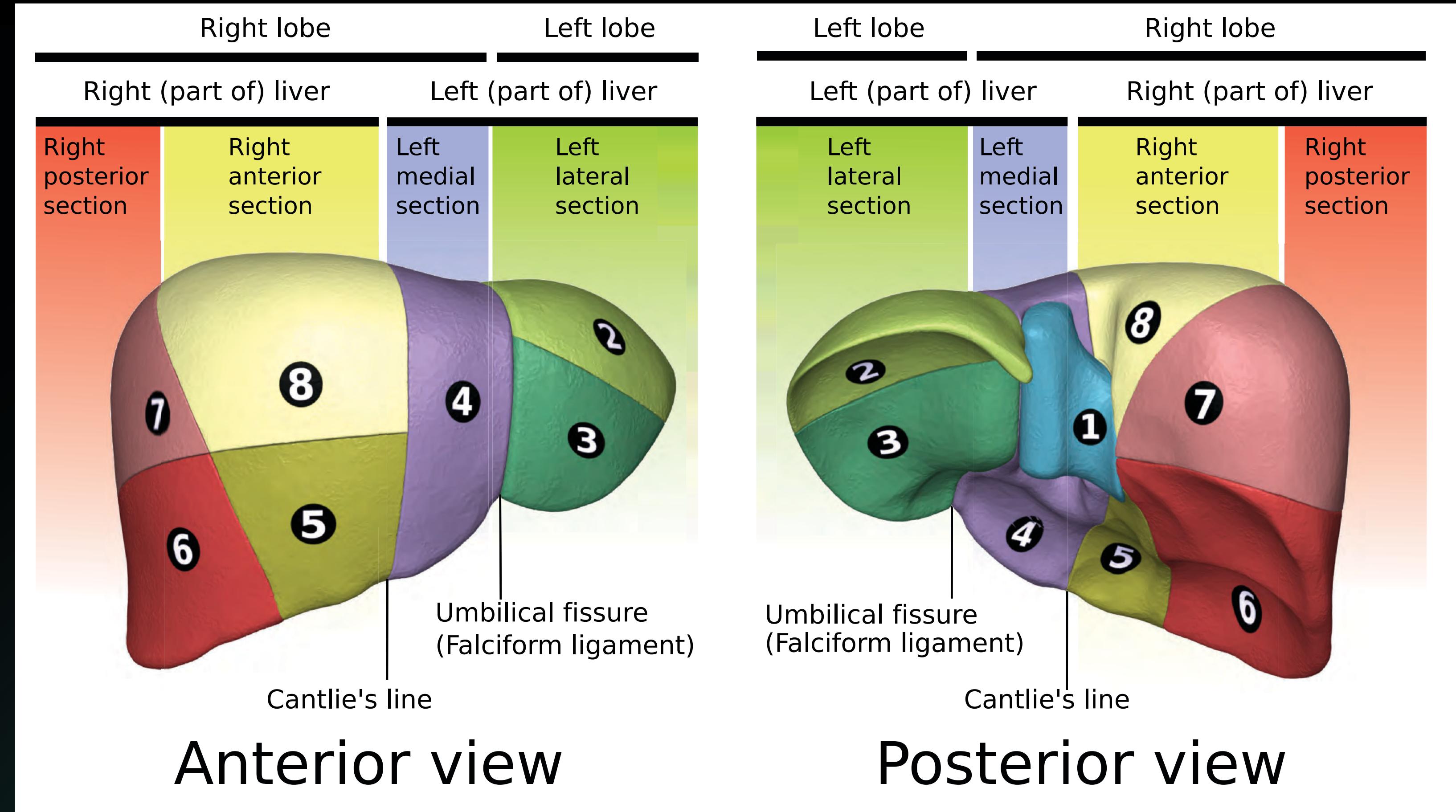


I have no financial disclosures

Objectives

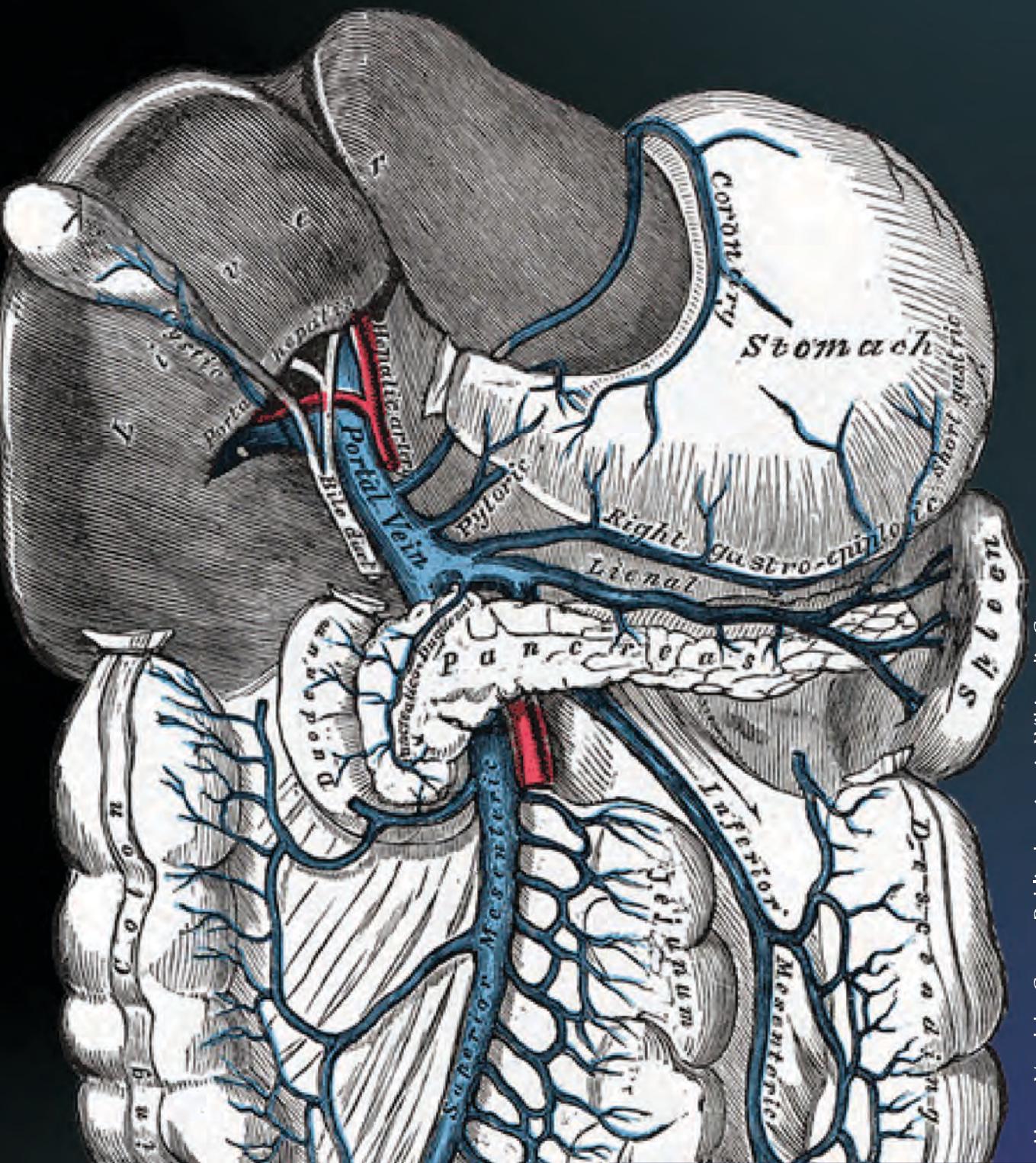
- Anatomy & Physiology
- Liver Disease
- High Yield Concepts
- Anesthetic Considerations
- Liver Transplant





Blood Supply & Regulation

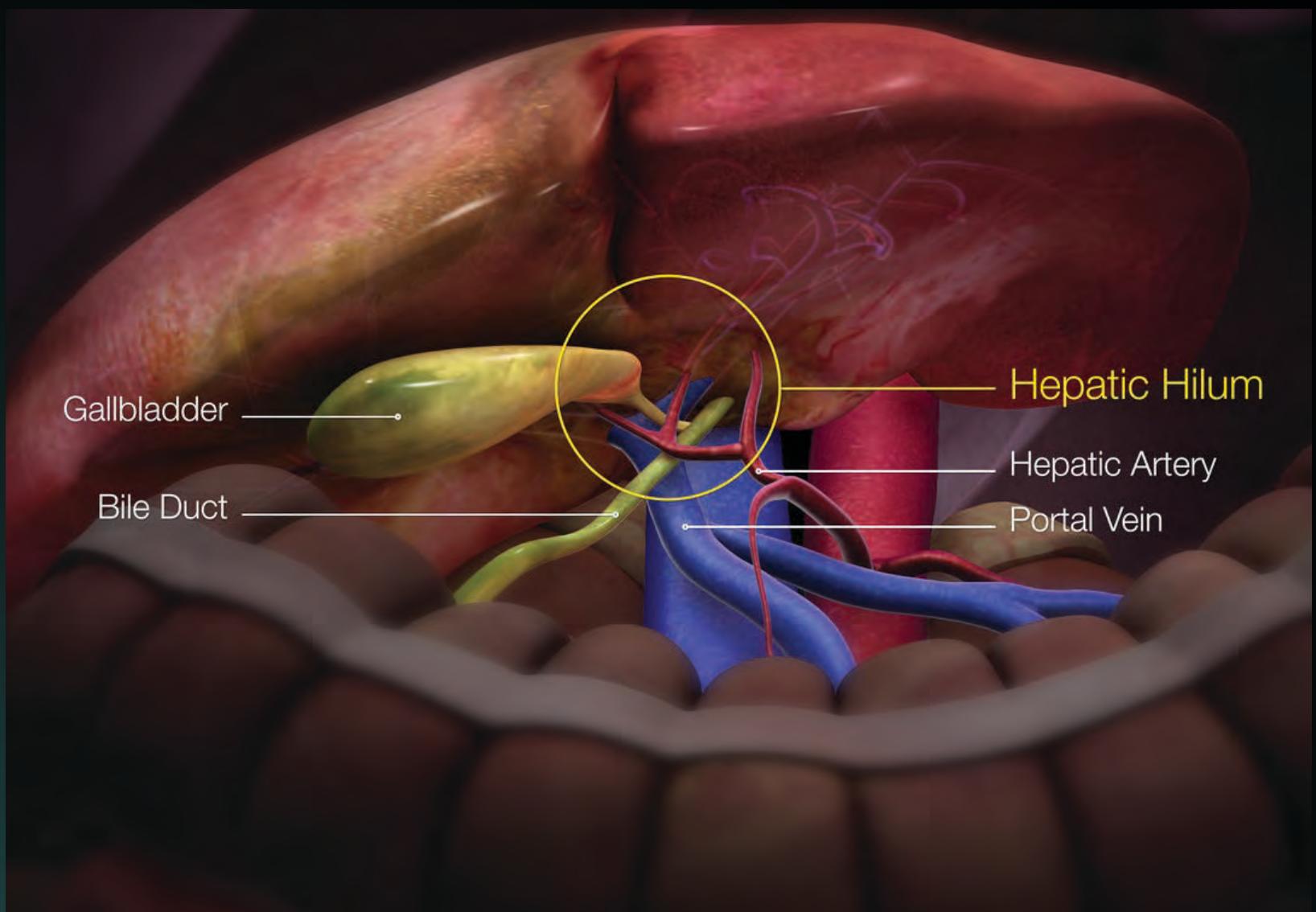
- 25% of resting cardiac output
 - Hepatic artery:
 - 25% of total hepatic blood flow | 50% oxygen supply
 - Arises from celiac trunk (80%) or SMA (20%)
 - Portal vein:
 - 75% of total hepatic blood flow | 50% oxygen supply
 - Confluence of SMA, IMV, splenic vein
- Hepatic Veins
 - Right, middle, and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



Henry Vandyke Carter, Public domain, via Wikimedia Commons

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



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 | oncotic pressure
 - Alpha₁-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

Objectives

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



Preoperative Assessment

History

- Jaundice, pruritus, malaise, anorexia
- Exposure to drugs, alcohol, toxins
- Paracentesis frequency
- Hospitalizations
- History of TIPS
- History of GIB

Comorbidities

- Cardiac
- CKD
- Diabetes w/ appropriate related testing

Physical Exam

- Stigmata of liver disease



Preoperative Optimization

- Coagulopathies
- Thrombocytopenia
- Ascites
- Volume
- Electrolytes
- Renal dysfunction
- Encephalopathy
- Inadequate nutrition

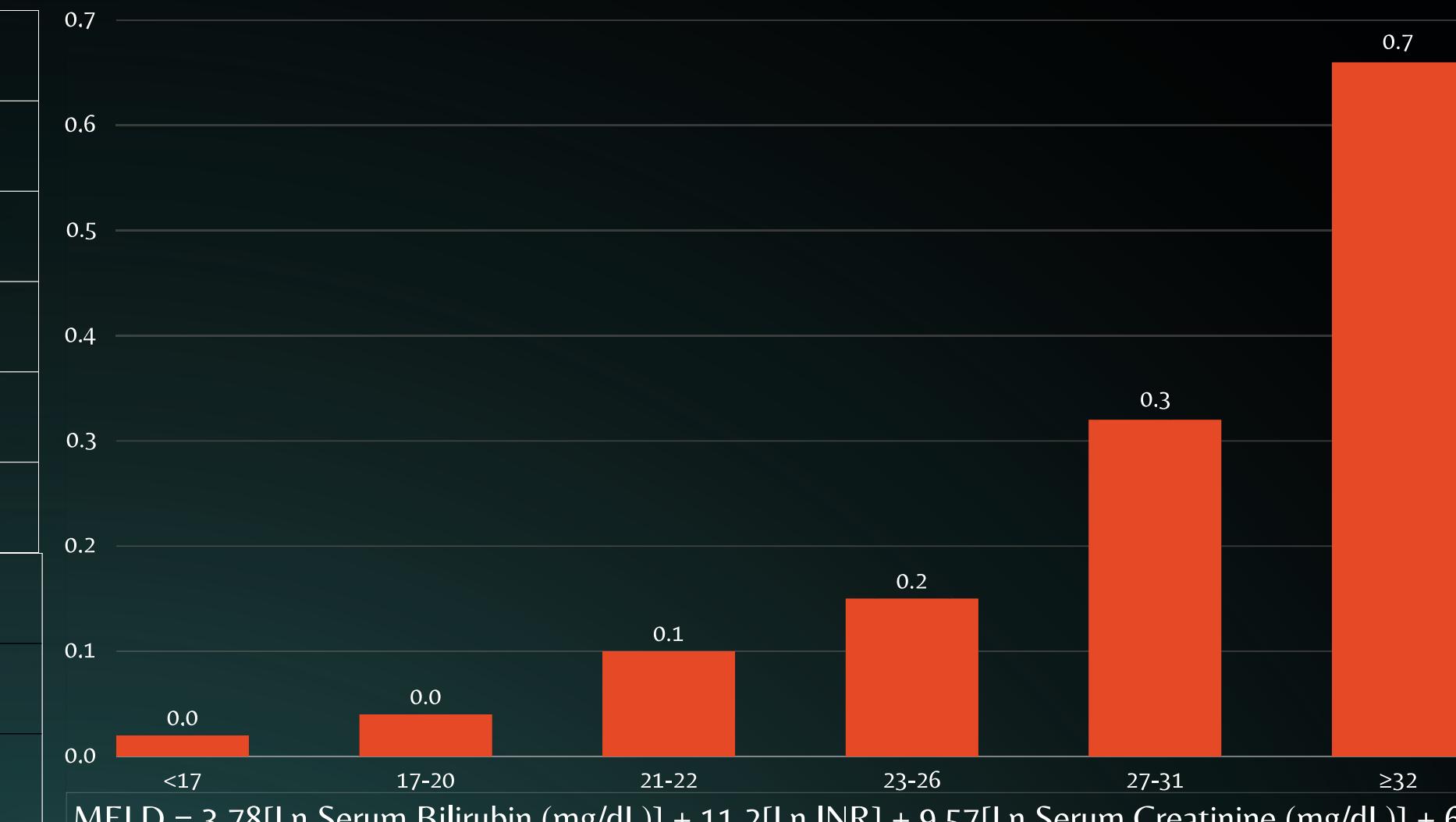


Prognostication

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



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

Acute Liver Failure



No Elective Surgery

CTP A | MELD <10



Proceed with Caution

CTP B | MELD 10-15



Proceed with Caution
post Optimization

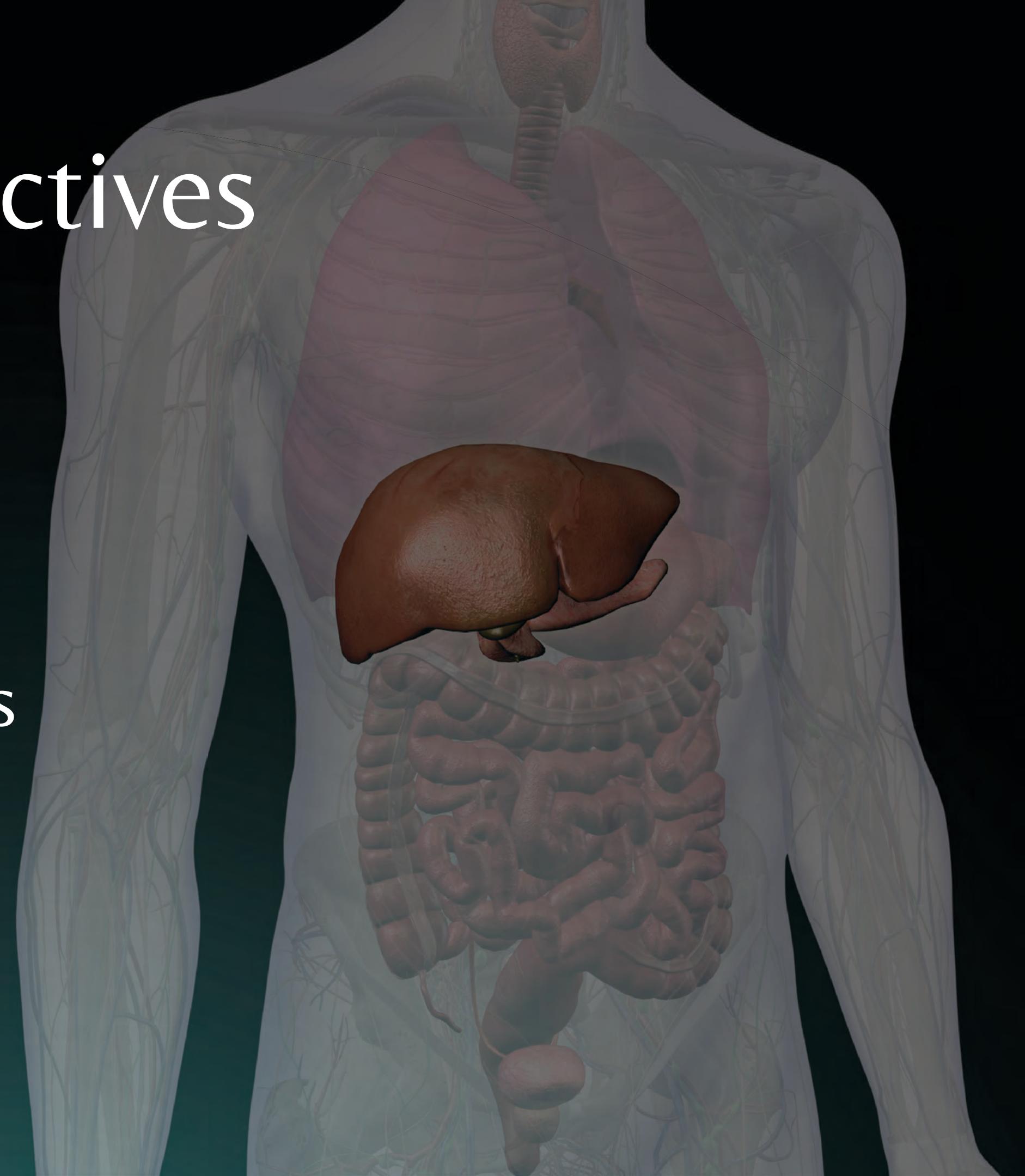
CTP C | MELD >15



No Elective Surgery

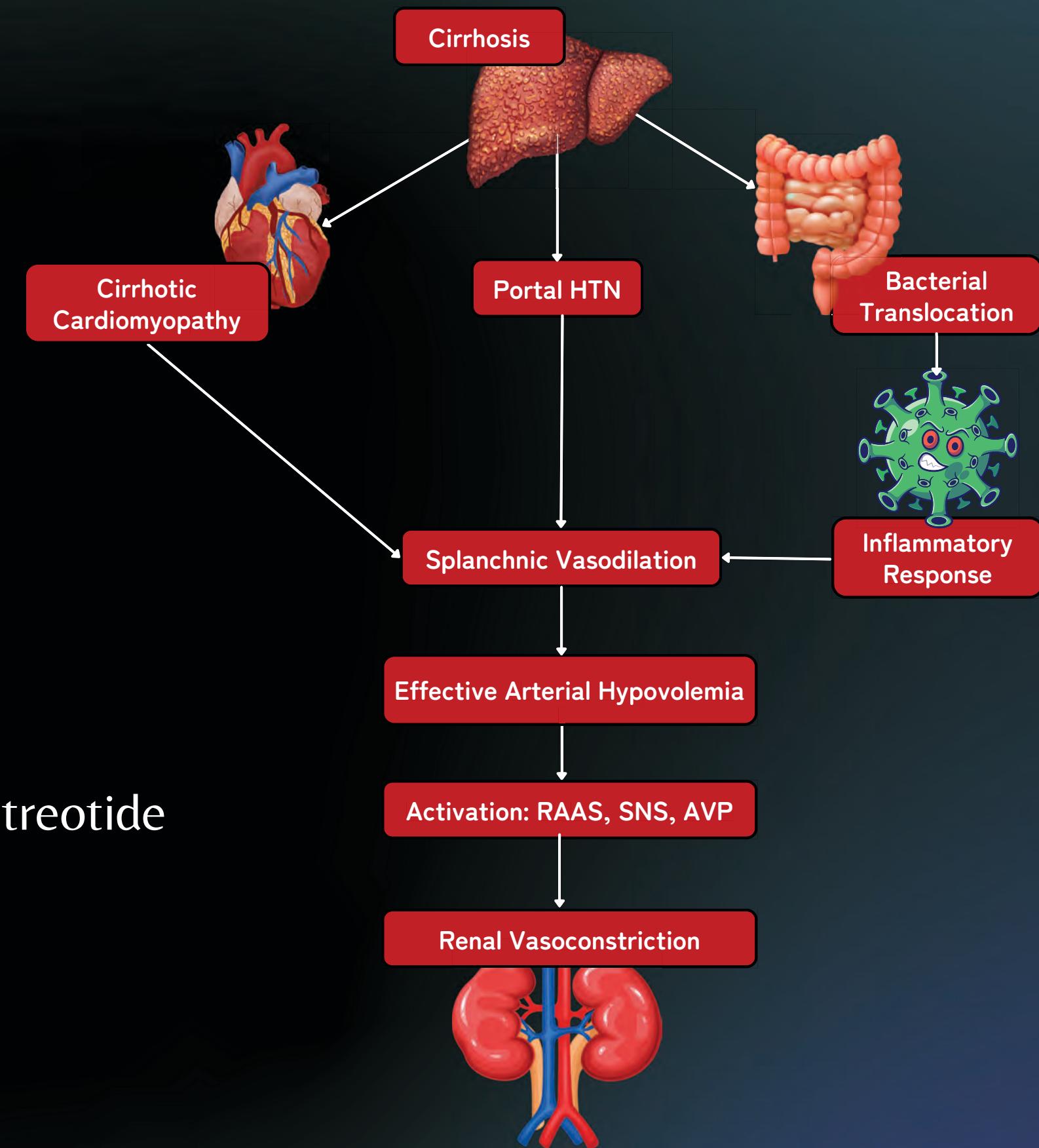
Objectives

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

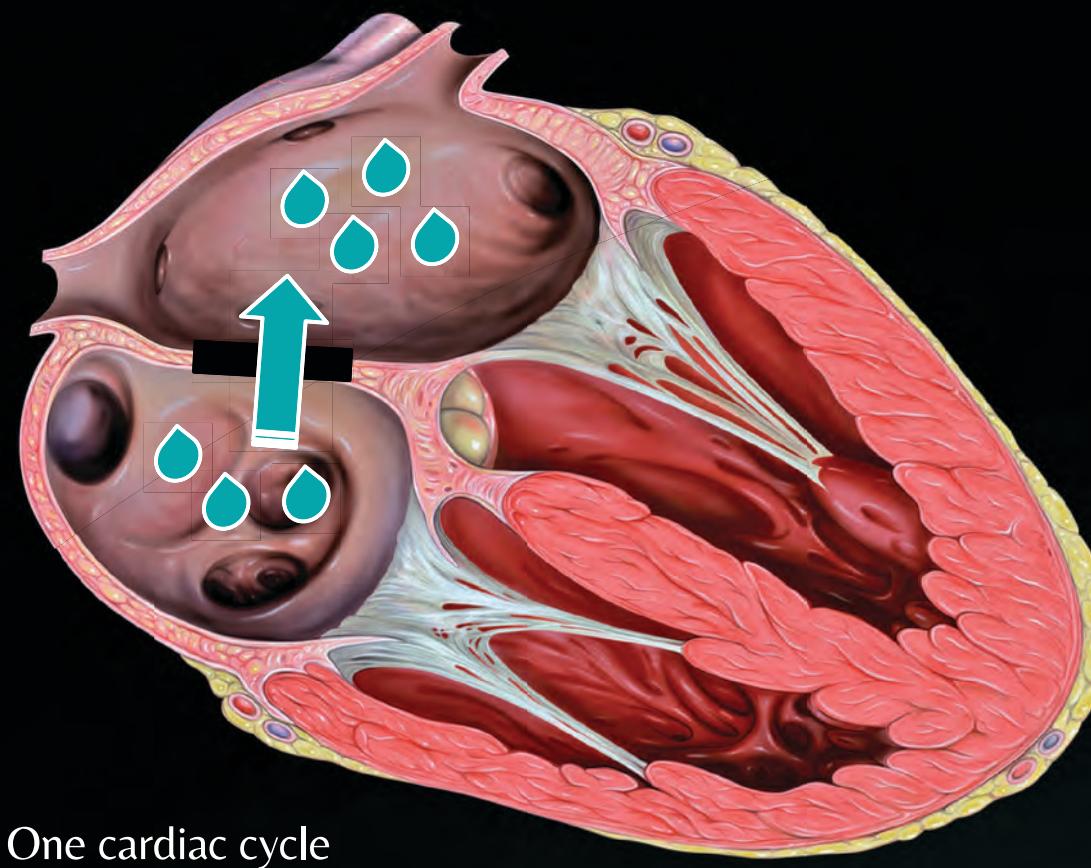


Hepatorenal Syndrome

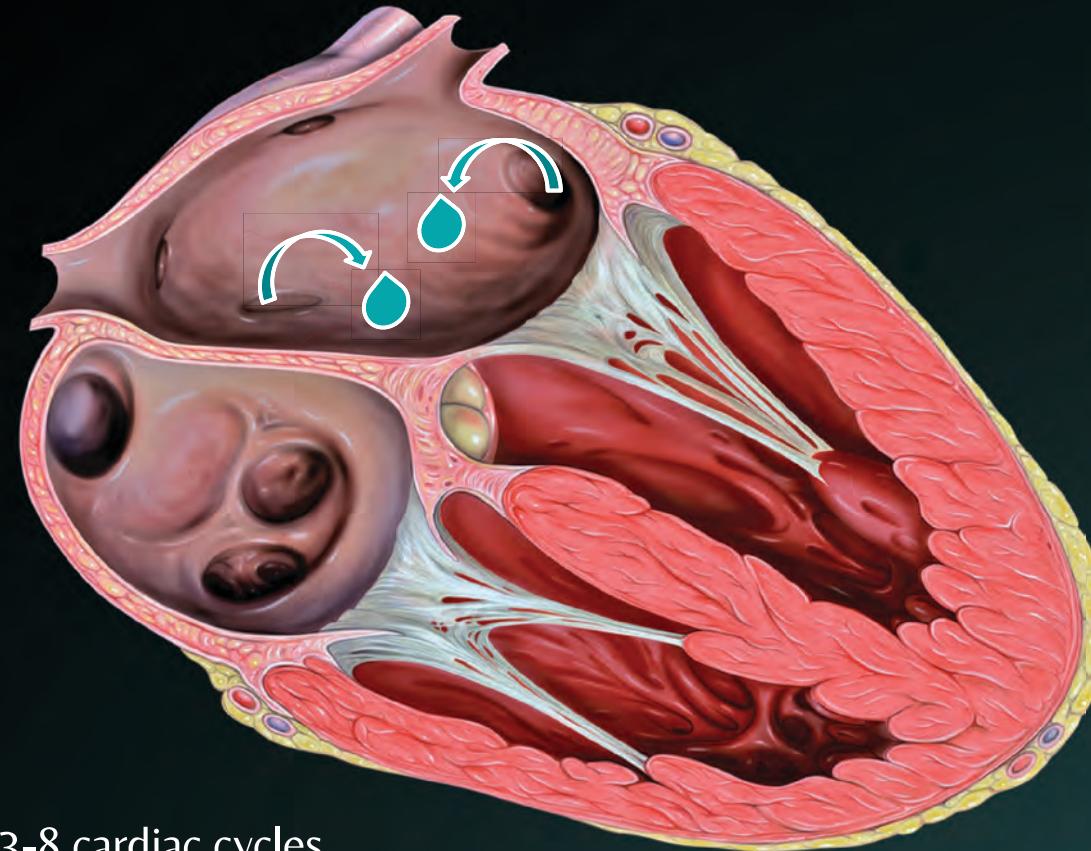
- Diagnosis of exclusion
- Poor prognosis
- Type 1 HRS aka HRS-AKI
- Type 2 HRS aka HRS-CKD
- ICU: norepinephrine + albumin +/- vasopressin
- Non-ICU: albumin + terlipressin or midodrine + octreotide
- TIPS, RRT as bridge



Hepatopulmonary Syndrome



One cardiac cycle

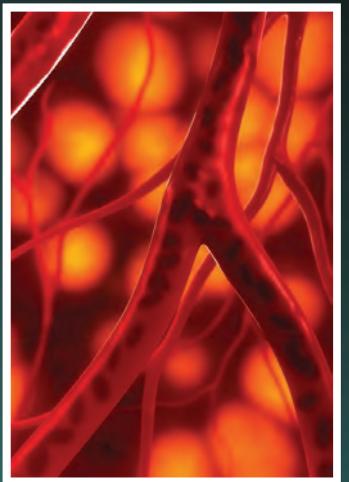


3-8 cardiac cycles

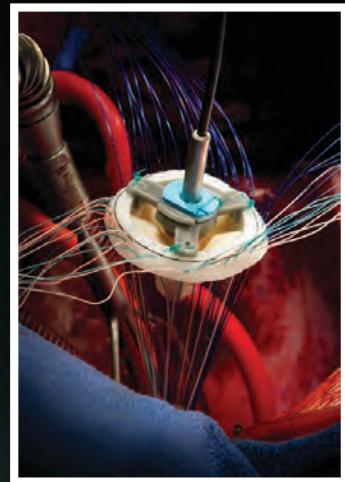
- Triad
 - Liver disease and/or portal hypertension
 - A-a gradient ≥ 15 mmHg on room air with $\text{PaO}_2 < 80$ mmHg
 - Intrapulmonary vascular dilatations (IPVD) | Intrapulmonary shunt
- Platypnea
 - Upright: increase in dyspnea
 - Recumbent: decrease in dyspnea
- Orthodeoxia:
 - Upright: decrease in PaO_2
 - Recumbent: increase in PaO_2

Portopulmonary Hypertension

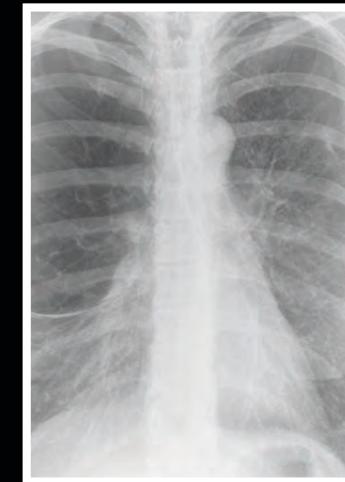
- mPAP \geq 25 mmHg + portal hypertension = portopulmonary hypertension (POPH)
- mPAP \geq 35 mmHg is a predictor of increased mortality following LT
- Screening: TTE, RVSP good estimate in diagnosing mod-severe PPHTN in absence of pulmonary stenosis
- Confirmation: RHC is the gold standard
 - Indicated if RVSP \geq 45 mmHg per AASLD
- RHC: confirm PVR \geq 240-dynes sec cm⁻⁵ m² and PCWP \leq 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

Cirrhotic Cardiomyopathy

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



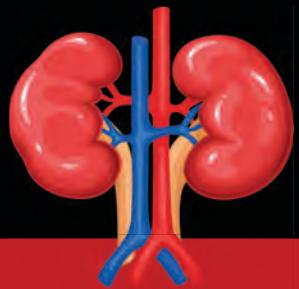
Intrahepatic Resistance
Portal Pressure
Vasodilators (NO)
Fibrosis
Endothelial Activation



Arterial Vasodilation
Splanchnic Resistance
Intravascular Volume



Cardiac Output
Heart Rate
SVR
MAP



SNS
Plasma Renin
Angiotensin II
Aldosterone

Cirrhotic Cardiomyopathy

Systolic Dysfunction
Blunted response to adrenergic stimulus
Rest LVEF <50%

Diastolic Dysfunction
Diastology on echo
LAE | LVH

Electrophysiologic Dysfunction
Prolonged QTc | LAE | LVH
BNP
Troponin

Objectives

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



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

- 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%

CAUTION

Anesthetics: Liver Disease

Benzodiazepines & Opioids

- Metabolism: hepatic
- Hypoalbuminemia: free fraction = potency
- Remifentanil cleared by nonspecific plasma esterases



Anesthetics: Liver Disease

Volatiles: preferred, eliminated primarily through respiratory system

Regional anesthesia: Coagulopathy | Thrombocytopenia

Acetaminophen: max dose 2g in 24 hours

NSAIDS should be avoided



Anesthetics: Liver Disease

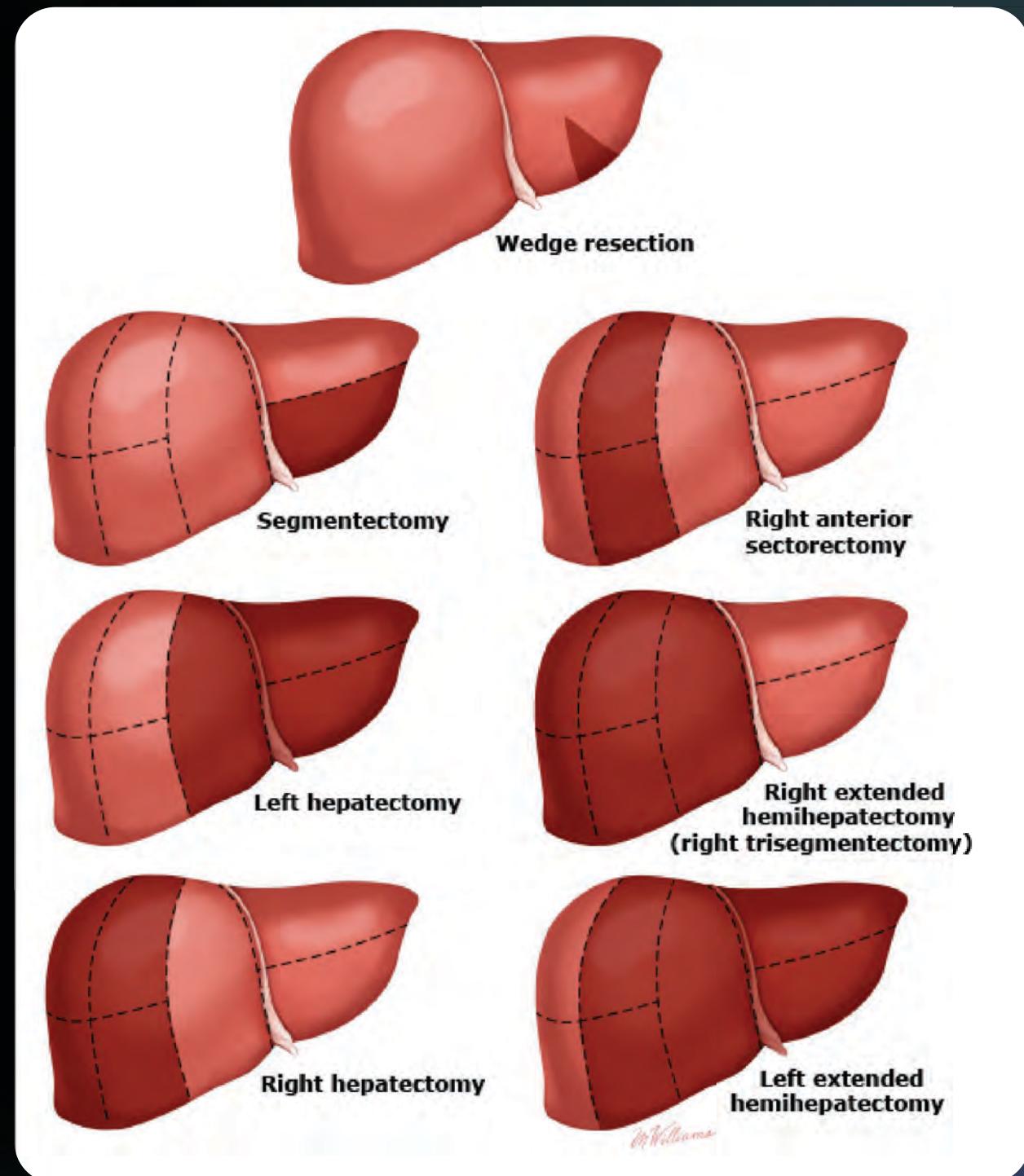


Neuromuscular blocking agents

- 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

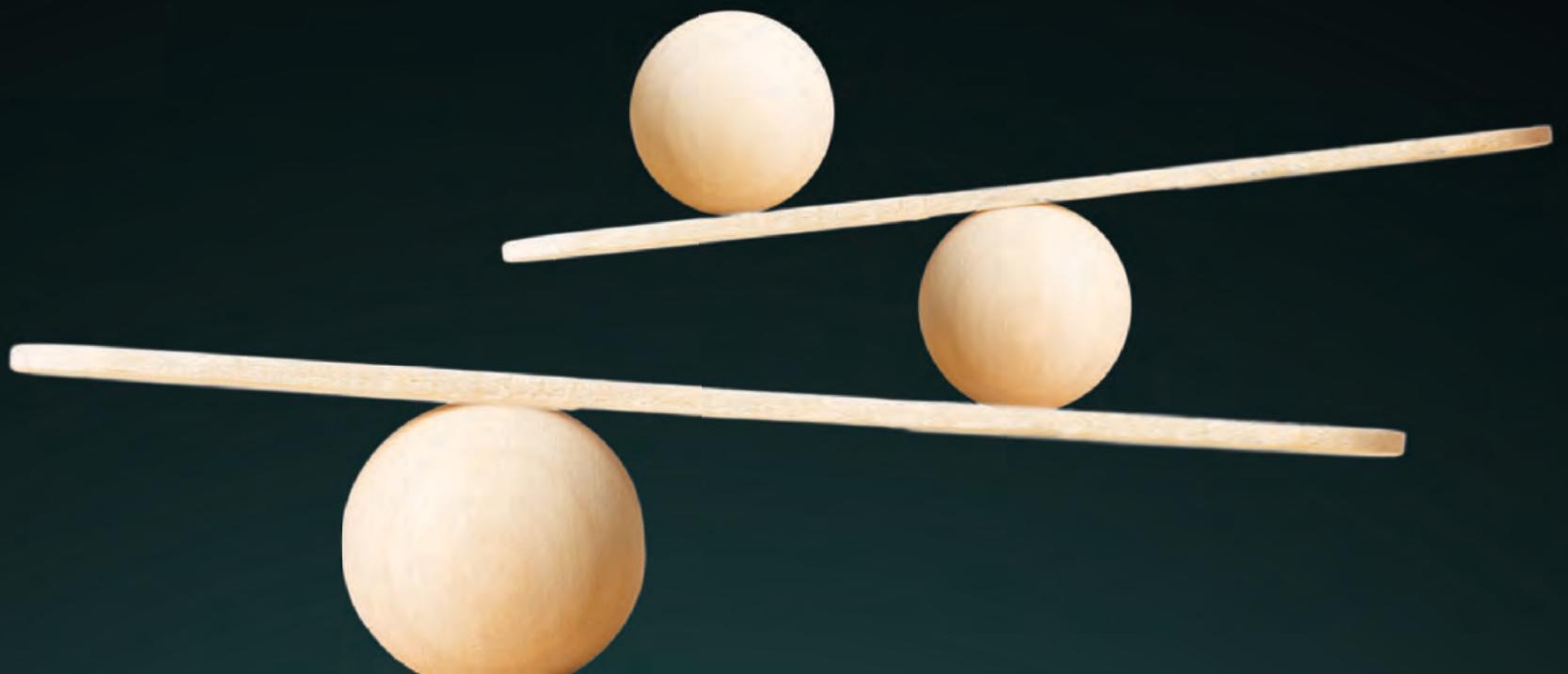
- Balance hepatic perfusion and blood loss reduction
- Decrease portal pressure with restrictive fluid therapy to minimize bleeding
- Volume expansion with albumin
- May require higher doses of vasopressors to maintain BP
- Surgical techniques to decrease blood loss
 - Total hepatic vascular exclusion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



Hemostasis

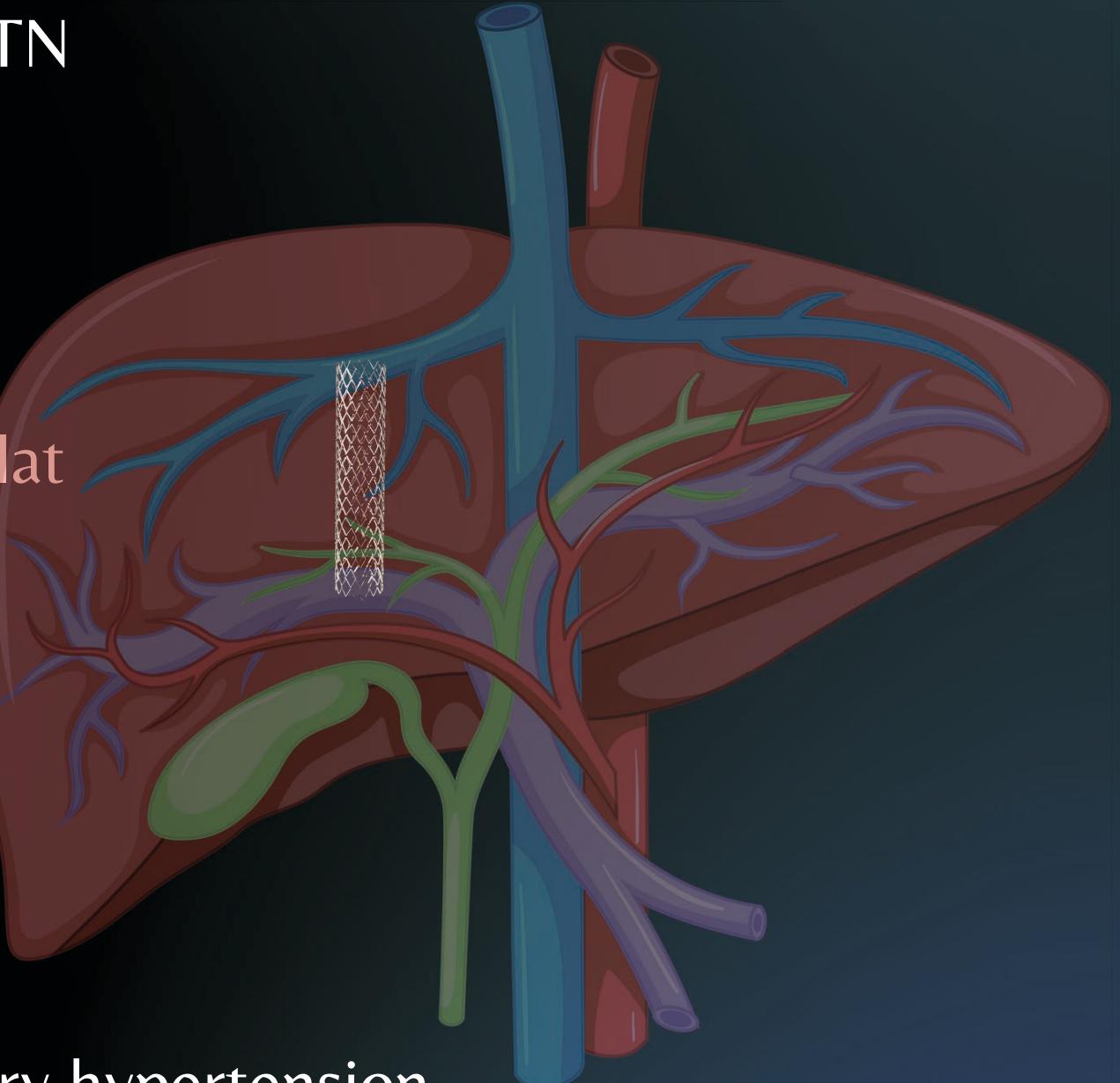
Thrombocytopenia
Decreased thrombopoietin synthesis
Decreased FII, V, VII, IX, X, and XI
Vitamin K deficiency
Dysfibrinogenemia
Increased tPA

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



Transjugular Intrahepatic Portosystemic Shunt (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

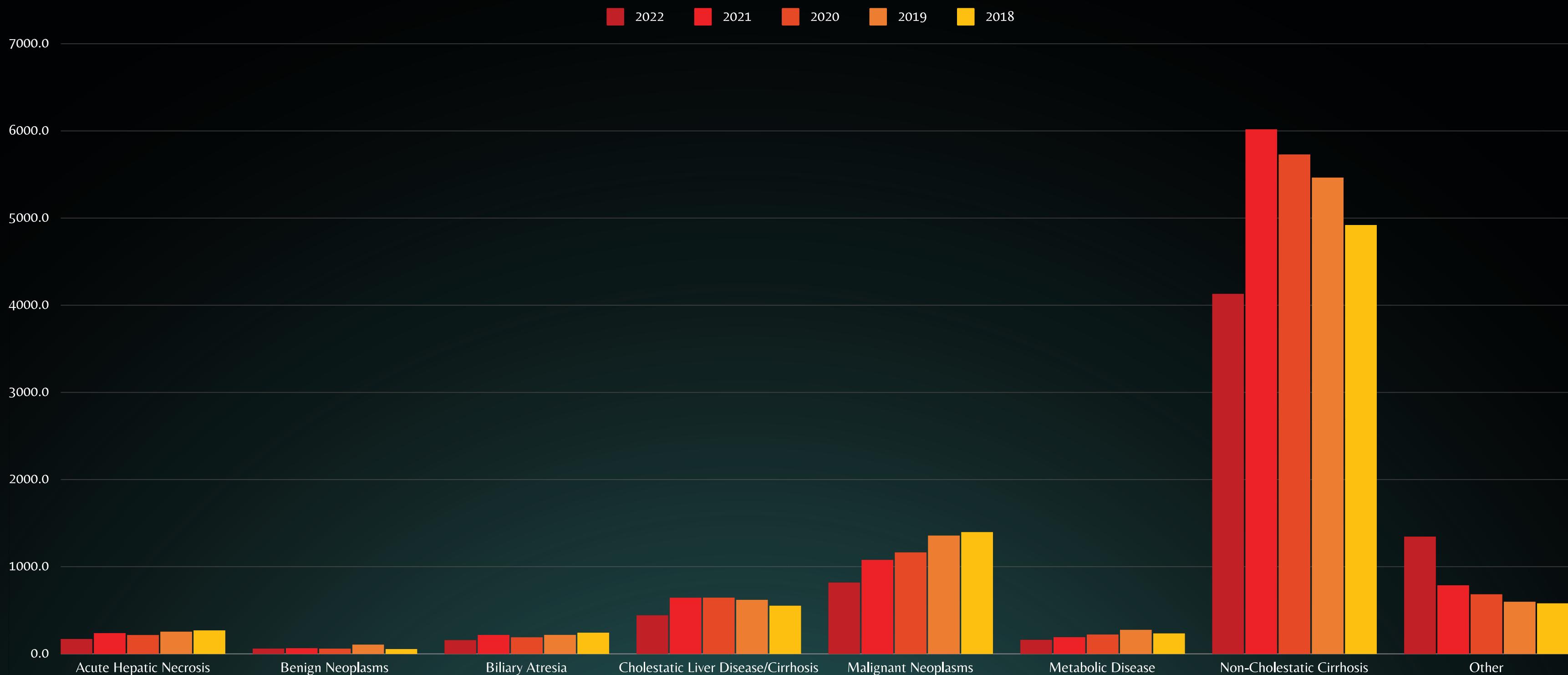


Objectives

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



Liver Transplant Indications



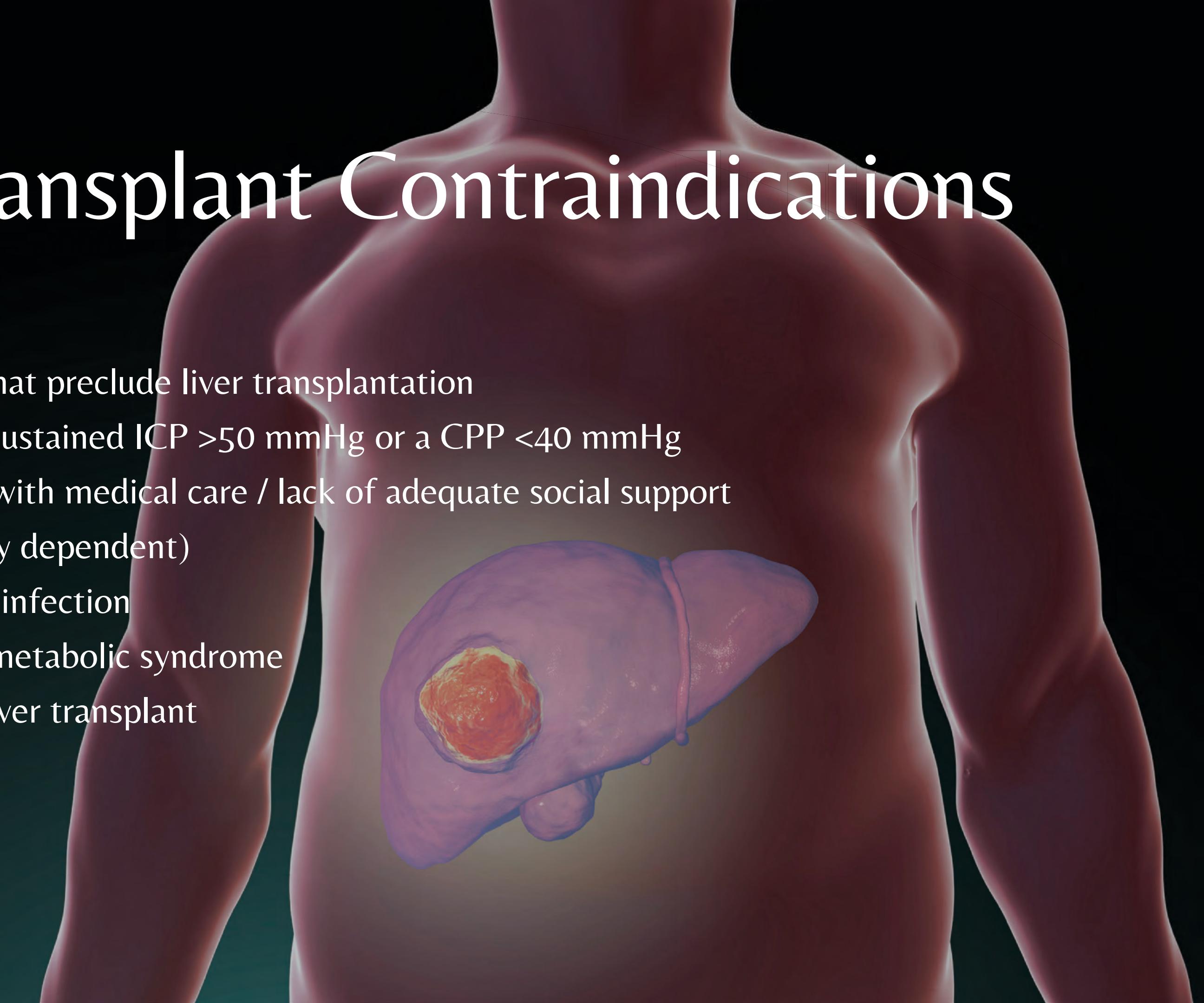
Liver Transplant Contraindications

- 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



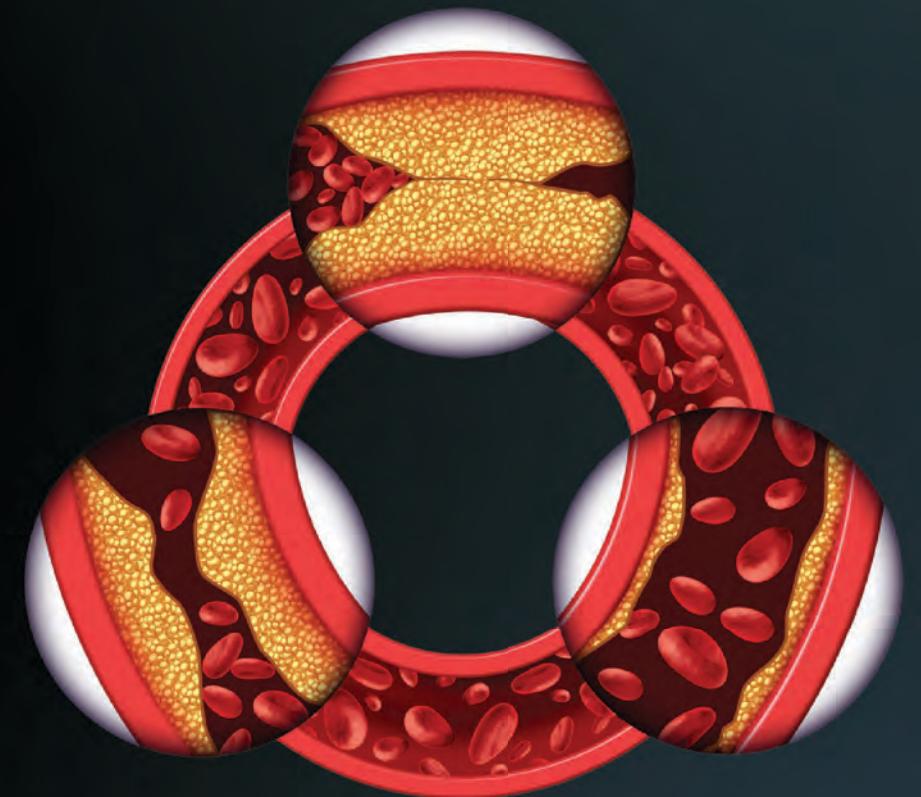
Liver Transplant Contraindications

- 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



Preoperative Evaluation

- 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

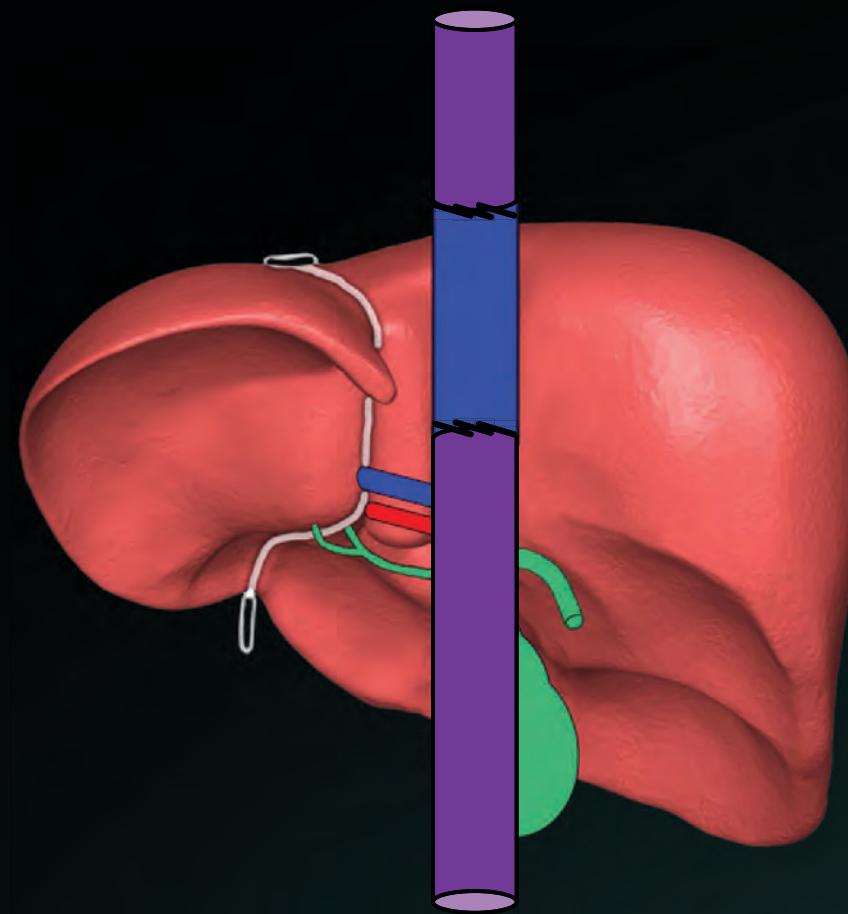
- DCD or brain death
- DCD fastest growing source of transplant organs
- Generally classified as emergent or urgent
- Recipients are older, sicker, and have multiple co-morbidities
- Expanded donor pool with marginal donors and increasing donor age

Graft Options

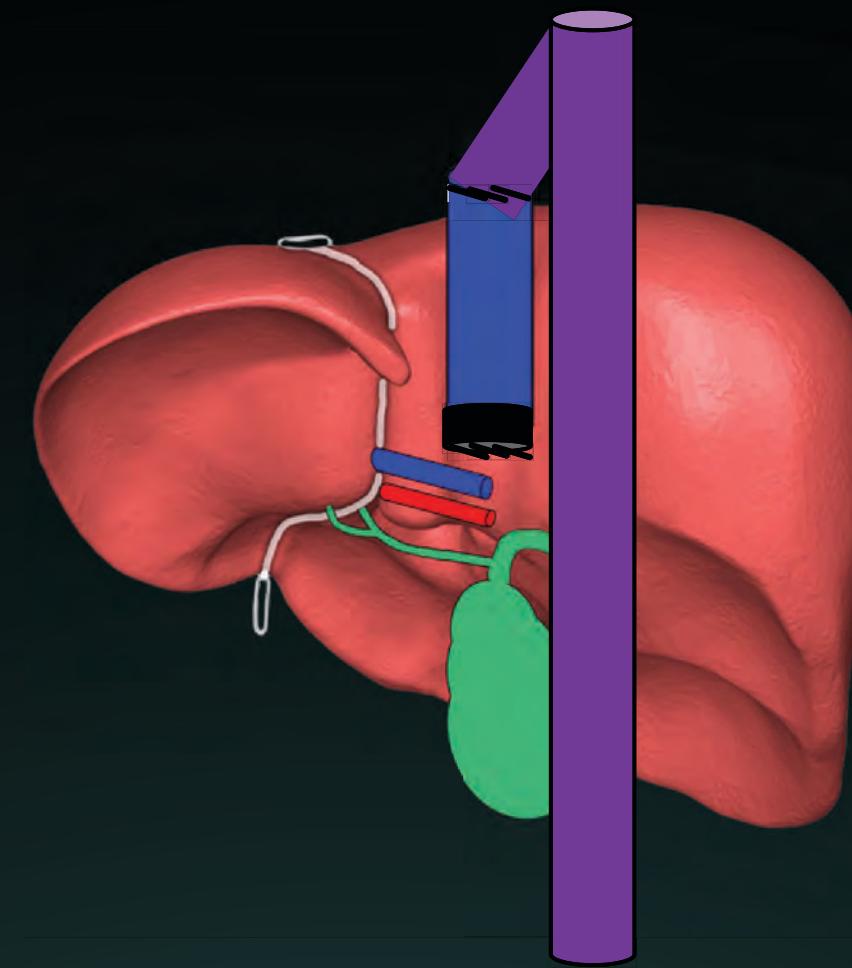
Living Donor

- 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

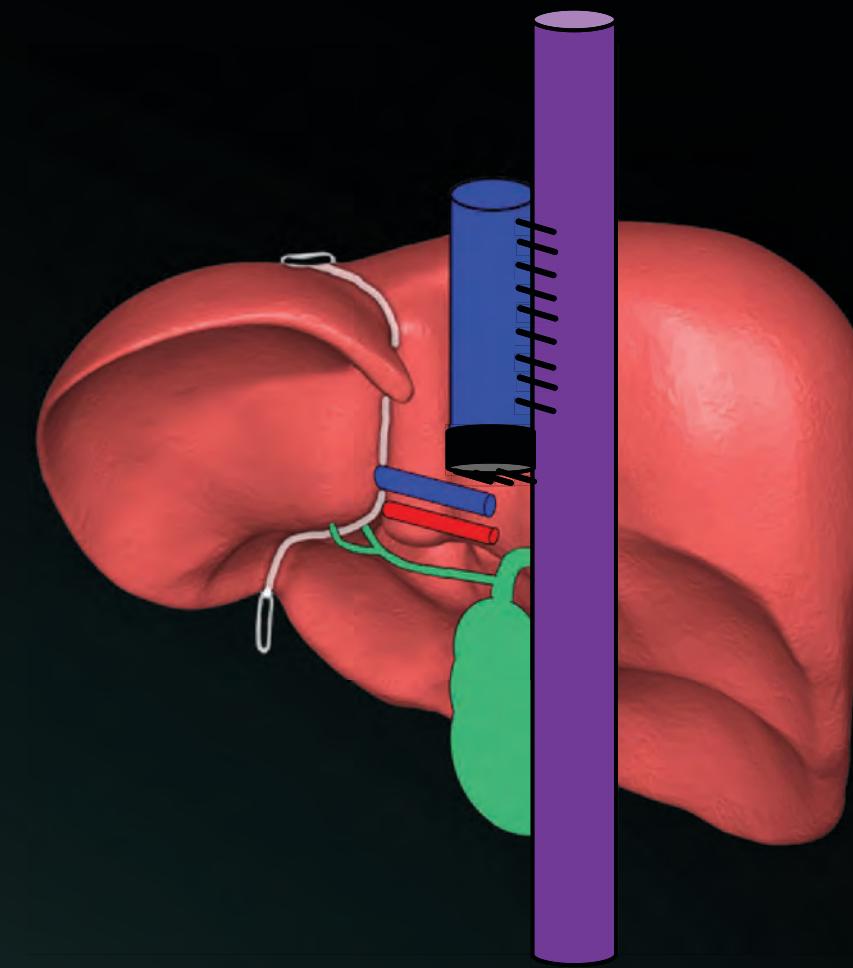
Surgical Technique



Intercaval Connection



Piggyback Technique

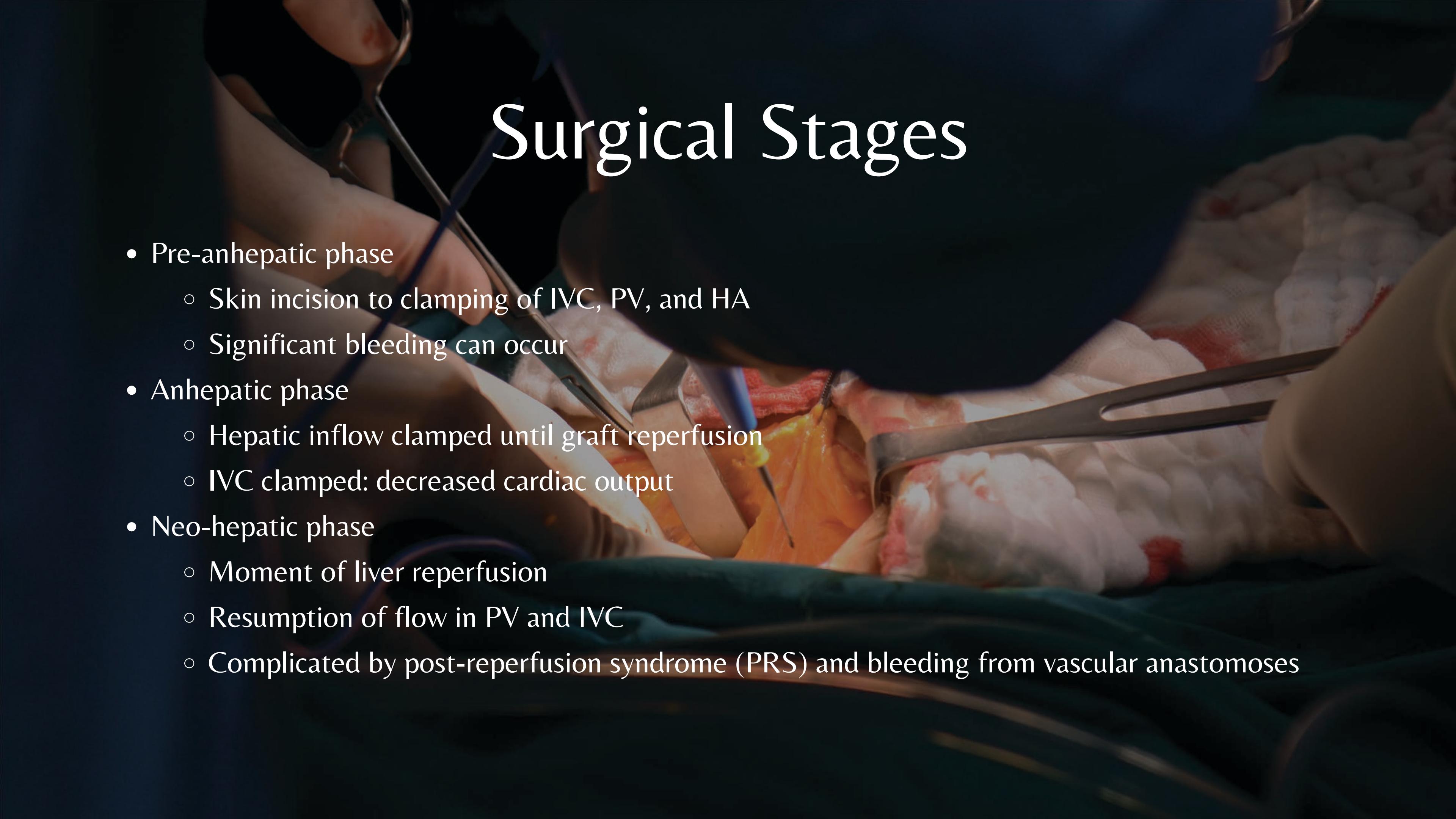


Cavo-Caval Anastomosis

Recipient IVC

Donor IVC

Surgical Stages



- 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 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

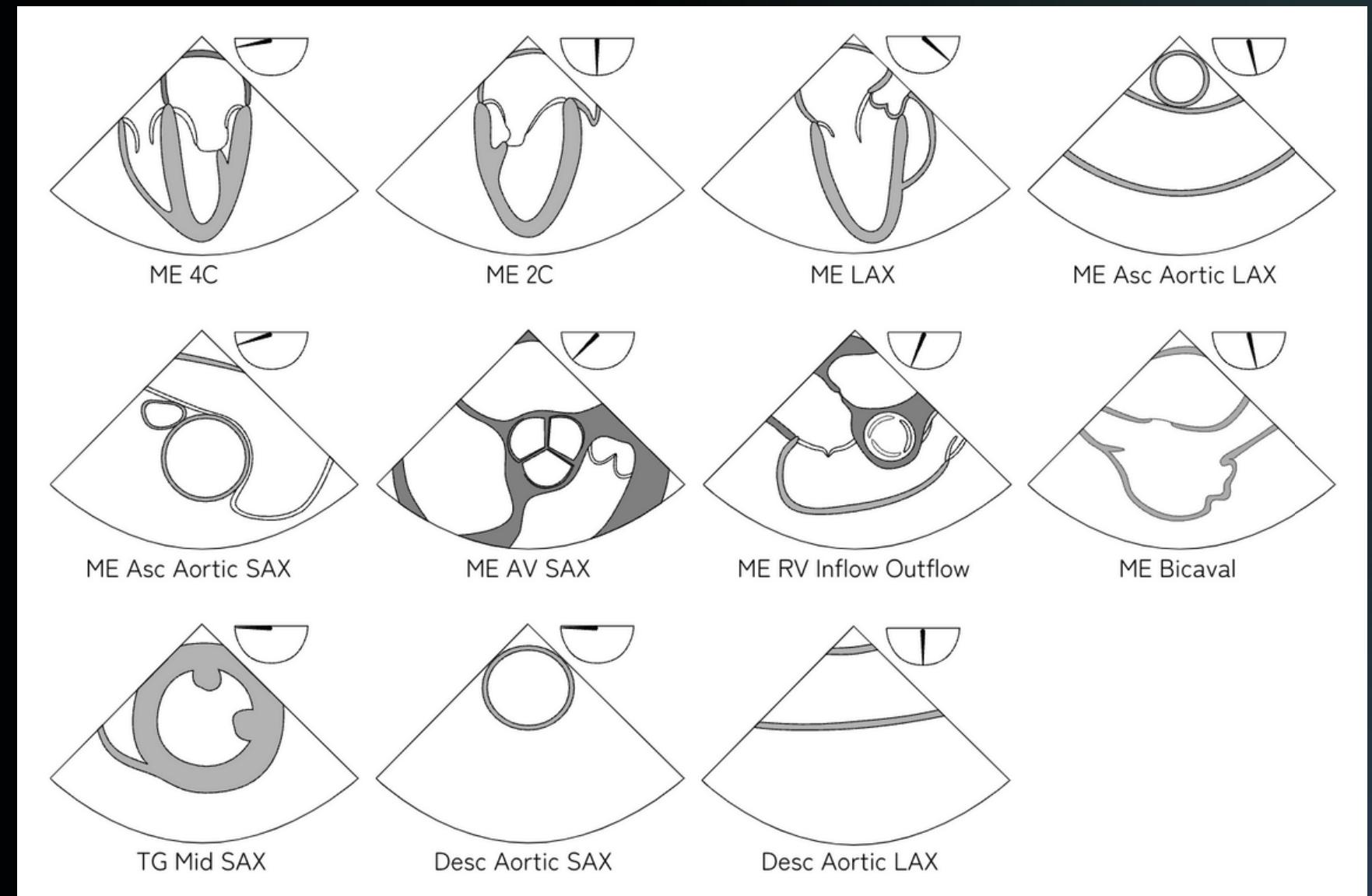
- Most challenging part – hepatic outflow obstructed and IVC may be clamped - decrease in preload, CO, and arterial pressures
- Extensive collaterals may contribute to cardiovascular stability
- Some may require surgical portosystemic shunt or portosystemic veno-venous bypass
- Total loss of liver function: 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

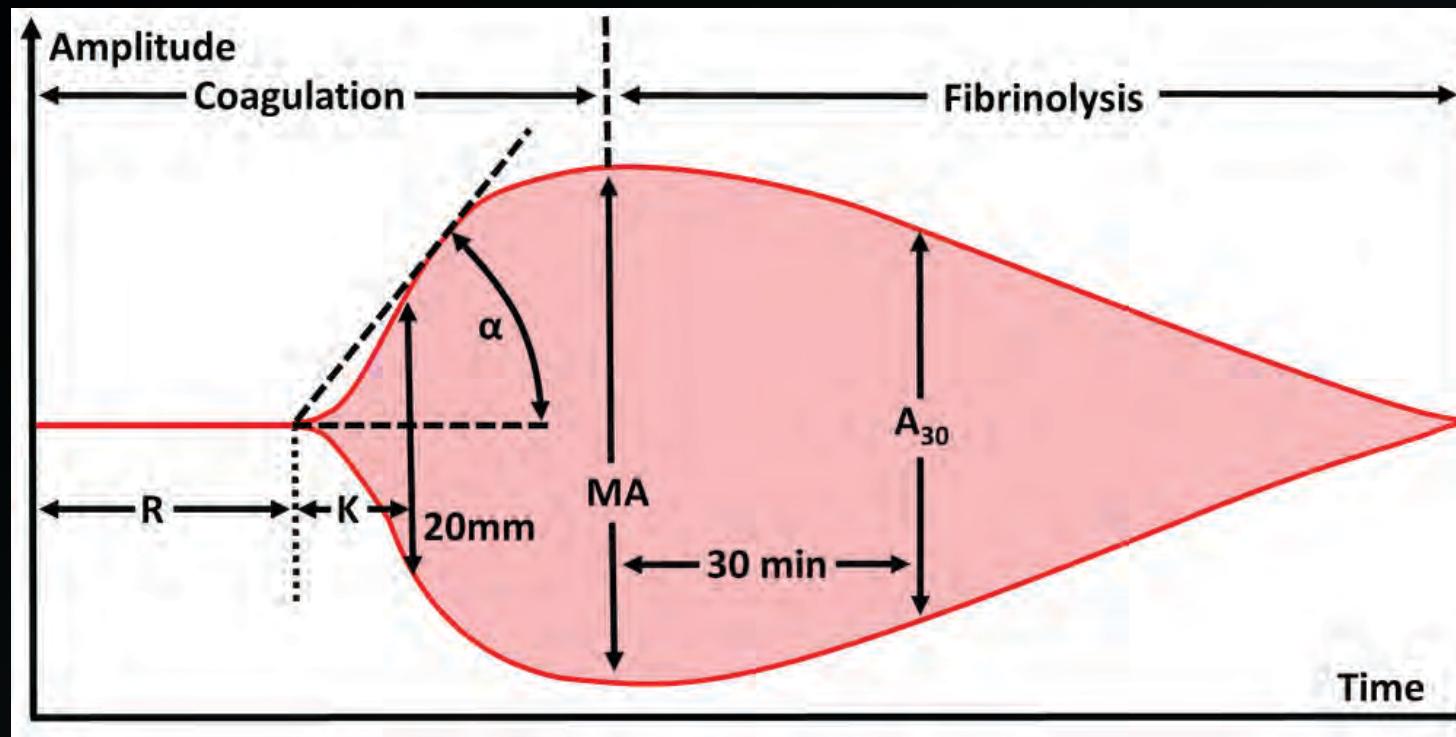
- Reperfusion: significant hemodynamic perturbations – sudden decrease in BP, HR, SVR and CO
- Can result in worsening pHTN and RV failure
- Rapid increase in K⁺ can lead to sinus arrest
- Sequestered blood from the portal and lower body venous system return to heart (no VVB)
- High K preservative solutions 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 as 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

Transesophageal Echocardiogram

- Direct visualization of heart in real time
 - Optimize euvoolemia – 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



Component	Definition	Normal Values	Problem	Treatment
R Time	Clot formation time	5-10 minutes	Coagulation Factors	FFP
K Time	Clot fixed strength	1-3 minutes	Fibrinogen	Cryoprecipitate
Alpha Angle	Fibrin accumulation speed	53-72 degrees	Fibrinogen	Cryoprecipitate
Maximum Amplitude (MA)	Highest vertical amplitude	50-70 mm	Platelets	Platelets and/or DDAVP
Lysis @30 minutes (LY30)	% amplitude reduction 30 minutes after MA	0-8%	Hyperfibrinolysis	Tranexamic Acid or Aminocaproic Acid

References

- Meirelles Júnior RF, Salvalaggio P, Rezende MB, et al. Liver transplantation: history, outcomes and perspectives. Einstein (Sao Paulo). Jan-Mar 2015;13(1):149-52. doi:10.1590/s1679-45082015rw3164
- Zarrinpar A, Busuttil RW. Liver transplantation: past, present and future. Nature Reviews Gastroenterology & Hepatology. 2013;10(7):434-440. doi:10.1038/nrgastro.2013.88
- Kaur H, Premkumar M. Diagnosis and Management of Cirrhotic Cardiomyopathy. Journal of Clinical and Experimental Hepatology. 2022;12(1):186-199. doi:10.1016/j.jceh.2021.08.016
- Gines P, Sola E, Angeli P, Wong F, Nadim MK, Kamath PS. Hepatorenal syndrome. Nat Rev Dis Primers. Sep 13, 2018;4(1):23. doi:10.1038/s41572-018-0022-7
- Weinfurtner K, Forde K. Hepatopulmonary Syndrome and Portopulmonary Hypertension: Current Status and Implications for Liver Transplantation. Current Hepatology Reports. 09/01 2020;19doi:10.1007/s11901-020-00532-y
- De Pietri L, Mocchegiani F, Leuzzi C, Montalti R, Vivarelli M, Agnoletti V. Transoesophageal echocardiography during liver transplantation. World J Hepatol. Oct 18, 2015;7(23):2432-48. doi:10.4254/wjh.v7.i23.2432
- Peiris P, Pai SL, Aniskevich S, 3rd, et al. Intracardiac thrombosis during liver transplant: A 17-year single-institution study. Liver Transpl. Oct 2015;21(10):1280-5. doi:10.1002/lt.24161

References

- Raevens S, Geerts A, Van Steenkiste C, Verhelst X, Van Vlierberghe H, Colle I. Hepatopulmonary syndrome and portopulmonary hypertension: recent knowledge in pathogenesis and overview of clinical assessment. *Liver International*. 2015;35(6):1646-1660. doi:10.1111/liv.12791
- Offer J, Green L, Houghton AR, Campbell J. A case of hepatopulmonary syndrome. *Echo Research and Practice*. 2015;2(2):K25-K27. doi:10.1530/erp-14-0100
- Hassoun PM. Pulmonary Arterial Hypertension. *N Engl J Med*. Dec 16 2021;385(25):2361-2376. doi:10.1056/NEJMra2000348
- Lee WS, Wong SY, Ivy DD, Sokol RJ. Hepatopulmonary Syndrome and Portopulmonary Hypertension in Children: Recent Advances in Diagnosis and Management. *The Journal of Pediatrics*. 2018;196:14-21.e1. doi:10.1016/j.jpeds.2017.12.068
- Wiese S, Hove JD, Bendtsen F, Moller S. Cirrhotic cardiomyopathy: pathogenesis and clinical relevance. *Nat Rev Gastroenterol Hepatol*. Mar 2014;11(3):177-86. doi:10.1038/nrgastro.2013.210
- Moller S, Danielsen KV, Wiese S, Hove JD, Bendtsen F. An update on cirrhotic cardiomyopathy. *Expert Rev Gastroenterol Hepatol*. May 2019;13(5):497-505. doi:10.1080/17474124.2019.1587293
- Groves H, del Rio Martin JV. Surgical Techniques in Liver Transplantation. In: Wagener G, ed. *Liver Anesthesiology and Critical Care Medicine*. Springer International Publishing; 2018:121-133.

References

- Sanyal R, Lall CG, Lamba R, et al. Orthotopic Liver Transplantation: Reversible Doppler US Findings in the Immediate Postoperative Period. *RadioGraphics*. 2012;32(1):199-211. doi:10.1148/rg.321115006
- Aniskevich S, Pai SL. Fast track anesthesia for liver transplantation: Review of the current practice. *World J Hepatol*. Sep 18, 2015;7(20):2303-8. doi:10.4254/wjh.v7.i20.2303
- Brezeanu LN, Brezeanu RC, Diculescu M, Droc G. Anaesthesia for Liver Transplantation: An Update. *J Crit Care Med (Targu Mures)*. Apr 2020;6(2):91-100. doi:10.2478/jccm-2020-0011
- Washburn WK, Lewis WD, Jenkins RL. Percutaneous venovenous bypass in orthotopic liver transplantation. *Liver transplantation and surgery : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society*. 1995;1 6:377-82.
- Gilbert-Kawai N, Hogan B, Milan Z. Perioperative management of patients with liver disease. *BJA Educ*. Mar 2022;22(3):111-117. doi:10.1016/j.bjae.2021.11.006
- Bhogal HK, Sanyal AJ. Transjugular intrahepatic portosystemic shunt: An overview. *Clinical Liver Disease*. 2012;1(5):173-176. doi:10.1002/cld.96
- Tyler PD, Yang LM, Snider SB, Lerner AB, Aird WC, Shapiro NI. New Uses for Thromboelastography and Other Forms of Viscoelastic Monitoring in the Emergency Department: A Narrative Review. *Annals of Emergency Medicine*. 2021;77(3):357-366. doi:10.1016/j.annemergmed.2020.07.026

References

- Bhogal HK, Sanyal AJ. Transjugular intrahepatic portosystemic shunt: An overview. *Clinical Liver Disease*. 2012;1(5):173-176. doi:10.1002/cld.96
- Tyler PD, Yang LM, Snider SB, Lerner AB, Aird WC, Shapiro NI. New Uses for Thromboelastography and Other Forms of Viscoelastic Monitoring in the Emergency Department: A Narrative Review. *Annals of Emergency Medicine*. 2021;77(3):357-366. doi:10.1016/j.annemergmed.2020.07.026
- Ahmad S, Hunt BJ. Coagulopathy of Liver Disease. In: Gonzalez E, Moore HB, Moore EE, eds. *Trauma Induced Coagulopathy*. Springer International Publishing; 2016:471-482.
- Manion SC, Brennan TJ, Riou B. Thoracic Epidural Analgesia and Acute Pain Management. *Anesthesiology*. 2011;115(1):181-188. doi:10.1097/ALN.0b013e318220847c
- Wall WJ. Liver Transplantation for Polycystic Liver Disease. *New England Journal of Medicine*. 2007;356(15):1560-1560. doi:10.1056/nejmcm055470
- Mendirichaga R, Fishman JE, Martinez CA. Chapter 7 - Imaging Modalities for Detection and Treatment of Cardiovascular Thrombus. In: Topaz O, ed. *Cardiovascular Thrombus*. Academic Press; 2018:99-113.
- Miller's Anesthesia, 9th Edition
- UpToDate