Blood Products (Products present in room should be checked early)

10U PRBC, in room

10U FFP, in room

Platelets and Cryoprecipitate do not need to be prepared at beginning of case, but be vigilant about need and give adequate time for blood bank to prepare. Most likely will be required in neohepatic phase.

Intraoperative: Timing of operating room should be discussed with surgeon, recognizing time needed for line placement and possible difficulties in placement.

Lab Monitoring during intraoperative period (Make sure adequate tubes are available):

Frequency based on clinical context and attending management. However baseline laboratory values should be sent early on for all labs and repeat should be done during neohepatic phase

ABG with Lactate

CBC

Coagulation studies (PT, PTT, and Fibrinogen)

TEG

Additional Monitoring:

Liver Function Tests during Neohepatic Phase

Induction: Once the patient is moved onto the operating room bed, defibrillation pads should be placed. Induction is at the discretion of the attending anesthesiologist, as is maintenance of anesthetic. Line placement is done after induction, specific lines will be planned prior during discussion between surgical and anesthesiology attendings. R IJ reserved for VV Bypass line. 2 Line minimum suggested in addition to bypass line(Introducer/Swan, plus either additional introducer or dialysis catheter) but anesthesiologist will determine final need. NG tube should be placed early on, verification by surgery. Baseline laboratory values can be sent during this time, organize setup, check blood products. Check to make sure antibiotics and steroids have been given, also verify other immunosuppression has been given in appropriate time frame.

Preanhepatic Phase: Incision -> Removal of native liver. Monitor pH, electrolytes, blood loss, and any coagulation defects. Baseline laboratory values should be sent including ABG, CBC and Coagulation studies (PT, PTT, Fibrinogen, TEG). While adequate MAP needs to be maintained, volume overload will cause hepatic congestion that can lead to worsening bleeding and hepatic function of the new liver. Judicious fluid management should be utilized. If VV bypass is to be utilized, it will be hooked up during this period. Discuss any planned IV Heparin utilization.

Anhepatic Phase: Clamping of hepatic vessels -> Reperfusion of donor liver. Issues include hemorrhage, coagulopathy, fibrinolysis, acidosis, hypothermia, and renal dysfunction. As in prehepatic phase, acidosis, hypocalcemia, glucose, coagulation, and other electrolyte abnormalities should be treated. Judicious management of fibrinolysis should be considered, especially during VV bypass due to embolism risk. Surgeon will hand sterile tubing during this period for hooking up to Liver Flush described above, place on pressure bag, open when required.

NeoHepatic: Reperfusion of new liver can lead to significant hemodynamic instability. Prior to reperfusion optimize pH, electrolytes, and MAP. Reperfusion can lead to significant acidemia, hyperkalemia, and hypotension/dysrhythmias all contributing to possible cardiac arrest. Volume, vasopressors, calcium, and bicarbonate should all be prepared for utilization prior and during reperfusion. Once reperfusion has passed and bile duct reconstruction begins, continue to monitor liver function while optimizing MAP, hemoglobin, and coagulation status. Labs should be sent to monitor these parameters including CBC, PT, PTT, Fibrinogen, ABG, LFTs, and TEG. Lasix might be utilized at this time to help reduce hepatic congestion. Repeat dosing of antibiotics and steroids should be given. Check with surgeon concerning immunosuppressant utilization.

Post-Operative Considerations: ICU bed should be present with monitor for transport. ICU should be aware and prepared for patient including post-operative ventilator requirements. VV Bypass line should be removed prior to transport to ICU. All blood products should be transferred from operating room to ICU for further utilization.

A Review Of Anesthesia for Liver Transplantation

- ESLD a complex multisystem abnormality is present
- Pre-transplant patients with critical illness are higher on waiting list
- Contraindicator to LT include
- Sepsis, ARDS, metastatic CA
  M.I. or Cerebral Disease

- Pulmonary Hypertension severity is a single direct indicator of intraoperative mortality risk, overshadows other hepatic diseases

- Organ Systems involved include:

- Cardiovascular
- Pulmonary:
- Parenchymal and Vascular
- Central Nervous System
- Renal
- Gastro Intestinal
- Metabolic
- Hemotalogic / hemostatic
- Psychological

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

Multi Organ System Abnormality In End Stage Liver Disease

CARDIO VASCULAR SYSTEM

- Hyper dynamic circulation in Cirrhosis 30%-60% Rakela J etal *Hepatology 1990*
- Cardiac Output >9-10 L/min
- Tachycardia
- Low Vascular Resistance
- Lower Blood Pressure

- ISHD increases with age >50

  5% - 27% Grose, RD etal *J. Hepatology 26:326 1995*

  Diabetes is a major risk factor

PULMONARY SYSTEM

Parenchymal Disease

- Atalectasis
- Obstructive airway disease
- Pneumonia, aspiration
- Pleural effusion
- Decreased lung volume, ascites

Vascular Disease

- Intrapulmonary Vasodilation

  Shunting, elevated SVO2
- Pulmonary Hypertension
  - **mPAP >25mmHg, PAWP <15mmHg**
  - **PVR > 120 dynes/cm**
- Hepatopulmonary Syndrome

  Hypoxemia with Intra Pulmonary Vasodilation

  Lack of oxygen diffusion at capillary level

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review.* Ch9, 2001

Multi Organ System Abnormality In End Stage Liver Disease Continued

CENTRAL NERVOUS SYSTEM

- Porto Systemic Encephalopathy:
  Acute hepatic failure associated with Intracranial Hypertension
- Chronic ESLD not necessarily associated with elevated ICP

RENAL SYSTEM

- Hepato Renal Syndrome
- Inappropriate water retention
- Renal vasoconstriction
- Renal Insufficiency:
  - **Inappropriate ADH secretion**
  - **Renin Angiotensin Aldosterone System**
  - **Prostaglandin Release**
  - **Sympathetic Nervous system alteration**
- HRS reverses after Liver Transplant
- Renal and Liver Transplantation improves outcomes.

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

Multi Organ System Abnormality In End Stage Liver Disease Continued

- GASTRO INTESTINAL SYSTEM
- Gastro esophageal varices
- Porto systemic shunting due to the cirrhosis
- Ascites
- Rapid sequence induction to GA

- COAGULOPATHY
- Liver is source pro-coagulants and anticoagulants

  Surgical Bleeding with poor clotting
- Thrombocytopenia

  Platelet sequestration in spleen due to portal hypertension

  Platelet Goal is >50,000/mm2
- Hyperfibrinolysis 10-20% Kang, Y *Anesthesiology 1987*

  Elevated tPA levels

  Low liver clearace of tPA
- Antifibrinolytic reduce surgical bleeding

  Heparin dose 3,000 units IV –Phase 1

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

LIVER TRANSPLANTATION PROCEDURE

- THREE PHASE SURGICAL PROCEDURE

- Pre- Anhepatic - Phase One 2-3 hours
  Induction GA , line placement, Skin incision to native liver removal

- Anhepatic – Phase Two 45 min to 1 hour
  Porto caval cross clamp to anastamosis and reperfusion of graft

- Post Graft Perfusion - Phase Three 5 to 7 hours
  Begins after graft reperfusion, homeostasis, biliary drainage, closure

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

LIVER TRANSPLANTATION - PHASE ONE

Anesthesia Management Plan

- Review PreOperative Assessment
- Patents arrive from home, admitted to nursing unit then to OR
- One PIV
- Premedication – Versed, Bicitra
- Rapid sequence Induction

Anesthesia Equipment Setup

- Team Assembly of monitors/OR
- Dedicated Surgical Suite
- Blood Bank Coordination
- Invasive monitoring lines placed after Induction of GA
- Tran Esophageal Echocardiography
- Rapid Infuser System used - Belmont

Phase One: Anesthesia Goals

- Maintain normothermia
- Optimize hemodynamic values
- Optimize laboratory values
- Renal perfusion and output
- Normal to Lower CVP
- Transfuse blood products
  Hemoglobin goal: 10 gm/dl
- Normosol IVF hydration (3-4L)
- Colloid use dependant upon case

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

LIVER TRANSPLANTATION - PHASE TWO

Anesthesia Management Plan

- Prepare for graft reperfusion
- Normovolemia
- Normal Lab Values
  - K+, Ca++, HbG, Ph, glucose
- "Venting" the graft possible
  500cc blood loss may lower PRS

Fresh Frozen Plasma

PRBC transfusion

Avoid Volume Overload:

Low dose vasopressor used:

Norepinephrine infusion 1-3 mcg/mn

- Post Reperfusion Syndrome
- Hypotension
- >30% decrease MAP Aggarwal, *Trans Proc. 1989*
- MAP < 60mmHg Gabrial, etal *Transplantation. 1993*
- Incidence PRS 8-30% Aggarwal, *Trans Proc. 1989*
- Arrhythmia – Bradycardia, Asystole

PRS symptoms worsened with :

- Hyperkalemia
- Acidosis and Hypocalemia
- Hyperglycemia >150 Gm/dl
- cerebral ischemia risk

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

LIVER TRANSPLANTATION - PHASE THREE

Anesthesia Management Plan

- Optimize physiology:
  - Hemodynamic Variables
  - Hematologic/Lab Values
    - Platelets
    - Cryoprecipitate
- Consider Post GA Management
  - SICU admission
- Analgesia considerations

  Fentanyl 20-40 mcg

Anesthesia Goal = hemostasis

- Coagulopathy predominates
- Fibrinolysis,elevated tPA Porte, *Transplant Proc.* 1989
- New graft release heparin Chapin, *Transpl Proc.* 1993
- Decrease FI,V,VIII, excess plasmin because of elevated tPA

Generalized proteolytic activity

Legnani, *transplantation.* 1993

Maintain Control of:

-Hypothermia

-Hypocalcemia

-Acidosis

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review.* Ch9, 2001

Successful liver transplant graft acceptance during Phase Three is characterized by:

- Citrate is metabolized, so calcium level stabilizes
- Acidosis and hypothermia improve
- Glucose level normalize
- ProThrombin Time /Partial ThromboplastinTime /Fibrinogen improve
- Thromboelastography trace is normal
- Full, non engorged surgical appearance of graft
- Urine output improves

- Thromboelastography is a useful intraoperative measure

Schwart, AJ, Majasko, MJ, Otto, CW. *ASA Review*. Ch9, 2001

REVIEW OF MEDICAL CARE OF LIVER TRANSPLANT RECIPIENT

- 30 year post transplant life Desai, *Liver Trans* 2008
- Improvement in long term survival
- General Long term Complications
  is not unlike our own

Challenge of health maintenance Gaglio 2008

- Regular Medical Checkups
- Follow lab values, glucose screens
- Regular Dental care
- Chest X-Rays
- Bone Mineral Density Testing
- Flu Shots, pneumovax
- Colonoscopy
- Blood pressure screening
- Take medications as ordered

Rule of Twos

- 2 days, 2 weeks, 2 months, 2 years

- Most Common complications:
- Osteoporosis
- Immunosuppressant complications
- Infections
- Neoplasm
- Recurrence of primary liver disease
  - Hepatitis
  - Cirrhosis
  - Vanishing bile duct syndrome

*Gaglio, R, Brown, R, Kaplan, Bonis. Medical Care of LT Recipient *UpToDate*. 2008

IMMUNOSUPPRESSION COMPLICATIONS IN POST LIVER TRANSPLANT PATIENTS

- Immunosuppresive therapy

Reduce rejection of transplant Liver

- Immediate Post Op period:
- Calcineurin Inhibitor (CNI)
  - CycosporinA (CYA)
  - Tacrolimus (TAC)

  Inactivates calcineurin, blocks tCell signaliing
  Mnimizes tCell activation, modulate FB Recogn.
- Azathioprine or
  - Microphenalate mofetil
- Glucocorticoid, like Prednisone
- MonoTherapy after 6 months - CNI

Glucocorticoid side effects

- Hypertension,
- Hyperlipedemia, glucose intolerance, infection, bone abnormality,
- Peptic Ulcer Disease,
- Psychological abnormality

Immunosuppressive side effects

- Hypertension – Ca Ch Blocker, BB
  - Avoid diuretics
- Hyperlipidemia –statin, diet control
- Diabetes 13%-25% John, P. 8:708 *Liver Transpl.* 2002

Gaglio, R, Brown, R, Kaplan, Bonis. Medical Care of LT Recipient *UpToDate. 2008*

Treatment of Complications After Liver Transplantation

Refer Patient to a Transplant Center

Other complications include:

- Obesity
- ISHD, CAD
- Renal Insufficiency
- Osteoporosis
- Chronic Rejection starts 2wk -2mos
  "Vanishing Bile Duct Syndrome "

- Elevated Liver Function Tests
  Increase in serum transaminase
- AST, ALT. bilirubin, alkaline phos.
- Malignancy - de novo neoplasia
- Hepatocellular carcinoma

- Recurrence of primary disease

Congential Disease:

- Biliary atresia, Polycystic Liver Disease, idiopathic fibrosis

Metabolic Disease:

- Wilson's, alpha1 antitripsin defic.
- Biliary cirrhosis
- Primary schlerosing cholangitis
- Autoimmune hepatitis
- Non Alcoholic fatty liver disease
- Hemochromoatosis
- Alcohol associated disease
- Hepatitis B / Hepatitis C

Gaglio, R, Brown, R, Kaplan, Bonis. Medical Care of LT Recipient *UpToDate*. 2008

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LIVER TRANSPLANTATION

SURGICAL CONSIDERATIONS

.iver transplantation is the treatment of choice for patients with acute and chronic end-stage liver disease (ESLD). The liver transplant operation can be ivided into three stages:

1. hepatectomy
2. anhepatic phase, which involves the implantation of the liver
3. post-revascularization, which includes hemostasis and reconstruction of the hepatic artery and common bile duct.

here are many variations in the technical aspects of the liver transplant operation that may result in physiologic changes during anesthesia. Examples of hese variations include:

1. cross-clamping of the vena cava during the implantation of the liver, which results in impairment of the systemic venous return with subsequent profound hypotension
2. utilization of the venovenous bypass, which may be associated with thrombus, air embolism and/or fibrinolysis
3. use of a "cut-down liver," which may result in significant bleeding from the raw surface following revascularization.

The **hepatectomy** may be a formidable task in patients with severe portal HTN, coagulopathy and previous surgery in the upper abdomen. In such circumstances, blood loss is significant and may be minimized by placing the patient on venovenous bypass or by creating a temporary portocaval shunt to relieve the portal HTN.

The hepatectomy is usually much easier in patients with acute fulminant hepatitis or primary biliary cirrhosis than in patients with shrunken cirrhotic livers, such as in post-necrotic cirrhosis from hepatitis B or C, alpha-1 antirypsin deficiency or Wilson's disease, among others. In general, contributing factors associated with increased blood loss in liver transplantation include…

- Severe coagulopathy
- Severe portal HTN
- Previous surgery in the right upper quadrant
- Renal failure
- Uncontrolled sepsis
- Re-transplantation
- Transfusion reaction
- Venous bypass-induced fibrinolysis
- Primary graft non function
- Intraoperative vascular complications

The **anhepatic phase** may be associated with significant hemodynamic changes, depending on the technique used for vascular control. This stage of the operation consists of implantation of the liver allograft, with or without venovenous bypass. The use of the venovenous bypass is particularly helpful in coagulopathic patients with severe portal HTN. In these high-risk patients, the goal of the venovenous bypass system is to relieve the portal HTN by "bypassing" the liver. Cannulas, placed in the portal and femoral veins, draw the blood out of the systemic and splanchnic venous systems into a Biomedicus pump that delivers the blood into the axillary vein, maintaining the venous return.

This system allows the interruption of the vena cava with mild-to- moderate hemodynamic changes, depending on the blood flow rate through the system. The benefits and potential complications of the venovenous bypass system are listed below. Wound complications and nerve injuries may be prevented by introducing the bypass cannulas percutaneously rather than approaching the vessels through a surgical incision.

Benefits and Potential Complications of the Venovenous Bypass System

Benefits

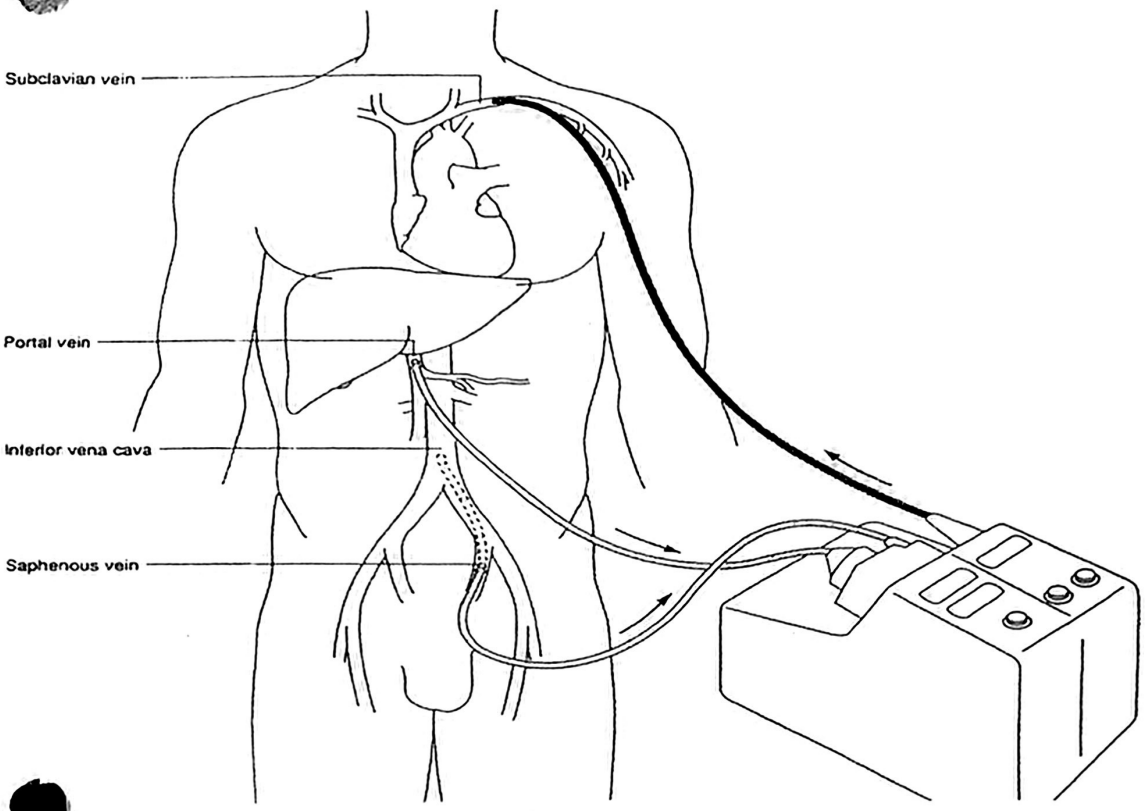
- *Improved hemodynamics during anhepatic phase due to maintenance of venous return from the lower extremities and portal circulation.*
- *↓Portal HTN ☐ ↓Blood loss ☐ ↓transfusion requirements*
- *Decreased intestinal edema ☐ improved surgical exposure of the liver bed.*
- *May improve perioperative renal function* ☐ improved venous drainage from the kidneys allowing urine production through maintenance of the trans-glomerular pressure gradient*

**In a prospective randomized trial comparing venovenous bypass with no bypass, no difference was found in the perioperative renal function between the two groups.*

Complications

- *PE/Air Embolism*

- *Brachial Plexus Injury*
- *Wound seroma/infection*



Setup for Venovenous Bypass During Hepatic Transplantation

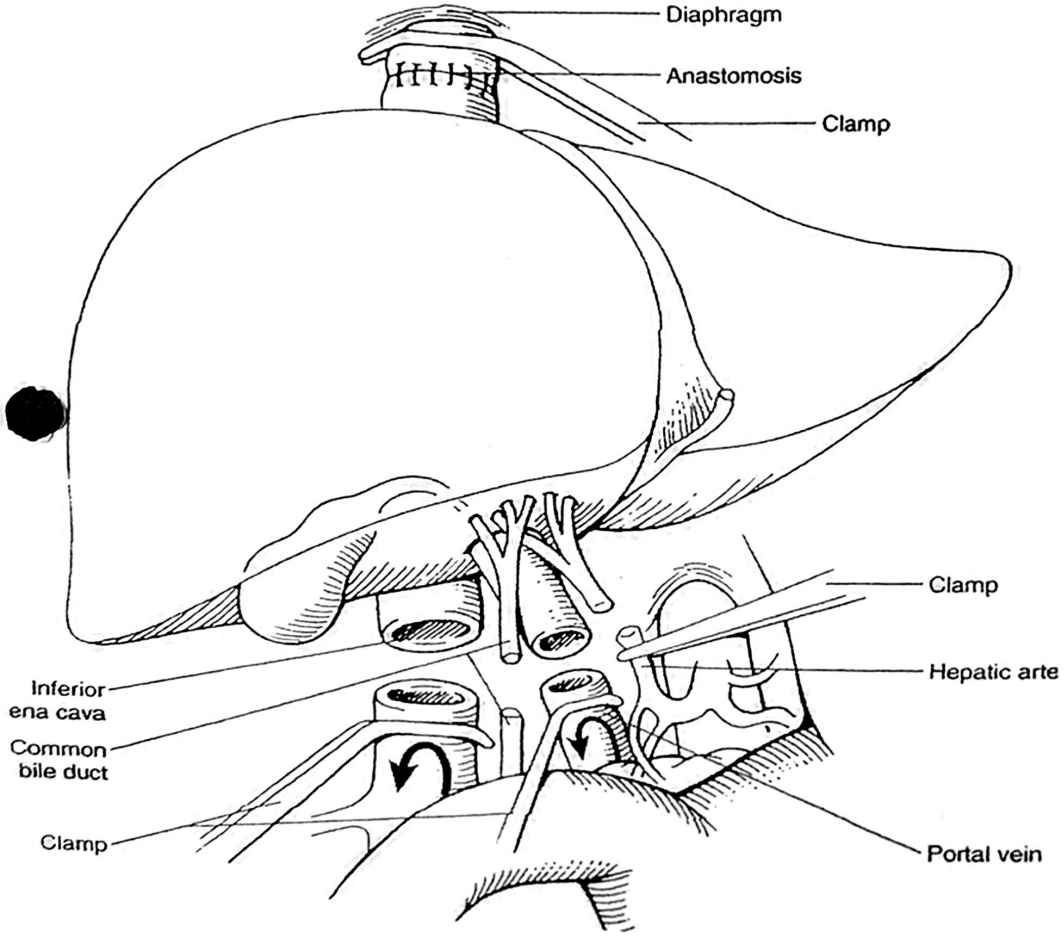
Cannulas are placed into the portal vein to decom press the splanchnic bed and inferior vena cava (through the greater saphenous vein) to decompress the lower extremities and kidneys during the anhepatic phase of the transplant. A

centrifugal pump is used to deliver bypassed blood to the central circulation by means of a cannula passed into the axillary vein.

[redacted] of these complications, several transplant teams have opted not to use the venovenous bypass. Vascular control is obtained by placing vascular [redacted] across the supra- and infrahepatic vena cava and the portal vein. The systemic and splanchnic venous return is interrupted during the anhepatic phase, leading to significant hypotension unless preventive measures, as reviewed in Anesthetic Considerations, are taken.

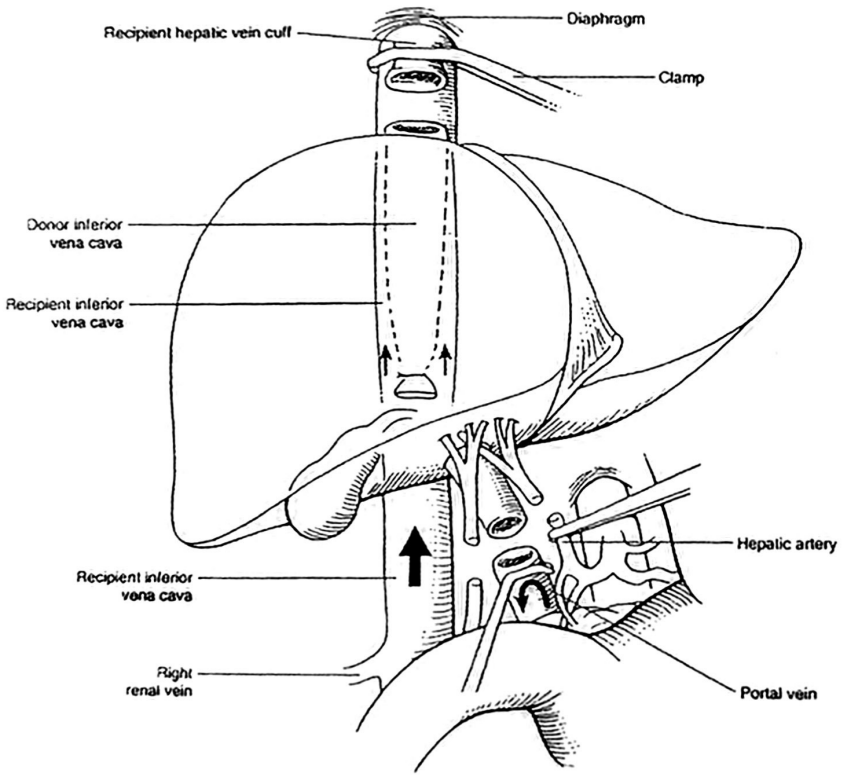
In a standard orthotopic liver transplantation, with or without venovenous bypass, the recipient's vena cava is removed, leaving two cuffs-one just below the diaphragm and the other above the entry of the renal veins. A cadaveric donor liver comes with a segment of the vena cava that is used for restoring the continuity of the recipient's vena cava. The first vascular anastomosis consists of an end-to-end anastomosis of the allograft supra hepatic vena cava and the cuff of the recipient's infra diaphragmatic vena cava. This is followed by the reconstruction of the infrahepatic vena cava with an end-to-end anastomosis. Lastly, the portal vein reconstruction is completed with an end-to-end anastomosis. At this point, the clamps are removed, ending the anhepatic phase of the operation.

Before **revascularization** (i.e., before removing the vascular clamps), the liver must be flushed with a cold solution (e.g., albumin 5%) through the portal vein and out the infrahepatic vena cava. This replaces the preservation solution, which has a very high content of K+ (145 mEq/L) and air. Hyperkalemia could be troublesome following revascularization, particularly from livers that sustained significant preservation (cold-storage) injury. Massive air embolism may lead to cardiac arrest following revascularization.



Standard liver transplantation without venovenous bypass ☐ Venous return is significantly impaired.

Venovenous bypass is not necessary in **piggyback liver transplantation** since the diseased liver is separated from the vena cava (systemic venous return remains unimpaired), and vascular control is obtained by placing a clamp across the confluence of the hepatic veins as they join the vena cava (see figure below). A temporary portocaval shunt may be created to minimize bleeding in cases with severe portal HTN. The first anastomosis is between the suprahepatic vena cava of the liver allograft and the cuff created from the hepatic veins. The infrahepatic vena cava of the liver allograft is ligated, and the portal vein reconstruction is completed. The clamps are then removed and the liver is revascularized.

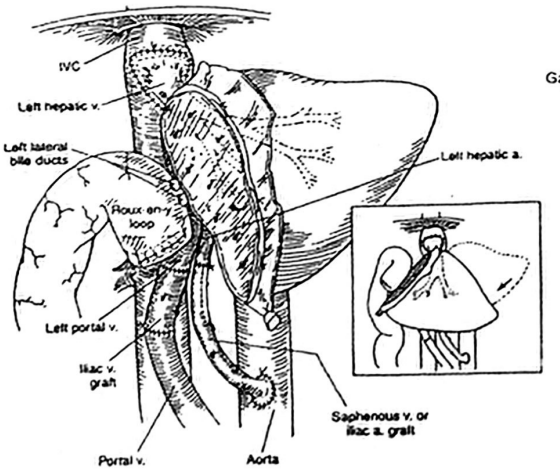


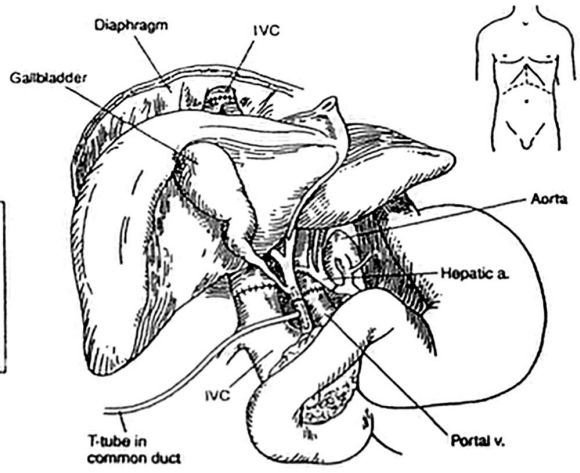
Piggyback Liver Transplantation

Note that the recipient's vena cava is left intact and systemic venous return is unimpaired

Post revascularization begins with the removal of the vascular clamps. The reperfusion of the liver may be the most critical part of the operation. It is during this stage that patients may experience pulmonary HTN, followed by RV failure and profound hypotension. This must be treated aggressively; otherwise, the liver is subjected to high outflow resistance leading to congestion and worsening of the preservation injury. The cause of this phenomenon is not well understood; fortunately, it is seen in very few patients.

The hepatic artery reconstruction is performed after stabilization of the patient following revascularization of the liver. The last part of the procedure involves hemostasis, removal of the gallbladder and reconstruction of the bile duct. There are two basic methods for the bile duct reconstruction: an end-to-end anastomosis, with or without a T-tube (in patients with normal common bile ducts); or a choledochojejunostomy to a Roux-en-Y (in patients with biliary atresia, primary sclerosing cholangitis or diseased common bile ducts, or when there is a size discrepancy between the donor and recipient common bile duct). In cadaveric or live-donor segmental transplantation, the technique for the recipient's hepatectomy and the implantation of the allograft is not different from that of full-size liver transplantation; however, the technique of piggyback liver transplantation must be used with live donors since the allograft segment does not include the vena cava. The anesthesiologist must be alert during the reperfusion of a segmental graft since significant bleeding may ensue from the raw surface of the liver.





Left: Anastamosis – including suprahepatic and infrahepatic IVC, portal vein, hepatic artery, and common bile duct – complete as shown here. Roux-en-Y loop of small intestine is an alternative biliary drainage conduit. Inset shows Chevron incision with midline extension.

Right: Liver transplantation (child) using left lateral segment from an adult liver. The hepatic artery and portal vein are extended with donor iliac artery and vein, respectively. The final position of the graft is shown (inset). A Roux-en-Y loop of small intestine is used to drain the bile ducts. The IVC is left intact. The cut surface of the liver can bleed excessively if CVP is too high.

Usual preoperative diagnosis: End-stage liver disease (ESLD)

SUMMARY OF PROCEDURE

Position: Supine; arms tucked. Left arm and left groin area out for access to the axillary and femoral veins if venous bypass is used.

Incision: Bilateral subcostal, in children; in adults, incision must extend cephalad to the xiphoid process.

Special Instrumentation: Upper hand retractor, venous bypass pump; rapid-infusion system; Cell Saver; argon beam coagulator.

Unique Considerations:

- Thrombus or VAE may occur during removal of clamps from vena cava
- RV failure, ↓BP and ↓SVR may be observed after revascularization
- Continuous arteriovenous hemofiltration may be required if renal failure is present.
- Head and extremities should be covered with plastic to maintain body temperature, particularly in children.

Antibiotics: Ampicillin (1g q 8hrs) and Ceftriaxone (1g q 24hrs) prior to making incision

Surgical Time: 4-12 h

EBL: 6 U average blood loss (range 0-100 U)

Post Operative Care: ICU ☐ 1-2 days. HTN commonly seen.

Mortality: 10% at 1 yr

Rejection: 35- 70% during first yr

Morbidity

- Infectious complications: 20-50%
- Biliary stenosis or leaks: 6-15%
- Retransplantation: 6-14%
- Primary graft non function: 2-6%
- Hepatic artery thrombosis: 0-6%
- Portal vein thrombosis: 1-4%

Pain Score ☐ 7 – 8

PATIENT POPULATION CHARACTERISTICS

Age Range: Neonate – 70 yrs

Male:Female ☐ 1:1

Incidence: 10/million/yr (15% pediatrics)

Etiology

- Adult: HCV cirrhosis, alcoholic cirrhosis, primary biliary cirrhosis, primary sclerosing cholangitis, HBV cirrhosis, hepatocellular carcinoma
- Pediatrics: Biliary atresia, inborn errors of metabolism

epatitis.

ANESTHETIC CONSIDERATIONS

PREOPERATIVE

atients presenting for liver transplantation represent a formidable challenge to the anesthesiologist. Frequently, these patients present for surgery with ıultiorgan system failure. Due to the emergent nature of the surgery, there may be insufficient time available for the customary evaluation and correction f abnormalities in this patient population.

tespiratory: These patients are often hypoxic because of ascites, pleural effusions, atelectasis, V/Q mismatch and pulmonary A V shunting. As a result, ıey are usually tachypneic and have a respiratory alkalosis. Evidence of pulmonary infection is usually a contraindication to surgery, but ARDS that may ccur with hepatic failure is not.

'ests:

- ABG; PFT, as indicated
- CXR: infection, effusions, atelectasis

Cardiovascular: These patients demonstrate a hyperdynamic state with ↑CO and ↓SVR (probably 2° AV fistulae and endogenous vasodilators). This nefficient circulatory state is manifested by a high SO2. The SVR usually is not responsive to α-agents. AV fistulae also occur across the pulmonary :irculation, so that precautions to prevent air embolism are important. Ejection fraction (EF) is usually high (> 60%). Pericardial effusions may be ›resent, and should be drained at surgery. Many of these patients will have dysrhythmias, HTN, pulmonary HTN (very high risk), valvular disease, :ardiomyopathy (alcoholic disease, hemochromatosis, Wilson's disease) and CAD. These patients will require appropriate preop consultation and workup.

Tests:

- ECG
- ECHO: Assess EF, contractility, pulmonary HTN, wall motion abnormalities, valve problems. If abnormal, consider a MUGA scan and/or right and left heart catheterization with coronary artery angiography.

Neurological: Patients are often encephalopathic and may be in hepatic coma; however, other organic causes of coma should be ruled out. In fulminant hepatic failure, ↑ICP is common, accounting for 40% of mortality (herniation), and may require prompt treatment (mannitol, hyperventilation, etc.).

Continuous ICP monitoring in fulminant hepatic failure

Hepatic: Hepatitis serology and the cause of hepatic failure should be determined. Vascular abnormalities, previous RUQ surgery or portal vein decompressive surgery places the patient in a high-risk group. Albumin usually low, with consequent low plasma oncotic pressure ☐ edema, ascites. The magnitude and duration of drug effects may be unpredictable but, generally, these patients have ↑sensitivity to all drugs and their actions are prolonged.

Tests: Bilirubin; PT/PTT; ammonia level; SGOT; SGPT; albumin

Gastrointestinal: Portal HTN, esophageal varices and coagulopathies ↑risk of GI hemorrhage. Gastric emptying is often slow and, together with the emergent nature of this surgery, warrants rapid-sequence induction. H2-antagonists are indicated preoperative.

Renal: Renal function, especially in fulminant hepatic failure (hepatorenal syndrome). The kidneys often recover after transplantation, but simultaneous kidney transplantation may be justified. These patients are often hypervolemic, hyponatremic and possibly hypokalemic. Ca^{2+} is usually normal. Metabolic alkalosis may be present. Consider preop dialysis and intraop continuous AV hemofiltration. Low-dose dopamine (2-4 μg/kg/min) and/or mannitol (0.5-1 g/kg) are often used intraop to maintain renal function.

Tests: BUN; creatinine, creatinine clearance; electrolytes; ABG

Endocrine: Patients often glucose intolerant or frankly diabetic, although acute hypoglycemia may be seen in acute hepatic failure. Hyperaldosteronism may be present.

Tests: Glucose; electrolytes

Hematologic: These patients are often anemic 2° either blood loss or malabsorption. Coagulation is impaired because of ↓hepatic synthetic function (all factors except VIII and fibrinogen are ↓), abnormal fibrinogen production, ↓/impaired Plt, fibrinolysis, and low-grade DIC.

Tests: PT/PTT; Plt count; bleeding time; fibrinogen; fibrin split products (FSP); TEG

edication: Low doses of benzodiazepines may be used judiciously, but often nothing is given prior to surgery. Usually good preop evaluation and ussion suffice. Intramuscular injection should be avoided. Full-stomach precautions are justified. Metoclopramide 10 mg IV, ranitidine 50 mg IV and Na citrate 0.3 M 30 ml PO should be given prior to surgery.

INTRAOPERATIVE

These patients are extremely complex to manage because of the hemodynamic variability, massive blood loss, coagulopathy and metabolic problems. It is convenient to divide the operation into three stages: preanhepatic, anhepatic and neohepatic (discussed below).

ıduction: Often, a narcotic (e.g., fentanyl 2-5 µg/kg) is given just prior to induction ☐ RSI is preferred. STP (3-5 mg/kg) or etomidate (0.3 mg/kg) with ıccinylcholine (1-2 mg/kg), together with cricoid pressure.

[redacted]ance: Standard maintenance with fentanyl 10-50 µg/kg. A benzodiazepine (e.g., midazolam 0.1-0.3 µg/kg) often is given to ensure amnesia ıring periods of hemodynamic instability when the volatile agent may need to be off. N2O is avoided because of bowel distention and possible air nbolism. Ventilation with FiO2 > 0.5 and PaCO2 = ~ 35 mmHg. Occasionally, PEEP (5 cm H2O) is added. Antibiotics and immunosuppressants should ɜ given per surgeon's direction. Muscle relaxation is usually maintained with pancuronium.

reanhepatic Phase: The preanhepatic phase starts at skin incision and ends with removal of the recipient liver. Pleural and pericardial effusions are rained, which may improve oxygenation. Hyperglycemia is common during this period. ↓filling pressures 2° hemorrhage or vascular compression. lemorrhage can be severe 2° portal HTN. Coagulation problems usually increase during this period, although fibrinolysis is not usually a problem. Blood ɔss replacement is accomplished with blood (PRBC) and FFP. Cryoprecipitate and Plt are given as needed, but a hypercoaguable state should be voided, particularly if venovenous bypass is contemplated. Hemodynamic instability is not uncommon during the hepatic vascular dissection 2°/2 ıanipulation of the liver and ↓venous return.

'enovenous bypass relieves most of the complications of portal and IVC X-clamping (↓venous return, low CO, tachycardia, acidosis, ↓renal function, ıtestinal swelling.) Blood is pumped from the femoral vein and the portal system (either portal vein or inferior mesenteric) via a centrifugal pump to the ɛft axillary vein. Generally, no heparin is used, but heparin-bonded cannulas and tubing are used. Bypass flows need to be at least 1 L/min to avoid ›ossible thromboembolism. Bypass flow depends on venous inflow and is drawn into the pump by negative pressure. Low flows may be caused by ıypovolemia or obstructed cannulae. Complications include unexpected decannulation, thromboembolism and air embolism, all of which may need rapid ermination of bypass and treatment of hypotension. Venovenous bypass is not always used.

ʌlassive blood transfusion is associated with ↓Ca and replacement is usually needed (~500 mg/1000 ml of blood/FFP/plasmalyte mixture). If ıyperkalemia occurs, it should be treated aggressively. Metabolic acidosis > 5 mEq/L should be treated with bicarbonate. Occasionally, inotropic support s needed, but α-adregenic agents should be avoided because of ↓renal and peripheral perfusion. UO needs to be maintained by ensuring adequate ntravascular volume; occasionally, low-dose dopamine and/or mannitol may be needed.

Anhepatic phase: The anhepatic stage begins with clamping of the hepatic vessels and vena cava and removal of the liver; it ends with the reperfusion of he donor liver. Problems during this period include hemorrhage, increasing coagulopathy and fibrinolysis, acidosis, hypothermia and ↓renal function. The hemodynamic instability associated with clamping of the hepatic vessels and the congestion of the bowel that occurs can be decreased by venovenous bypass. Care should be taken to maintain intravascular volume, while avoiding volume overload, since this will worsen fluid overloading on reperfusion. At the completion of vena caval anastomoses, the liver is flushed via the portal vein to remove air, preservation fluid and metabolites. [redacted]usion may take place after completion of the portal vein anastomosis or after both portal vein and hepatic artery anastomoses are completed. As in [redacted]eanhepatic phase, acidosis, ↓Ca, glucose, coagulation and other electrolyte abnormalities should be treated. Fibrinolysis usually starts in this period, but is not usually treated unless severe because of the potential for embolism during venovenous bypass.

Neohepatic Phase: The neohepatic phase begins with the unclamping of the portal vein, hepatic artery and vena cava and reperfusion of the donor liver. Preparation for this phase is important because this may be a period of great hemodynamic instability. Before removal of the clamps, acidosis should be corrected, ionized Ca should be normal and K should be < 4.5 mEq/L. CaCl2, NaHCO3 and epinephrine should be readily available. Fluid overload prior to unclamping should be avoided. High venous filling pressures decrease hepatic perfusion, especially prior to hepatic artery anastomosis. Unclamping can be attended by ↓BP, ↓HR, dysrhythmias, hypothermia, lactic acidosis, coagulopathy and hyperglycemia.

Reperfusion Syndrome: The "reperfusion syndrome" (which can occur in this phase) is characterized by ↓HR, ↓BP (30% develop MAP < 70% of baseline), conduction defects and ↓SVR in the face of acutely ↑RV filling pressures. Cause unknown. CO is often maintained. A rapid ↑K can lead to cardiac arrest. (Rx: ensure normal pH and electrolytes prior to unclamping, rapid therapy when it occurs.) ↓BP and HR are treated with epinephrine (10 µg increments), while CaCl2 and NaHCO3 are used to correct hyperkalemia and acidosis. Pulmonary edema may occur as a result of fluid overload and can be treated with diuretics, inotropes and phlebotomy. A high venous pressure will cause graft congestion and should be avoided. Reperfusion is associated with severe coagulopathy due to fibrinolysis (usually primary), release of heparin and hypothermia. As liver function returns, there should be an improvement in coagulation, acid-base status (metabolic alkalosis may occur), ↓lactic acidosis, return of glucose to normal and bile production.

Hypokalemia may occur 2°/2 uptake by the liver. HTN may be a problem. (Rx: SNP infusion.) Graft failure is associated with coagulopathy, ↑lactic acid, citrate intoxication, hyperglycemia and ↓bile formation.

Emergence: Extubation is deferred to ICU, with patient intubated and ventilated. These patients are generally ventilated postop until they are stable and able to be weaned from ventilatory support. Apart from the usual tests, hepatic function needs to be monitored, immunosuppression provided, infection controlled, analgesia ensured (usually morphine) and peptic ulcer prophylaxis given (ranitidine preferred).

Blood & Fluid Requirements: Massive blood loss IV: 10 Fr x 2. Generally, IV's are placed in the right antecubital fossa, left or right IJ or EJ. The left arm is avoided because the axillary vein is used for venovenous bypass.

- Plasmalyte A or Normasol to keep UOP > 1 ml/kg/h
- Warm all fluids, humidify gases
- [redacted] Rapid-infusion system Cell Saver
- 20 U PRBC
- 20 U FFP
- 20 U PLT

Plasmalyte A or Normasol are preferred (absence of glu cose, Ca and lower Na content) over NS/LR. Hyperna tremia can be a problem due to administration of NaHCO3. The ability to give up to 1.5 L/min of blood should be avail able. Usually a mixture of Normasol (250 ml), PRBC (1 U) and

FP (1 U) is used, yielding Hct = 26-30%. Actual blood loss estimation is extremely difficult, and usually replace ment is judged by hemodynamic status, O and SvO2. Cell Savers are used to conserve blood. Anticoagulation is with a citrate solution to avoid heparin contamination and cells are washed ith Normasol/Plasmalyte A. D/C use before bil iary reconstruction (infection) or in neoplasms, hepatitis B or spontaneous bacterial peritonitis.

s: Standard monitors +

- 5-lead ECG
- bladder temperature ☐ These pa tients sustain significant temperature loss
- ETN_2
- Arterial Line: One or two arterial lines are placed at the outset ☐ one in the right radial, for ongoing lab and blood gas sampling, with 1 port being designated as heparin-free; another line, in the right femoral artery is utilized for continuous pres sure measurement. All flush solutions contain citrate for anticoagulation in order to avoid heparin contamination.
- PA Catheter/SvO2/CO: PA catheter is essential for management of hemody namics in these patients because of the rapid changes in vital signs. A catheter capable of measuring SvO2 sat is very useful, as it gives early clues to impending decompensation. Coagulopathy complicates the place ment of central lines, and the use of ECHO or ultrasound guided needles is useful.
- TEE is useful to monitor cardiac filling and function and to diagnose problems such as PE or air embolism. Care needs to be taken in placing the TEE, since many of these patients have esophageal varices.
- ICP should be measured in patients with fulminant he patic failure if ↑ICP is a concern.
- Labs: ABG, acid base status, electrolyte, lactate, osmolality, Ca, PT/PTT, Plt, Hct all should be monitored on a regular basis (hourly or half-hourly and, occasionally, more frequently).
- TEG: The thromboelastograph (TEG) is useful for monitoring coagulation.

A full-time anesthesia technologist and lab/blood bank runner are useful. Lab and blood bank should be notified of the expected transplant. An automated data acquisi tion system also is useful, since there are times during the case when the record may be neglected in favor of working with the patient.

Coagulation Management: Patients are prone to a variety of coagulopathies (↓Plt, ↓coagulation factors, DIC, fibrinolysis, etc.) because of preoperative factors, massive hemorrhage, anhepatic period and reperfusion of the new liver; therefore, monitoring and treatment are necessary. Also, states of hypercoagulopathy need to be avoided because of unheparinized venovenous bypass. Therefore, check…

- PT/PTT
- PLT
- Fibrinogen
- FSP
- TEG

While PT/PTT, Plt counts, fibrinogen and FSP may provide relevant information, they may not reflect the true coagulability of patient's blood and tend to take considerable time to perform. Thus, in some centers, TEG has gained in popularity. It measures whole blood coagula bility, not specific factors. TEG works by measuring vis coelastic properties of blood as it forms clot (fibrin con nections) between a rotating cuvette and a spindle. Char acteristic patterns are formed by the various coagulo pathies with the common types shown below.

Evaluation of the TEG leads to more rational transfusion therapy, reducing the number of units of blood/blood pro ducts used. Comparing specimens of native whole blood vs. blood mixed with EACA or protamine can guide pharmacologic therapy of coagulopathies. The table below gives specific recommendations.

Coagulation Therapy Guided by TEG Monitoring
Maintenance Fluid ☐ RBC:FFP:Plasmalyte = 300:200:250
Replacement Therapy • *FFP (2U) for prolonged reaction time (r > 15 min)* • *Plt (10U) for small MA (<40 min)* • *Cryoprecipitate (6 – 12U) for persistent slow-clot formation (α < 40°) with normal MA*
Pharmacologic Therapy • *Compare coagulability of whole blood, blood treated with protamine, and blood treated with ε-ACA* • *ε-ACA 1g for severe fibrinolysis (F < 60 min)* • *Protamine 50 mg for severe heparin effect* • *Heparin 1000 – 2000 U for hypercoagulable state*

Positioning: Table and arm boards should be very well padded. Head should be placed on a foam rest. Particular care should be taken to pad the retractor supports where they may impinge on the arms and on the radial nerve as it curls around the humerus.

- Check and pad pressure points
- Check eyes

Temperature Control: Patient's arms, head, and legs should be wrapped in plastic to protect against heat loss. Plastic drapes and the use of a cesarian section-type drape to protect the ECG electrodes and direct fluid flow off the table are useful to prevent the patient from lying in a pool of fluid. A warming blanket under the patient and over the lower legs is very useful.

Complications:

- Coagulopathy
- Hemorrhage
- Air Embolism
- RV failure
- Metabolic Acidosis

POSTOPERATIVE

Monitoring of Hepatic Function:

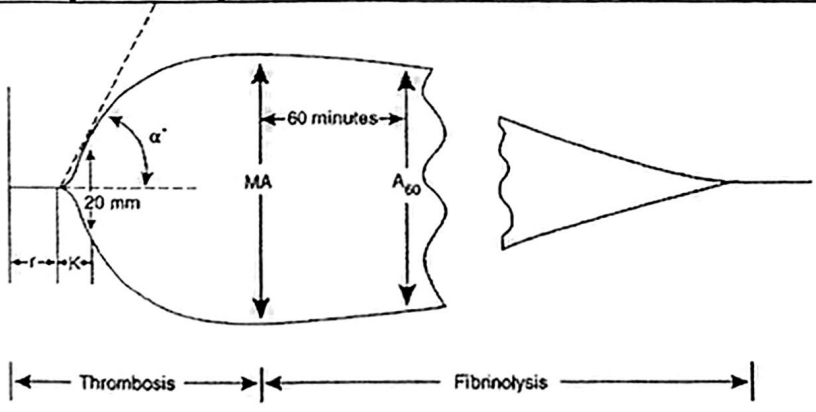
- Serial LFT's: Initial LFT's often show very high liver enzymes, which subside over a period of days.
- PT/PTT: PT generally improves to normal levels
- Lactate: Lactic acidosis usually corrects quickly. Often a metabolic alkalosis follows and may need treatment with HCl
- NH3 level
- TEG
- Bile output

Complications:

- Bleeding
- Partial vein thrombosis
- Hepatic artery thrombosis
- Biliary tract leaks
- Primary nonfunction
- Rejection
- Infection
- Pulmonary complication
- HTN
- Electrolyte abnormalities (hypokale mia, ↓Ca, ↑Na)
- Alkalosis
- Renal failure
- Peptic ulceration
- Neurologic

This is not a complete list. Feared complications which may result in graft loss include portal vein thrombosis, hepatic artery thrombosis, bile leaks and rejection. These are attended by ↑LFTs, lactic acidosis, coagulopathy, hypoglycemia, ↓renal function, and poor bile formation.

Quantification of Thromboelastograph (TEG) Variables



r = reaction time (time from sample placement in the curette until TEG amplitude reaches 2 mm. The normal r time is 6 to 8 minutes and represents the rate of initial fibrin formation. Prolongation of the r time may be the result of coagulation factor deficiencies, anticoagulation (heparin), or severe hypofibrinogenemia. A short r time may be present in hypercoagulability syndromes.

K = clot formation time (normal range 3 to 6 minutes) as measured from the r time to the point where the amplitude of the tracing

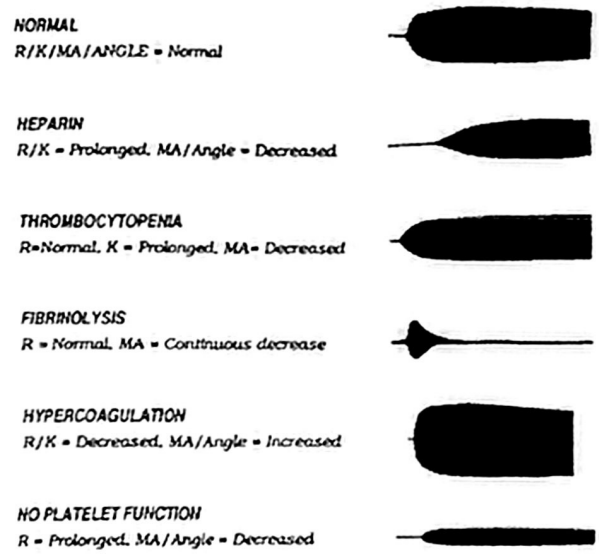
r + K = coagulation time ☐ 10 – 12 min

[redacted] alpha angle (normal range 50 to 60 degrees) is the angle formed by the slope of the TEG tracing from the r to the K value. [redacted]tes the speed at which solid clot forms. Decreased values may occur with hypofibrinogenemia and thrombocytopenia.

MA = The maximum amplitude (MA) ☐ normal range 50 to 70 min. greatest amplitude on the TEG trace and is a reflection of the absolute strength of the fibrin clot. Platelet abnormalities alter the MA.

A60 (normal range = MA - 5 mm) is the amplitude of the tracing 60 minutes after MA is achieved. This is a measure of clot lysis or retraction.

F = the interval from MA to return to a zero amplitude, is a measure of the rate of fibrinolysis. In normal subjects F is sufficiently long that the test is usually terminated before this time elapses.



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