Liver Transplant Resident Guide

The Liver Team:

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General Game Plan:
1. General via endotracheal tube.
2. ALWAYS preoxygenate!
3. One adequately running peripheral IV is usually sufficient to start the case.
4. Rapid sequence or modified rapid sequence induction with Propofol and Rocuronium or Succinylcholine.
5. Maintenance with volatile with fentanyl and cisatracurium infusions
6. Consider premed with Midazolam if the patient is very anxious and has no signs of encephalopathy.

Overview of Setup

1. Medications to Order
   a. Order 3 medications from pharmacy as soon as you start setting up
      i. Albumin 5%, 3L (500ml x6)
      ii. Octreotide 500mcg/vial. One vial for most livers, two for living donor
      iii. Insulin 1unit/ml, 100 unit bag
   b. Ask your tech to pick up
2. Basic equipment
a. Heated, humidified circuit
b. Laryngoscope
c. ETT
d. Oral airway
e. Tegaderm for eyes
f. Bite block
g. OG tube

3. Liver table and auxiliary equipment
   a. 8 syringe pumps, 1L NS carrier on micro-drip, 8 stopcocks, extension, built by anesthesia techs
   b. Blue top (Coags) and Purple top tubes (CBC), lots of ABG syringes.
   c. 3 hot lines with Plasma-Lyte (2 on liver table, plus 3rd on IV pole to patient's right)
   d. Liver auxiliary cart (yellow)
      i. Contains extra medication, syringes, equipment for lines
   e. Triple transducer (Arterial, CVP, PA)
   f. Zoll pads and defibrillator
   g. Radiometer ABG machine—make sure it's plugged in (lives in back room off of OR 12)
   h. Ultrasound with linear probe (for lines)
      i. Consider TEE probe

4. Drugs
   a. Infusions
      i. Norepinephrine: 4mg in 250ml NS to make 16mcg/ml. Draw up in 60ml syringe. Set pump at 5mcg/min
      ii. Calcium: Draw up three 10mL syringes of 100mg/ml in a 30ml syringe. Set infusion at 500mg/hr
      iii. Fentanyl: 10ml of 50mcg/ml. Set infusion at 100mcg/hr.
      iv. Cisatracurium: 10ml of 2mg/ml. Set infusion at 1mcg/kg/min
      v. Octreotide: Dilute one 500mcg vial in 49ml NS to make 10mcg/ml. Set infusion at 100mcg/hr. Then go to options—bolus and set a 100mcg bolus over 15 mins. When the bolus is done, the pump will automatically start the infusion if you set it this way.
      vi. Zosyn 3.375g – load one syringe in 20mL and set to deliver over 30 mins. We will give a dose every 2 hours for 3 doses. After third dose, move to q6 hour dosing.
   b. Bolus syringes
      i. Phenylephrine
      ii. Norepinephrine
      iii. Epinephrine 10mcg/mL (1mg in 100mL saline bag)
      iv. Calcium Chloride 100mg/mL
   c. Other considerations
      i. Vasopressin 1unit/ml (20ml), for sicker patients, omit phenylephrine
      ii. Furosemide 10mg/ml (10ml), for volume overload, CKD
iii. The infusion line connects to the side port of introducer, VIP port or triple lumen catheter.

iv. Methylprednisolone (Solumedrol) 500mg IV over 30 minutes
   1. Reconstitute in 100ml NS with microdrip, or run in syringe pump
   2. Give this through a separate port since it can precipitate with other infusions.

v. Code dose epinephrine 100mcg/ml

vi. ample supply of calcium chloride 100mg/ml (liver auxiliary cart should have extra)

vii. Bicarbonate (no need to open)

viii. Atropine (no need to draw up, just make sure it’s available)

d. Induction medications
   i. Propofol
   ii. Lidocaine
   iii. Rocuronium, rarely succinylcholine
   iv. Esmolol

5. Lines (usually in this order)
   a. 20g left radial arterial line
   b. 14g or 16g right upper extremity volume line
   c. 7 French left antecubital rapid infusion catheter (RIC)
      i. Placed with prep, sterile towels and gloves
   d. 8.5 or 9 French PSI introducer with double-lumen insert or MAC catheter in right internal jugular (Typically, if the RIC goes in nicely, PSI introducer is placed; otherwise MAC.
      Occasionally, trialysis catheter is placed, in which case RIC is usually not needed.)

6. Monitors
   a. Standard ASA
   b. Typically temp Foley is placed (unless doing a combined liver kidney, in which case a three way foley is used and you will need a separate temp probe)
   c. Arterial line
   d. CVP
   e. Zoll pads
      i. Turn on the defibrillator and check that you have ECG trace through the pads!
   f. 3rd pressure channel (PA) occasionally used to check portal pressures (routine in living donor cases)

Starting the case

● 1 reliable PIV for induction.
● Position on table, most likely supine with right arm tucked and left arm out on arm board.
● IV RSI as above
● After induction, place left radial arterial 20G catheter and eft arm RIC
● 14G or 16G PIV in R-arm before tucking
● Right IJ Cordis or MAC with DLIC
• Place 18Fr OG after all lines are in.
• Temperature monitoring is usually done via a temperature foley
• Temperature control: Heated, humidified circuits, 3 hotlines as above, Forced air warming
• Labs: Use Collection Manager to scan patient ID armband and generate specimen label. Call your anesthesia tech for CBC, coags. ABGs are run in OR.

Goals and Objectives for Anesthesia Residents on the Liver Transplant Service

Introduction
Anesthesia residents at UCSF perform anesthesia on the liver transplant service as part of the senior resident rotation and during night call as the senior resident. The liver transplant service is a multidisciplinary service comprised of surgeons, hepatologists, anesthesiologists and nurses. Approximately 180 liver transplants are performed each year, providing each resident with roughly 8 transplants each.

Goals

• Describe the surgical course of a liver transplant
• Understand the management of a donor hepatectomy
• Understand the preoperative evaluation of a patient with cirrhosis
• Understand blood component therapy

Objectives

Interpersonal Communication Skills

• Communicate effectively with other healthcare professionals
• Demonstrate professionalism and interpersonal/communication skills with patients and families
• Communicate with patients and their families in easily understood and culture-sensitive language.
• Work effectively as a member of the liver transplant team
• Maintain comprehensive, timely, and legible medical records

Professionalism

• Demonstrate respect, compassion and integrity
• Demonstrate a commitment to excellence and ongoing professional development
• Demonstrate a commitment to ethical principles pertaining to confidentiality of patient information, informed consent, and resource utilization
• Demonstrate sensitivity and responsiveness to patients’ culture, age, gender, and disabilities
• Demonstrate organizational skills to care for patients in a competent and efficient manner

Medical Knowledge
Liver Transplant Specific

- List what vessels are “cross” clamped during the anhepatic stage
- Define veno-veno bypass
- Define a “piggy back” transplant
- Define the “anhepatic period”.
- Distinguish heterotopic transplant from orthotopic transplant

Cirrhosis

- List the factors that are used to calculate a MELD score.
- List several factors used to determine Childs-Pugh classification
- Define portopulmonary hypertension
- Define hepaticolymphatic syndrome
- Define the approximate perioperative mortality in a patient with cirrhosis
- List elements of coagulation abnormalities in a patient with cirrhosis

Transfusion

- Define indications for Factor VIIa and PCC use
- Define a dose range for Factor VIIa and PCC
- Define the indication for use of FFP
- Define the indication for use of cryoprecipitate
- Define the indication for use of platelets
- Define “massive transfusion”
- Define dilutional coagulopathy and the hemostatic abnormalities associated with it
- List blood components most associated with citrate toxicity

Practice-based Learning and Improvement

- Perform literature search and retrieve relevant literature
- Access UNOS website and relevant data
- Access Licage and Litac and relevant data

Systems-based Practice

- Demonstrate awareness of the role transplantation plays in the health care system
- Understand efforts being made to expand organ donation, both living and deceased

Case Discussion

Preoperative Evaluation

The severity of illness and prognosis of patients with chronic liver disease can be estimated by a number of different scoring models, including the Child-Pugh-Turcotte and MELD (Model for End-Stage Liver Disease).
Child-Pugh-Turcotte Classification
Originally developed in 1973, the Child-Pugh score was used to estimate the risk of operative mortality in patients with bleeding esophageal varices and has since been repurposed to predict survival of patients with cirrhotic liver disease without transplant. The score is based on 5 laboratory and clinical criteria, as indicated in the table below; scores will range from 3 to 15 points.

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 Point</th>
<th>2 Points</th>
<th>3 Points</th>
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</thead>
<tbody>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
<td>2-3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
<td>2.8-3.5</td>
<td>&lt; 2.8</td>
</tr>
<tr>
<td>Encephalopathy grade</td>
<td>None</td>
<td>1-2</td>
<td>3-4</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Slight (or medication responsive)</td>
<td>Moderate to Severe (or refractory)</td>
</tr>
<tr>
<td>PT (seconds &gt; normal)</td>
<td>&lt; 4</td>
<td>4-6</td>
<td>&gt; 6</td>
</tr>
</tbody>
</table>

Child-Pugh-Turcotte scoring system

<table>
<thead>
<tr>
<th>Class</th>
<th>Score</th>
<th>One year survival</th>
<th>Two year survival</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>5-6</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>B</td>
<td>7-9</td>
<td>80%</td>
<td>60%</td>
</tr>
<tr>
<td>C</td>
<td>10-15</td>
<td>45%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Child-Pugh-Turcotte survival prediction

Model for End-Stage Liver Disease (MELD)
The Child-Pugh score fell victim to the subjectivity of the evaluator in the burden of ascites and extent of encephalopathy, and as such, was considered too subjective. The MELD score was initially devised as a 3-month predictor of survival for patients undergoing TIPS (transjugular intrahepatic portosystemic shunt) using objective criteria. In the initial study, it was also validated to predict 1-year survival of the same cohort. It was later found to be prognostic of short- and long-term survival in patients with end-stage liver disease of varying etiologies and since 2002 has been adopted by UNOS to prioritize patients to receive liver transplantation.
The initial formula was based on creatinine, bilirubin, INR, and etiology of disease (giving lower scores to cholestatic or alcoholic liver disease). The etiology of disease was found to be too subjective and when removed from the formula, it was found the predictive value of the score did not change. Additionally, as of 2016, a model including serum sodium (using hyponatremia as a proxy for ascites burden) has been found to be prognostic for survival in patients with ascites and/or hyponatremia.

\[
\text{MELD} = 9.57 \times \ln (\text{Creatinine}, \text{mg/dl}) + 3.78 \times \ln (\text{Bilirubin}, \text{mg/dl}) + 11.20 \times \ln (\text{INR}) + 6.43
\]

(calculator at [https://www.mdcalc.com/meld-na-score-liver-cirrhosis](https://www.mdcalc.com/meld-na-score-liver-cirrhosis))

UNOS has made the following modifications to the score:
- If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0
- Patients with a diagnosis of liver cancer will be assigned a MELD score based on how advanced the cancer is (details available here: [https://www.uptodate.com/contents/model-for-end-stage-liver-disease-meld#H16431878](https://www.uptodate.com/contents/model-for-end-stage-liver-disease-meld#H16431878))
- Other modifications to score (known as exception points) may be made based on sequelae or concomitant conditions (also found at link above)

### Organ System-Specific Considerations

**Neurological**

Hepatic encephalopathy should be assessed. In fulminant liver failure patients, you should look for signs of high ICP. Find out if the patient has had a CT scan looking for cerebral edema. Some patients may have ICP monitoring. Usually, these patients are intubated for coma.

**Pulmonary**

Gas exchange deficiencies are common. While hepatopulmonary syndrome (intrapulmonary shunting from liver failure causing (likely) nitric oxide mediated intrapulmonary vasodilation) may occur, most gas exchange deficiencies in this patient population are due to more common etiologies. These may include atelectasis, decreased FRC from ascites, pneumonia, underlying lung disease, and pleural effusions (common in cirrhotic patients). Often the effusions can be drained through the diaphragm after incision, so despite a bad effusion, the issue will not ultimately be severe during surgery.
Pulmonary Hypertension and Portopulmonary syndrome

Cirrhosis is associated with pulmonary hypertension similar to primary pulmonary hypertension (pulmonary arterial hypertension, WHO Group 1). The cause is not clear. However, these patients may do poorly, and severe enough forms may be a contraindication to transplantation. Pulmonary hypertension is difficult to screen for preoperatively, and can be asymptomatic. All patients will have had a cardiac echo, which should have estimated PA pressures. Even echo may be a poor screening tool, and right heart catheterization may be performed to look for pulmonary hypertension.

Portopulmonary hypertension is defined as pulmonary arterial hypertension (PAH) with mean PAP > 25mmHg and PCWP < 15 mmHg (to rule out LH etiology or volume overload) in addition to portal hypertension. It has been established that patients with portopulmonary hypertension have poorer outcomes in the setting of liver transplantation, but frequently, liver transplantation in addition to medical therapy for PAH is the best treatment and can lead to complete resolution of portopulmonary hypertension.

Cardiovascular

Cardiac evaluation is a routine component of the liver transplantation preparation. Liver transplantation is an extremely stressful surgery, and may not be tolerated by a patient with significant coronary artery disease. Stress tests, e.g. P-Thal and dobutamine echo, are routinely performed. There is a low threshold for getting left and right cardiac catheterization. In the vasodilated state of liver failure, cardiac function should be hyperdynamic, with an elevated ejection fraction, often 70- 80%. Even a mildly reduced ejection fraction, e.g. 55%, may be distinctly pathologic. Cirrhotic cardiomyopathy can occur, and refers to increased diastolic pressures and inability of the heart to compensate with increased work load. Cardiac dysrhythmias are common. Hemochromatosis (e.g. Wilson’s disease as an example of hereditary hemochromatosis) can also have implications on the heart. Iron infiltration of myocardium can impair cardiac contractility and conduction. Hemochromatosis is common, and because of additional diseases such as hepatitis C, it may be missed. In any adult patient with IDDM that developed after cirrhosis, hemochromatosis (bronze diabetes) should be suspected.

Cardiac workups from patients referred from outside centers are usually found under “Care Everywhere” or “Scanned Outside Documents” in Apex or may need to be requested from the liver transplant service.

Gastrointestinal

History of GI bleeding, ascites, portal hypertension, TIPS performed should be noted. History of prior abdominal surgery can also lead to dissections that can be more difficult, longer, and result in more blood loss. While NPO status is ascertained, we consider that most patients may have full stomachs due to poor emptying with ascites, and possible GI bleeding. A Blakemore tube may be necessary during surgery if the patient has active and significant upper GI bleeding.
Renal
Hepatorenal syndrome and other causes of renal insufficiency should always be assessed. Some patients may be scheduled for combined liver and kidney transplantation. Because large volumes of blood product are often necessary, some form of fluid removal (diuresis, or CVVH) may be necessary. In fluid overload states where patients are ESRD or oliguric/anuric, factor VIIa (Novoseven) or PCC (prothrombin complex concentrate, Kcentra) can also be used to achieve hemostasis in these patients. This should always be discussed with the surgical team if indicated, since factor VIIa has been associated with thrombosis and both therapies can be very costly.

Every electrolyte may be abnormal and should be considered. Hyperkalemia and hypokalemia are both common due to renal failure and diuretic use. Hyponatremia is common due to diuretic use, low intravascular volume and excessive free water retention and/or replacement. Although debated, central pontine myelinolysis may be related to overly-rapid correction of hyponatremia, and has been reported in the setting of liver transplantation. \( K^+ \), \( Mg^{2+} \) and ionized \( Ca^{2+} \) levels should be noted and corrected prior to the anhepatic phase.

Hematology
Patients are often hemodiluted due to volume overload with low Hb/HCT. Hb may also be low in the setting of GI bleeding or concurrent kidney disease. Platelet counts can be reduced due to poor production (from low thrombopoietin state) as well as sequestration secondary to portal hypertension. Platelet function may also be affected by liver and/or renal disease, reducing the number of effective platelets from what is seen on the CBC. Coagulation status is also affected by liver disease. Coagulation studies, PT/INR, may be abnormal in patients with affected synthetic function. This does not necessarily mean patients are coagulopathic, however. Patients with liver disease are in a brittle, but rebalanced coagulation homeostasis due to the decreased production of not only factors 2,7,9, and 10 but also protein C and S and antithrombin, as well as inability to clear tPA, in addition to many other purported causes. Focus has traditionally been on correcting laboratory test values, but ultimately surgical hemostasis is the treatment endpoint.

Blood is set up by protocol, but the order to thaw FFP needs to be sent to the blood bank, and in a patient with a severe coagulopathy, factors need to be requested for possible transfusion before line placement. This should be anticipated during the preop evaluation. We currently order 5 RBC, 5 FFP and 2 plt in room before start of the case for a patient with near normal coagulation studies, or 10 RBC/10 FFP/2 PLT for coagulopathic patients. Talk to your attending regarding this point.

Surgical details

General Considerations
Liver transplantation is almost always performed as an "orthotopic liver transplantation", meaning the transplanted liver is placed in the same position as the native liver (as compared to renal transplantation where the kidney is typically transplanted into a heterotopic location, the pelvis). Types of grafts may vary. In pediatric patients, surgeons may use a variety of "reduced-size" grafts: pared-down segments
from adult donors, small segments (left lateral segment) from live donors, or "split-livers", which harvests two grafts from one donor. Adult-to-adult living related transplants typically use the right hepatic lobe from the donor.

Donor organs come from two broad categories, living and deceased donors. Living donor surgeries are scheduled cases and the health of the organ is well known. Additionally, ischemia times of the organ are kept to a minimum as the donor and recipient surgeries are timed together.

Deceased donors (or cadaveric donors) are then broken into two types, depending on the state of the donor at the end of life. One type is the brain-dead donor. Brain-dead donors are typically intubated at the end of life and may be on vasopressors for various reasons. Once the decision for organ donation has been made, these patients will be kept hemodynamically stable to maintain perfusion of organs. Once the organ harvest surgeons have opened the body and are ready to clamp vasculature and harvest, circulatory and ventilatory support is ceased. This maintains perfusion until the last possible minute prior to harvest.

The second type is a donation after cardiac death (DCD). These patients have suffered either controlled (withdrawal of life support) or uncontrolled (cardiac arrest, dead on arrival, unsuccessful resuscitation) circulatory arrest. As such, the organs harvested may have experienced a substantial amount of warm ischemic time (ischemia outside of ice bath). These organs used as transplant grafts have shown to contribute to worse outcomes in recipients. However, given the large pool of patients in need of transplant, these organs are still offered to surgeons as an alternative to no transplant at all.

Surgical technique can have anesthetic implications, as will be discussed later. The arterial and portal venous anastomoses are straightforward end to end anastomoses. The venous anastomosis can vary based on how well preserved the donor vasculature is and how accessible the recipient vasculature is. The “conventional technique” involves a full clamp of the infrahepatic and suprahepatic IVC, excision of native liver, and end to end anastomoses of the donor infrahepatic and suprahepatic IVC to their respective vessels in the recipient. A "piggyback" refers to partial, semilunar, occlusion of the IVC, with an end-to-side anastomosis of donor hepatic veins to native IVC.
Regardless of the surgical technique, liver transplantation involves an abdominal dissection, removal of the native liver, placement of the liver graft, reperfusion, additional work on the graft, and then closure. For a variety of studies and discussions, we break the operation down into three stages. Breaking the procedure into these stages will permit a better delineation of specific anesthetic goals and physiology.

**Stage I: “DISSECTION Phase”**
This phase consists of incision, exposure, dissection, and recipient hepatectomy. In another context, consider it major abdominal surgery in the presence of coagulopathy, portal hypertension, and frequently severe scar tissue from prior abdominal surgery or from post-necrotic hepatitis. The goal of this portion of the surgery is to mobilize the vascular structures around the liver (suprahepatic vena cava, infrahepatic vena cava, portal vein, and hepatic artery) and isolate the common bile duct. In addition, adhesions between the liver, diaphragm and retroperitoneal areas must be dissected to allow full mobilization of the liver within the right upper quadrant. Be wary of the effects of hepatic manipulation on the venous return: i.e., surgically induced hypotension. This must be distinguished from other causes of hypotension, which are common during liver transplantation.

Toward the end of this stage, we prepare for the anhepatic period by a technique of volume loading. Colloid solution and/or blood product are administered and titrated to filling pressure (e.g. CVP of 10-15 mmHg) in anticipation of a significant decrease in filling pressures after the caval clamps are applied. In the conventional technique, preload is decreased very significantly when the portal vein and IVC are clamped, as the clamps are completely obstructing flow. Piggyback technique allows for preservation of preload by only partially obstructing the IVC and as a result requires less volume loading and promotes hemodynamic stability. However, until just before cross clamp, low CVP is preferred (= 5 mmHg if tolerated) to reduce blood loss from portal venous congestion during dissection. In addition, a general goal during the dissection phase of the operation is to promote a diuresis (either naturally or with pharmacologic assistance), which will allow transfusion of sufficient blood products during the remainder of the case without volume overloading or hemodiluting.
Stage II: "ANHEPATIC Phase"

This is the period of time when no liver is in the circulation. At UCSF, this is nearly always managed without the use of venovenous bypass, and consequently, this stage has significant metabolic and cardiovascular implications. This is the most challenging part of the anesthetic management. The hemodynamic considerations depend on the planned surgical procedure.

The bicaval technique is more challenging from a hemodynamic standpoint. The stage begins with the applications of multiple vascular clamps: 1) Hepatic Artery 2) Portal Vein 3) Infrahepatic Vena Cava 4) Suprahepatic Vena Cava. The mobilized liver is quickly removed, and the ice-cold liver graft is placed in the field.

During the next 30-45 minutes, 3 anastomoses are completed: 1) Suprahepatic vena cava (right beneath the diaphragm, look over and see the hepatic veins draining into the cava of the new liver), 2) Infrahepatic vena cava, and 3) Portal vein - a smaller vessel but critical for providing flow into the liver. Fluid management with the caval clamps can be extremely difficult, as we must anticipate the return of volume when the clamps are released at the completion of the vascular anastomoses. The use of volume must be balanced with use of pressors and inotropes so as not to create a volume overload state with release of the clamps.

Currently, a staged-release is performed: the suprahepatic caval clamp is released and the anastomosis is inspected and small leaks repaired. The infrahepatic caval clamp is then released and the anastomosis is inspected and repaired if needed. Finally, the portal vein clamp is removed allowing recipient blood flow into the donor liver. With the release of the caval and portal venous clamps, preload is brought back to pre-anhepatic levels and will simulate a volume load. In a bicaval technique, this volume load will be exaggerated as compared to the piggyback technique. At this point the anhepatic period ends and the next phase begins.

At UCSF venovenous bypass (VVB) is almost never used in liver transplantation, however, many other transplant centers employee this technique to overcome the negative effects of caval and portal clamping during the anhepatic phase. In VVB, the femoral vein and portal vein are each cannulated. These outflow cannulas divert blood from the splanchnic and systemic circulation to an extracorporeal pump, which then returns the blood to a third cannula placed in the axillary vein so that the blood can return to the heart via the SVC. The benefits of VVB include reduction of hemodynamic instability during the anhepatic phase, preservation of renal function (by avoiding renal congestion associated with IVC clamping), reduction of blood loss (via reduction in portal pressure), and prevention of portal and splanchnic congestion. However, incidence of complications associated with the use of VVB has been reported to be between 10 and 30% and include decannulation of the bypass circuit, air or thrombotic emboli, hypothermia, blood clotting in the bypass system, vessel thrombosis, lymphocele formation, hematoma, vascular and nerve injury, wound infection or dehiscence, hemothorax and prolonged operative and warm ischemic time.

Stage III: "REPERFUSION Phase"
This covers the time from vascular reperfusion of the liver graft until the end of the procedure. The actual moment of reperfusion can have profound cardiovascular effects (i.e. arrhythmias, profound hypotension, and about a 3-5% incidence of hyperkalemic or other cardiac arrest) and anesthetic management is directed at maintaining or recovering cardiovascular stability. Multiple factors likely combine to produce this hemodynamic insult: ionic composition (K⁺) of the preservative solution, hypothermia, metabolic acidosis, "vasoactive" peptides from the gut, other cytokines, and sudden atrial stretching in response to the unclamping and reperfusion. Initially, profound bradycardia can occur, which can progress to asystole if untreated. This can be treated with glycopyrrolate or atropine, but we usually use epinephrine in small doses, 10-30 μg at a time. After the initial bradycardia, the hypotension appears to be due to very low SVR with adequate filling pressures and high cardiac output (15-20 L/min). As the new liver begins to function and vasoactive peptides are metabolized, SVR increases and the hypotension improves.

Following reperfusion, attention is paid to the diagnosis and management of a significant coagulopathy (dilution/consumption of clotting factors, platelet entrapment, heparin effect, primary fibrinolysis, DIC), and resultant bleeding. Platelets should be administered to correct thrombocytopenia. Most of the necessary treatment is FFP. Factor VIIa (Novoseven) or PCC (prothrombin complex concentrate, or Kcentra) can be used in patients with significant volume overload, although it may be best to wait some time until fibrinolysis resolves. Antifibrinolytics (aminocaproic acid or Amicar) can be given if fibrinolysis is suspected. Protamine can be administered to treat any heparin effect. Factor VIIa, PCC, antifibrinolytics, and protamine should be discussed with your attending and the surgeons prior to use. Laboratory analysis and blood product support guide the management of the coagulopathy. Bleeding tends to be of mixed, multifactorial etiology: coagulopathy as mentioned above, extensive raw surfaces above and behind the liver, effects of portal hypertension, and multiple anastomoses.

In addition, we monitor evolution of liver graft function (PT/INR, base deficit, lactate), and recovery from renal ischemia. During this time, the surgeons are completing the hepatic artery anastomosis, controlling bleeding, performing a cholecystectomy on the liver graft, and providing for biliary drainage via an end-to-end (duct-to-duct) anastomosis or a choledochojejunostomy with a Roux-en-Y loop.

Toward the end of the procedure, we shift the anesthetic emphasis to consider postoperative disposition. One option is to provide analgesia and sedation in anticipation of postoperative mechanical ventilation. If the liver is functioning adequately, and the patient is hemodynamically stable with adequate gas exchange, tracheal extubation can be considered. This has been very successful in a high percentage of patients.

Hypertension may develop toward the end of the procedure in about 20-30% of cases. Relative hypervolemia, activation of endogenous reflexes during the anhepatic period, and possibly activation of the renin/angiotensin or endothelin systems probably combine to produce the relative hypertension. It is important to identify a tendency to hypertension before leaving the operating room and provide treatment since hypertension could promote bleeding at the arterial anastomosis.
Intraoperative Hemodynamics: A General Depiction

During the liver transplant procedure a general pattern of hemodynamic changes usually evolve in each patient. This typically reflects the common cardiovascular changes that accompany chronic liver disease, and the manifestations of "reflex responses" to the anhepatic period, and the acute effects of reperfusion as described above. Below, data gathered in one patient during the critical part of the operation are displayed: end of dissection phase, anhepatic period and reperfusion.

<table>
<thead>
<tr>
<th>Stage</th>
<th>HR</th>
<th>MAP</th>
<th>CVP</th>
<th>PA</th>
<th>CO</th>
<th>CI</th>
<th>SVRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissection (II-5)</td>
<td>84</td>
<td>78</td>
<td>5</td>
<td>19</td>
<td>9.9</td>
<td>5.8</td>
<td>589</td>
</tr>
<tr>
<td>Anhepatic (II+10)</td>
<td>99</td>
<td>72</td>
<td>2</td>
<td>4</td>
<td>3.8</td>
<td>2.2</td>
<td>1472</td>
</tr>
<tr>
<td>Anhepatic (III-5)</td>
<td>96</td>
<td>78</td>
<td>5</td>
<td>5</td>
<td>4.3</td>
<td>2.5</td>
<td>1356</td>
</tr>
<tr>
<td>Reperfusion (III+10)</td>
<td>86</td>
<td>72</td>
<td>7</td>
<td>21</td>
<td>11.5</td>
<td>6.7</td>
<td>452</td>
</tr>
<tr>
<td>Reperfusion (III+30)</td>
<td>91</td>
<td>76</td>
<td>8</td>
<td>22</td>
<td>10.0</td>
<td>5.8</td>
<td>543</td>
</tr>
</tbody>
</table>

Please understand that this is the data from one patient, a 60-year-old woman with primary biliary cirrhosis, with the usual manifestations of end stage liver disease. These values are representative for a typical patient undergoing liver transplantation. Note that the initial cardiac output/index is evidence of a hyperdynamic circulation associated with a decreased systemic vascular resistance. During the anhepatic period, marked reductions in filling pressures and cardiac index do not result in systemic arterial hypotension. The ability to increase the SVR three or four fold results in a relatively stable blood pressure. Not all patients will demonstrate the same reflex responses to the anhepatic period, and support of blood pressure may require additional volume and/or pressor support. Not evident in this data are the acute and transient changes that occur upon reperfusion of the liver graft. Despite a
sudden increase in central filling pressures, a period of hypotension (2-3 minutes) usually accompanies graft reperfusion, and usually requires immediate intervention (consider: prophylactic calcium, blood pressure support with norepinephrine or epinephrine.)

Anesthetic considerations

Overview
As mentioned earlier, the cases will be scheduled when a donor liver has been identified. Deceased donor surgeries will be scheduled as information about donors becomes available to surgeons. Because of multiple logistic considerations regarding the procurement of the donor liver, it is not uncommon for the scheduled "start" time to change on short notice. It is important to discuss the various risks with the patient, and specific mention should be made of transfusion and post-operative intubation with care in the ICU. The anesthesia attending should complete this discussion with the patient. As with any operation, there is no ideal anesthetic - there have been no controlled trials comparing different anesthetic agents or techniques during liver transplantation. Anesthetic induction can be performed with propofol. Desflurane, isoflurane, or sevoflurane for maintenance is adequate, with opioid (usually fentanyl). Any reasonable anesthetic technique is possible, but must take into consideration the intricacies of intercurrent illness (i.e. hepatic failure to some extent) and surgical requirements (in this case, management of the anhepatic phase without the use of venovenous bypass). Central to our anesthetic management is preparation and anticipation: at critical points of the operation we look for and expect certain responses from the patient, and are ready to intervene during those critical moments, mostly during the anhepatic phase and with graft reperfusion. An arterial line is absolutely essential. This is usually placed in the left radial artery, because this arm can remain out, while the right arm is tucked. This leads to fewer problems. Femoral arterial lines can be necessary. A right IJ 8.5 or 9 Fr introducer should be placed, with a PA catheter if indicated, or alternatively with a DLIC. A left antecubital RIC (7.0 Fr) is the preferred volume line, which can be attached to the rapid infusion device (Belmont).

Laboratory and Blood Sample Protocol
There is no shortage of intraoperative laboratory tests during this operation. In general, arterial blood samples are sent at baseline and serially during the operation. During critical phases of the operation, labs are usually sent every 30 minutes. We now have the ability to do point of care ABG analysis, which has eliminated problems with delays. This also provides complete electrolytes, hemoglobin, glucose and lactate. CBC and coags are sent to the main laboratory.

Fluid Management
It is fairly common to expect a blood loss of 1-1.5 blood volumes (i.e. 5-8 liters), and total intravenous fluids administration between 15-20 liters. This fluid will consist of crystalloid, colloids, blood products, and "rapid infusion" support. The rapid transfusion device is an important part of the anesthetic management and support of the liver transplant patient. At UCSF, we have a transfusionist available for all of our cases, and following the induction of anesthesia, they can prepare 1-2 liters of modified whole blood consisting of washed packed red blood cells (washed to remove K+ and acid) reconstituted with
fresh frozen plasma at our discretion based on starting hematocrit and coagulation studies. This solution is administered via a Belmont, usually through a left antecubital 7.0 Fr RIC. We are typically able to obtain flow rates of 300-600 cc/minute with a reasonable line pressure, and the transfusionist will administer this volume under the direction of the anesthesia team. Standard blood products are set up for liver transplant. This includes 5 or 10 u PRBC and 5 or 10 u FFP to be brought to the OR, with 2 or 4 single donor platelet units available on request. Thawing of the FFP is delayed until the start of the transplant is confirmed. The circulating nurse may ask you about thawing FFP. If there are any questions about blood banking issues, refer them to your attending. Blood products are brought to the OR in coolers, and the platelets and cryoprecipitate in a soft blue insulated bag. The nurses and transfusionist will check these against our patient for us, but you should always confirm that each unit has been checked before administering (look for the two signatures).

Anesthetic Record
There is a "Liver Transplant" macro on Apex that will insert a collection of drugs and fluids for a liver transplant. It may not be complete, but it is largely accurate.

Currently, Apex does not track “units” of blood, instead requiring entry of volumes of blood products administered. To keep track of numbers of units as well as approximate volume, we have created a system to enter a volume such as 301 ml, which makes reporting units much easier. Please enter unit donor identification numbers (usually starting with W and 12 digits long). Blood from the transfusionist can be totaled at the end per their verbal report, and a quick memo referring to their record for unit numbers can be made. Blood gas data should automatically transmit to the anesthesia record.

Other Useful Links
Liver Intensive Care Group of Europe (Licage) - http://www.licage.org/
United Network for Organ Sharing (UNOS) - https://www.unos.org/
Scientific Registry of Transplant Recipients (SRTR) - https://www.srtr.org/
Organ Procurement and Transplantation Network (OPTN) - https://optn.transplant.hrsa.gov/

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