

LIVER TRANSPLANT HANDBOOK



THE UNIVERSITY OF
CHICAGO
MEDICINE

AT THE FOREFRONT OF MEDICINE®

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Education

MELD	
Transplant Donor Selection	

Important Contacts

Virtual Transplant p8767

Fresh Kidney p5969 Covered by APP or attending in the immediate postop period

Kidney Group Pager 11520

Liver Group Pager 11525

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Clinic Appointments

2-4500

Clinic Appointments immediately post kidney transplant

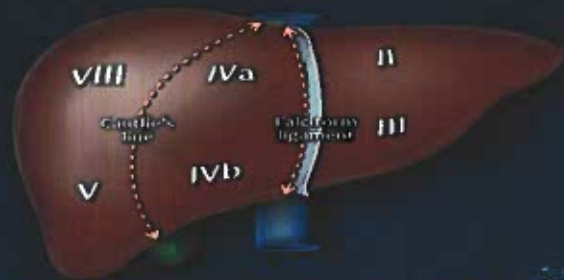
2-6867

Liver Anatomy

Segmental anatomy



Segmental anatomy according to Couinaud. Click to enlarge.



On a frontal view of the liver the posteriorly located segments VI and VII are not visible.

Couinaud classification

The Couinaud classification of liver anatomy divides the liver into eight functionally independent segments. Each segment has its own vascular inflow, outflow and biliary drainage.

In the centre of each segment there is a branch of the portal vein, hepatic artery and bile duct. In the periphery of each segment there is vascular outflow through the hepatic veins.

Right hepatic vein divides the right lobe into anterior and posterior segments.

Middle hepatic vein divides the liver into right and left lobes (or right and left hemiliver). This plane runs from the inferior vena cava to the gallbladder fossa.

The Falciform ligament divides the left lobe into a medial-segment IV and a lateral part - segment II and III.

The portal vein divides the liver into upper and lower segments.

The left and right portal veins branch superiorly and inferiorly to project into the center of each segment.

The illustration above is a schematic presentation of the liver segments.

In reality however the proportions are different. On a normal frontal view the segments VI and VII are not visible because they are located more posteriorly.

The right border of the liver is formed by segment V and VIII. Although segment IV is part of the left hemiliver, it is situated more to the right.

Couinaud divided the liver into a functional left and right liver by a main portal scissure containing the middle hepatic vein. This is known as Cantlie's line.

Cantlie's line runs from the middle of the gallbladder fossa anteriorly to the inferior vena cava posteriorly.

Liver surgery

Right hepatectomy

segment V, VI, VII and VIII (\pm segment I).

Extended Right or right trisectionectomy
segment IV, V, VI, VII and VIII (\pm segment I).

Left hepatectomy

segment II, III and IV (\pm segment I).

Extended Left or left trisectionectomy
segment II, III, IV, V and VIII (\pm segment I).

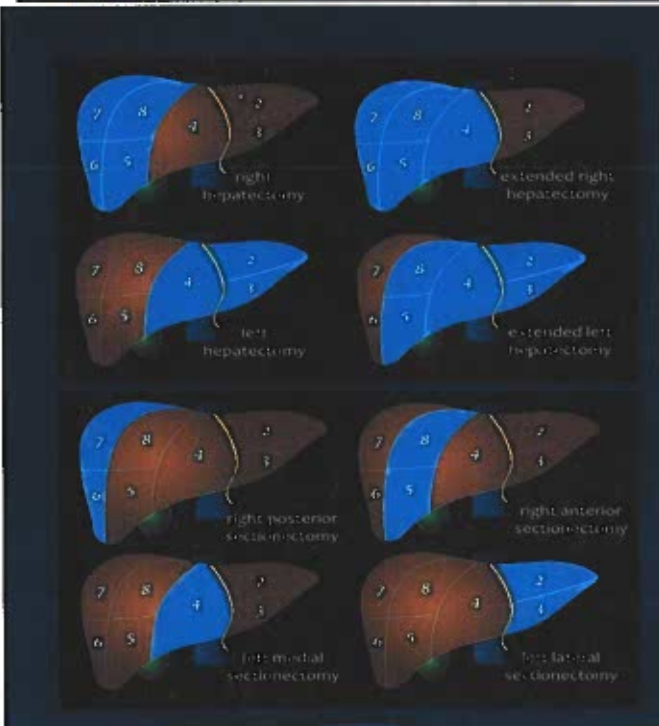
Many surgeons prefer to use the term "extended" instead of trisectionectomy to indicate that some adjacent tissue of segment 4, or 5/8, as applicable is included rather than the entire segment 4, or 5/8.

Right posterior sectionectomy
segment VI and VII

Right anterior sectionectomy
segment V and VIII

Left medial sectionectomy
segment IV

Left lateral sectionectomy
segment II and III



PROGRESSION OF LIVER DAMAGE

HEALTHY LIVER



A healthy liver is able to perform its normal functions effectively, e.g. aiding digestion and breaking down harmful drugs and poisons.

FIBROTIC LIVER



Continuous inflammation of the liver caused by hepatitis C can lead to fibrosis - the formation of scar tissue within the liver.

CIRRHOTIC LIVER



Extensive scarring can block the flow of blood through the liver and cause liver function to deteriorate over time - this is called cirrhosis.

LIVER CANCER



Hepatitis C is a leading cause of liver cancer - the formation of a malignant tumour in the liver.

Transplant Abbreviations

SPK-Simultaneous kidney/pancreas transplant	LRD-Living related donor
PAK-Pancreas after kidney transplant	LURD-Living unrelated donor
PTA-Pancreas transplant alone	B2M-Beta-2 Microglobulin
DDRT-Deceased donor renal transplant	DGF-Delayed graft function
LRRT-Living related renal transplant	AMR-Antibody mediated rejection
LURT-Living unrelated renal transplant	ACR-Acute cellular rejection
LDRT-Living donor renal transplant	DSA-Donor specific antibody
DCD-Donation after cardiac death	ESRD-End stage renal disease
DBD-Donation after brain death	ATN-Acute tubular necrosis
KDPI-Kidney donor profile index	AKI-Acute kidney injury
FSGS-Focal segmental glomerulosclerosis	RRT-Renal replacement therapy
CAN-Chronic allograft nephropathy	CKD-Chronic kidney disease
HD-Hemodialysis	
CVVH-Continuous veno-venous hemofiltration	ATG-Thymoglobulin
GFR-Glomerular filtration rate	HLA-Human leukocyte antigen
OLT-Orthotopic liver transplant	MHC-Major histocompatibility complex
ESLD-End stage liver disease	ABO-blood type
PBC-Primary biliary cirrhosis	OPO-Organ procurement organization
PSC-Primary sclerosing cholangitis	UNOS-United Network for Organ Sharing
HCC-Hepatocellular carcinoma	PVT-Portal vein thrombosis
HCV-Hepatitis C virus	ERCP-Endoscopic retrograde cholangiopancreatography
HBV-Hepatitis B virus	SBP-Spontaneous bacterial peritonitis
HAT-Hepatic artery thrombosis	GVHD-Graft versus host disease
RFA-Radio frequency ablation	STR-Short tandem repeats(tests for GVHD)
TARE-Transarterial radioembolization	CMV-Cytomegalovirus
TACE-Transarterial chemoembolization	
NASH-Nonalcoholic steatohepatitis	
NAFLD-Nonalcoholic fatty liver disease	
EBV-Epstein Barr virus	
BK-BK virus(polyomavirus)	
ANC-Absolute neutrophil count	
MMF-Mycophenolate Mofetil	
MF-Myfortic	
FK-FK506 Tacrolimus	
CSA-Cyclosporine	
CNI-Calcineurin inhibitor	



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ADULT LIVER TRANSPLANT EVALUATION

Tests that must be done at University of Chicago Medical Center

- Baseline CT of upper abdomen and pelvis using a triple phase contrast or cirrhosis protocol or an MRI of upper abdomen using triple phase contrast plus noncontrast CT abdomen and pelvis
- Annual CT of upper abdomen or MRI of liver using triple phase contrast
- Ultrasound of the liver with Doppler annually (every 6 mos once MELD \geq 22)
- CXR PA-L annually
- EKG annually
- Blood Type x 2
- Resting echocardiogram every year (with PA pressure estimate)
- Cardiac Calcium Score by CT scan (if indicated by cardiac workup protocol)
- PFTs with ABG (for patients with history of or at risk for lung disease)
- GFR by serum cystatin, urine protein to creatinine ratio

For patients at risk:

- Upper GI Endoscopy to screen for esophageal varices (every year if not on beta blocker or every 2 years if on a beta blocker)
- Colonoscopy (patients at age \geq 50 years, AA patients at age \geq 45 years)
- Bone Density using dual photon absorbitometry
- Dental clearance (dental exam or panorex or cone CT; potential infection sources should be identified and treated before activation for transplantation)
- Mammogram (annually at age \geq 40 years)
- Pap smear and pelvic exam (annually for age \geq 18 years)

Recommended Immunizations

- Pneumonia vaccine: Prevnar13 and pneumovax 23
- Tdap vaccine
- Annual flu vaccine
- Hepatitis vaccines
 - Hepatitis B vaccinations if HBsAg and HBsAb negative (3 doses)
 - Hepatitis A vaccine if HAV IgG is negative needed (2 doses)
 - Or Twinrix (combined Hepatitis A & B vaccine if HBsAb & HAV IgG are both negative; 3 doses)
- Shingrix vaccine (age \geq 50)
- HPV vaccine for young women, transgender or immunocompromised patients at age \leq 26 years and young men at age \leq 21 years or men who have sex with men

Laboratory Studies

- CBC, CMP, PT, zinc, magnesium,
- Quantiferon TB Gold Blood test
- EBV IgG & IgM (IDPA case only for insurance requirement)
- CMV IgG
- VZV (varicella zoster virus) IgG & IgM (IDPA case only for insurance requirement)
- HIV
- RPR
- Hepatitis A Total Ab
- HBsAg, HBsAb, total HbcAb —HBsAg positive patients need HBV DNA by PCR, HBeAg and HBeAb
- Hepatitis C Ab (HCV RNA, HCV genotype if HCV Ab positive)
- HCC risk panel (at baseline and every 6 months, every 3 months for patients with HCC)
- Urine toxicology and urine cannabinoids
- **Troponin T**
- PSA (all men over 50 years of age)
- AIH patients - ANA, ASMA
- PBC patients - AMA if not done, vit ADE
- PSC patients - CEA and CA19-9 every 6 months, vit ADE

Other transplant team evaluations:

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University of Chicago Center for Liver Disease Acute Liver Failure Protocol

1. Criteria to enter this protocol

- a. No prior history of liver disease except Wilson's disease
- b. PT/INR > 2.0 OR presence of any stage of hepatic encephalopathy
- c. ALT \geq 300
- d. bilirubin \geq 2.5

2. Admit to ICU

3. Baseline labs

- a. Blood type and screen (on two separate draws)
- b. Complete blood count with differential
- c. Chemistries
 - i. Complete metabolic panel plus magnesium and phosphate
 - ii. Arterial blood gas (ABG)
 - iii. Arterial lactate
 - iv. Lipase
 - v. Ammonia level (arterial if possible)
- d. AFP
- e. Prothrombin time/INR, PTT, factor V, TEG if available
- f. Acetaminophen level
- g. Toxicology screen
- h. Viral hepatitis serologies
 - i. Anti-HAV IgM
 - ii. HBsAg
 - iii. Anti-HBc IgM,
 - iv. Anti-HEV (if suspected)
 - v. Anti-HCV
 - vi. Herpes Simplex Virus IgM Ab and HSV PCR
- i. Ceruloplasmin level - if Wilson's disease is suspected, also obtain:
 - i. serum copper
 - ii. 24 hr urine copper
 - iii. Slit lamp exam (ophthalmology consult)
- j. Pregnancy test (females)
- k. Autoimmune markers
 - i. ANA
 - ii. ASMA
 - iii. Immunoglobulin levels
- l. HIV status
- m. Blood cultures x 2
- n. TSH
- o. Prealbumin

4. Radiologic and other testing

- a. Hepatic ultrasound with doppler study – to evaluate for evidence of chronic liver disease and for vascular patency
- b. Non-infused head CT – for baseline brain image prior to possible neurological deterioration and to rule out other causes of encephalopathy
- c. Echocardiogram if MELD >20

5. Nursing orders

- a. Peripheral IV placement
- b. Foley catheter
- c. BP, P, RR, SpO₂, Temp q2h
- d. Glucose accuchecks q4h
- e. Diet (if alert): 3000 cal, low glutamine
- f. Neurologic checks q2h for hepatic encephalopathy stage 1-2.
Neurologic checks q1h for hepatic encephalopathy stage 3-4.
- g. Accurate 24 hr urine output; I/O
- h. Daily weights

6. Medications

- a. Administer NAC
 - i. intravenously for acetaminophen toxicity – order as “acetylcysteine IVPB acetaminophen toxicity panel”
 - 1) 150 mg/kg (max 15,000 mg) in 250 ml D5W IV over 15-60 minutes, followed by
 - 2) 50 mg/kg (max 5,000 mg) in 500 ml D5W IV over 4 hours, followed by
 - 3) 100 mg/kg (max 10,000 mg) in 1000 ml D5W IV over 16 hours
 - ii. intravenously for non-acetaminophen toxicity with stage 1-2 hepatic encephalopathy – order as “acetylcysteine IVPB acute liver failure panel”
 - 1) 150 mg/kg (max 15,000 mg) in 250 ml D5W IV over 60 minutes, followed by
 - 2) 50 mg/kg (max 5,000 mg) in 500 ml D5W IV over 4 hours, followed by
 - 3) 150 mg/kg (max 15,000 mg) in 1000 ml D5W IV over 24 hours, followed by
 - 4) 150 mg/kg (max 15,000 mg) in 1000 ml D5W IV over 24 hours, followed by
 - 5) 118.75 mg/kg (max 11,875 mg) in 1000 ml D5W IV over 19 hours, then
 - 6) discontinue NAC
 - 7) Note: The final dose of 418.75 mg/kg over 67h is split into three different infusions for stability reasons. Consider lower volume diluents for patients with hyponatremia; the max concentration is 58.4 mg/ml.⁵
 - iii. orally - 140 mg/kg by mouth or nasogastric tube diluted to 5% solution, followed by 70 mg/kg by mouth q 4 h for 17 doses
- b. Protonix or other PPI IV bid
- c. Vitamin K 1 mg IV
- d. Zosyn IV, vancomycin IV, and diflucan IV if patient has at least one of the following conditions:
 - i. Stage 2 hepatic encephalopathy AND hemodynamic instability (hypotension, tachycardia, increased work of breathing), fever, or acidosis
 - ii. Stage 3 or 4 hepatic encephalopathy
 - iii. Hemodynamic instability, fever, or acidosis

7. Medical monitoring

- a. Assess q 6 h:
 - i. NH₃

- ii. PT/INR
- iii. CMP
- iv. Lactate
- b. ABG q 12 h
- c. Assess daily in addition to above:
 - i. CBC
 - ii. lipase
 - iii. Random urine sodium
 - iv. Phosphorus
 - v. Magnesium
 - vi. Blood and urine cultures
 - vii. AFP on day 3
- d. Daily MELD/MELD-Na score

8. Consults:

- a. Hepatology – will activate liver transplant team consult, hepatology attending to discuss case with transplant surgery attending
- b. Transplant surgery team (pager 8767)
- c. Neuro ICU team (pager 6228)
- d. Psychiatry (in cases of drug overdose)

9. Hyponatremia (<130) management

- a. Assess volume status
- b. Check cortisol level
- c. Check urine sodium and osmolality
- d. Change all IV fluids and piggybacks to 0.9 NS
- e. Administer 0.9 NS, albumin, 3% NSS cautiously
- f. Serum sodium correction should be limited to 10 meq/ml per day
- g. Consider nephrology consult

10. Coagulopathy management – correct only when there is active bleeding or when invasive procedures are being performed

- a. Obtain TEG prior to procedure
- b. If bolt placement is planned:
 - i. Novo 7 or
 - ii. 4 units FFP plus 1 unit cryoprecipitate if Novo 7 is not available
 - iii. 6 pack platelets for thrombocytopenia
- c. After bolt placement:
 - i. Keep INR <1.5 for at least 24 hours if possible
 - ii. Keep platelets >100K

11. Encephalopathy management

Staging of hepatic encephalopathy:

- | | |
|-----|---|
| I | Changes in behavior with minimal change in level of consciousness |
| II | Gross disorientation, drowsiness, possibly asterixis, inappropriate behavior |
| III | Marked confusion, incoherent speech, sleeping most of the time but arousable to vocal stimuli |
| IV | Comatose, unresponsive to pain, decorticate or decerebrate posturing |

***Central venous access - avoid central venous access through the internal jugular vein as much as possible to avoid impairing cerebral venous drainage and causing ICP elevation. Subclavian vein access, or if not feasible, femoral vein access, are preferred for central venous or dialysis catheter placement.**

- a. If stage I/II Encephalopathy:
 - i. Avoid stimulation, avoid sedation if possible
 - ii. Complete Transcranial Doppler (TCD) x 1 - to obtain baseline flow velocities and Pulsatility Indexes
 - iii. Lactulose: 30 ml PO (or per NGT) q12h and titrate to 3 soft formed stools/day
 - iv. Rifaximin 550 mg PO or per NGT bid
- b. If stage III/IV Encephalopathy:
 - i. Avoid stimulation
 - ii. TCD daily for patients without an ICP monitor (to non-invasively assess for increased intracranial pressure)
 - iii. Dobhoff feeding tube placement for nutrition
 - iv. Lactulose: 30 ml PO (or per DHT) q12h and titrate to 3 soft formed stools/day
 - v. Rifaximin 550 mg PO or per NGT bid
 - vi. Intubation
 - vii. Elevation of head of bed $\geq 30^\circ$
 - viii. Induce mild hypernatremia (serum Na⁺ goal: 145-155 mEq/L) to prevent/ameliorate the development of cerebral edema. Be careful to not increase serum Na >0.5 mEq/L/hour to avoid osmotic demyelination syndrome.
 - ix. Consider placement of ICP monitoring device by Neuro ICU team
 - 1) Indications for ICP monitoring:
 - a) Stage III hepatic encephalopathy AND need for intubation and sedation (lack of ability to follow the neurological exam)
 - b) Stage III encephalopathy AND presence of cerebral edema on head CT
 - c) Stage IV Encephalopathy
 - d) Large and unreactive pupils or nonphysiologic anisocoria
 - e) Clinical signs of brain herniation
 - f) Descerebrate or decorticate posturing
 - g) Rapid neurological decline to Grade III or IV hepatic encephalopathy
 - x. Staged management of increased ICP (ICP >20 mm Hg) – maintain cerebral perfusion pressure (MAP – ICP) >50 mm Hg (ideally CPP of 60 mm Hg) under the guidance of Neuro ICU team.
 - 1) Head of bed ≥ 30 degrees
 - 2) Head in neutral position
 - 3) Pain control and sedation as needed
 - 4) Avoid obstruction/compression of the jugular venous drainage, including insertion of internal jugular venous lines
 - 5) Mannitol (0.5 - 1 gram/kg IV delivered in a 10-15 minutes infusion to avoid arterial hypotension): use for severe elevation of ICP or first clinical signs of herniation. Monitor the serum osmolarity every 6 hours and use sparingly in renal failure (although for patients in CVVHD it can be used regularly. Promote an extra 200 cc of negative fluid balance after each dose of mannitol). In cases

- of brain herniation, a dose of up to 1.5 grams x 1 can be used.
- 6) Induced hypernatremia – with careful titration to serum sodium of ~150 – 160 mEq/L
 - a) Use 3% saline as bolus and maintenance drip as needed. In cases of severe intracranial hypertension and/or brain herniation, 23.4% NaCl IV can be used
 - 7) Hyperventilation – best guided by jugular A-V O₂ content difference, Transcranial Dopplers and ICP.
 - 8) Hypothermia to 33-34 degrees Celsius core body temperature
 - 9) CVVHD to lower ammonia levels that are >150 despite aggressive medical therapy or in those with worsening mental status
 - 10) Barbiturate coma – may use short-acting pentobarbital
 - 11) High-dose Propofol
 - 12) Indomethacin (avoid due to bleeding risks and splanchnic ischemia, unless last resource)

12. Seizure management

- a. EEG assessment
- b. CT scan of head, if not performed
- c. NeuroICU consultation, if not yet on consulted
- d. Treatment options:
 1. Phenytoin
 2. Benzodiazepines
 3. Propofol (in intubated patients)

13. Prognostication – predictors of poor prognosis for recovery

- a. Etiology of acute liver failure
 - i. Idiosyncratic drug injury
 - ii. Nonhepatitis A infection
 - iii. Autoimmune hepatitis
 - iv. Mushroom poisoning
 - v. Wilson disease
 - vi. Budd-Chiari syndrome
- b. Stage 3 or 4 encephalopathy at admission
- c. King's College criteria
- d. Clichy's criteria

King's College Criteria:

Acetaminophen-induced ALF:

- Arterial pH <7.3 (following adequate volume resuscitation) irrespective of

coma grade

OR

- PT >100 seconds

Non-acetaminophen-induced ALF:

- PT >100 seconds (INR >6.5) irrespective of coma grade

OR

- Any three of the following, irrespective of the coma grade:
 - Drug toxicity, indeterminate cause of ALT
 - Age <10 years or >40 years
 - Jaundice to coma interval >7 days
 - PT >50 seconds (INR >3.5)
 - Serum bilirubin >17.5 mg/dL

Clichy's Criteria

- Hepatic encephalopathy
- Factor V level
 - <20% in patients <30 years of age
 - <30% in patients ≥30 years of age

**Acute Alcoholic Hepatitis Guidelines for *Expedited* OLT evaluation and listing
University of Chicago Medicine, Center for Liver Diseases**

Committee Members: Anjana Pillai, Andrew Aronsohn, Barrett Gray, Daniel Fridberg, Sonali Paul, Talia Baker, Helen Te, Amanda Burress, Christine Trotter, Katherine Wherity, Joan Schulz, John Fung

Activation Date: December 2017

Background:

It is well-documented that patients with severe acute alcoholic hepatitis refractory to medical therapy have a high short term mortality without a life-saving organ transplant. It is also known that these patients only respond to medical therapy 50% of the time and 6 month mortality exceeds 70-80%. Validity of the six month rule in predicting alcohol relapse is controversial and there is data that shows duration of abstinence prior to liver transplant is a poor predictor of relapse. Carefully selected patients may have low risk of relapse despite not adhering to the strict 6 month abstinence rule.

Prevalence of recidivism varies from 10-60% across different studies due to variations in definition (any vs harmful alcohol use). Recidivism is most likely to be reported 2 years post LT and the majority of patients use ETOH intermittently with low risk of graft and patient loss.

Primary Outcome:

1 year survival – patient and graft

Action Items: Remove mandatory period of sobriety (assess on an individual basis) *unless* patient is in the transplant evaluation process and found to have + urine ETG/Utox

Inclusion Criteria:

- patients with severe alcoholic hepatitis refractory to medical therapy
- first known decompensation of liver disease due to ETOH use

Absolute contraindications:

- previous decompensation with known ETOH use and known liver disease
- lack of adequate and durable social support
- active, uncontrolled psychiatric illness
- significant legal conflicts due to alcohol
- progressive neurologic illness/deficits
- medical noncompliance leading to adverse medical complications (ie uncontrolled DM leading to amputations/multiple DKA admissions, non-compliance with medications leading to significant CV disease, non-adherence to meds due to ETOH or drug use)
- re-transplant due to alcohol disease of 1st graft
- unwillingness to admit to alcohol dependence/abuse or enter rehab program
- active polysubstance abuse (excluding marijuana unless insurance mandates)

-SIPAT score >70

Relative contraindications:

- ongoing opioid use (methadone vs active narcotic dependence)
- nicotine use (quantity, duration, affiliated cancer or CV risk) – assess on individual basis (ie will PVD/CAD in setting of active tobacco use be a contraindication)
- multiple failed rehab attempts

Mandate:

- post OLT f/u and contractual agreement and resources as recommended by transplant social worker
- random urine ETG/urine tox while undergoing evaluation, during listing, and after transplantation
- expectation that patient follows through with the rehab plan dictated in the initial assessment and treatment plan as well as the plan agreed upon in the signed treatment contract
- treatment plans dependent upon individual situations and risk factors in addition to insurance coverage and location

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9. Stroh G, Rosell T, Dong F, et al. Early Liver Transplantation for Patients with Acute Alcoholic Hepatitis: Public Views and the effects on organ donation. *Am J Transplant* 2015; 15: 1598-1604
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EKG and Resting Echo (add bubble study if with dyspnea or hypoxia)

**History of CAD, CHF
cardiac surgery,
arrhythmia,
cerebrovascular disease,
peripheral vascular
disease, angina,
cardiomegaly on imaging**

**Consult and
cardiac cath**

**Abnormal EKG*, abnormal
resting echo** or
presence of intracardiac
shunt, cardiac arrhythmia**

**Consult ±
Cardiac CTA or
cardiac cath**

**Normal EKG and
resting echo**

**Age ≤35,
No risk factors**

**No additional
testing**

**Age >35 or
age >30 with
risk factors**

CCS ≤10

**No additional
testing**

**Cardiac calcium
Score (CCS) CT
scan**

CCS ≤10

**No additional
testing**

CCS 11-400

**Cardiac CTA ±
consult**

**Normal renal
fxn, able to hold
breath**

CCS >400

**Consult and
cardiac cath**

- Risk factors:**
1. DM
 2. Smoking
 3. Hyperlipidemia
 4. Family hx of CAD (age <60)
 5. HTN
 6. History of cocaine use
 7. Morbid obesity

**Consult; Dobutamine
stress echo (CCS ≤100)
or cath (CCS >100)**

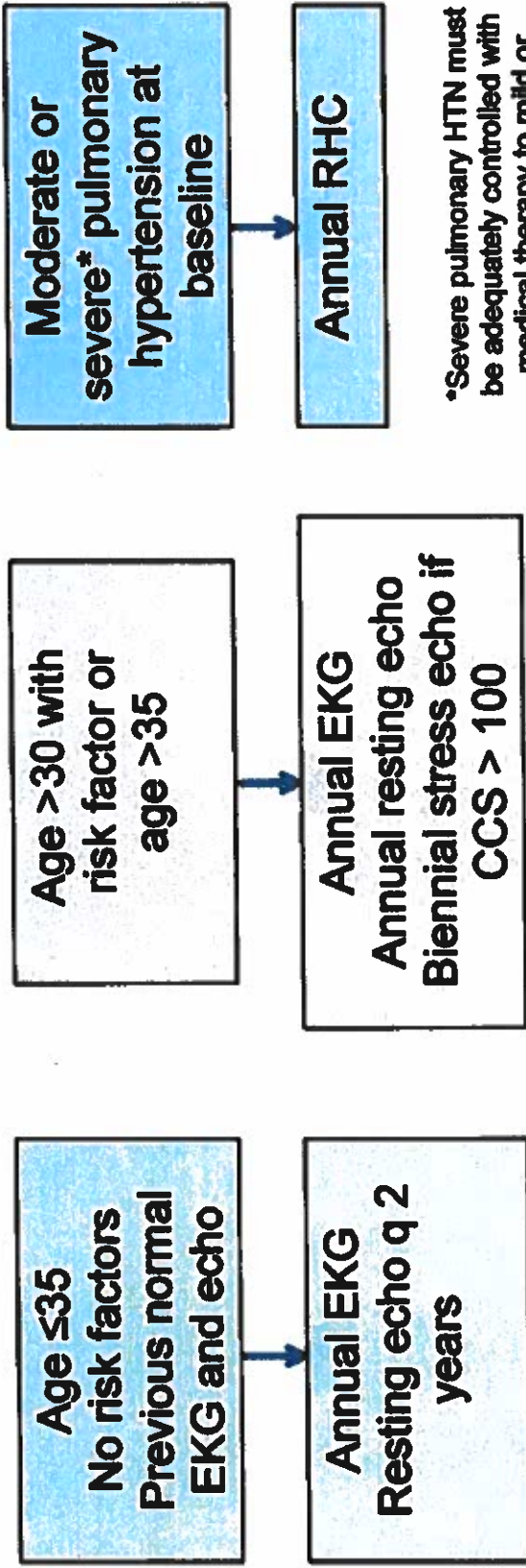
*Abnormal EKG - indicative of ischemia - STTW changes, Q waves, LBBB, arrhythmia.
**Abnormal resting echo - presence of regional wall motion abnormalities, EF <50%, mod to severe valvular disease, mod to severe pulmonary HTN, or presence of RVH, RV dilatation, RA dilatation.

yes

no



FOLLOW-UP CARDIAC EVALUATION FOR OLT CANDIDATES



Risk factors:

1. History of angina
2. History of CAD (MI, CABG, PTCA)
3. History of CHF
4. History of cardiac arrhythmia (Afib, VT)
5. History of cerebrovascular disease (CVA, TIA)
6. History of peripheral vascular disease
7. DM
8. Smoking
9. Hyperlipidemia
10. Family hx (age <60)
11. HTN
12. History of cocaine use
13. Abnormal resting echo (regional wall motion abnormalities, EF <40%, mod to severe valvular disease, or mod to severe pulmonary HTN, or presence of RVH, RV dilatation, RA dilatation)
14. Abnormal EKG (indicative of ischemia - STTW changes, Q waves, LBBB, arrhythmia)
15. TIPS
16. Morbid obesity

Approach to Liver Transplant in Adult Jehovah's Witness Recipients

No previous right upper quadrant surgery

Recombinant human erythropoietin. Adjunctive folic acid, vitamin B12, oral or intravenous iron supplements.

Serum creatinine < 2 mg/dL and absence of proteinuria.

INR minimum 1.5 after 2x10 mg doses of Vitamin K given parenterally

Allowance of normovolemic hemodilution (3 units phlebotomized but kept in circuit with central line

Use of cryoprecipitate and recombinant Factor VIIa allowed. Consideration for the use of Octaplas, Pooled Plasma (Human), Solvent/Detergent Treated or FFP

Platelet count >75,000 /mm³ – use of thrombopoietin mimetics (Romiplostim or Eltrombopag) allowed to increase platelet counts

Intraoperatively, strategies for reducing risk of blood product transfusion include lowering CVP to 5 mm Hg and maintenance of BP with use of vasopressors; avoidance of hypothermia (T > 35°C); minimal blood sampling (1 cc x 4 samples); and return of blood scavenged from the operative field.

Use of amicar and/or epsilon amino caproic acid and/or pre-emptive Factor VIIa.

Early re-exploration for evidence of bleeding.

Paralytics and mechanical ventilation for Hgb <6 gm/dL and increase in FiO₂ to decrease oxygen demand and maximize oxygen delivery. Continue daily recombinant human erythropoietin until post-transplant Hgb > 9 gm/dL.

UCM DCD Protocol

Donor must meet below criteria:

- Age \leq 50 yo
- Donor ICU Stay \leq 5
- BMI \leq 32
- Bilirubin \leq 2.5
- Local
- HCV negative
- Time from extubation to perfusion \leq 30 minutes
- Expected CIT \leq 8
- Estimated steatosis \leq 10

Recipient Criteria:

- Primary transplant
- No extensive RUQ surgery
- Low risk cardiovascular (no HPS or PPHTN)

Donor Procedure:

- Two attendings vs. attending and fellow
- Bring 1 vial tPA
- Bring 10 HTK
- Need to arrange or bring scale for donor liver
- Heparin and tPA protocol:
 - 30,000 units of heparin is administered systemically prior to withdrawal of life support, if local policies permitted it. Otherwise, 30,000 units of heparin were mixed in the initial bag of cold preservation solution.
 - tPA dosage is determined by liver graft weight (0.5mg tPA/100g graft) which is injected into the hepatic artery on the back table.
 - Clamp hepatic artery and store liver in preservation solution
- Upon flush contact recipient surgeon regarding usability of liver

Recipient Procedure

- To be in preop at time of extubation
- Upon acceptance of liver patient to wheel back to OR
- Attending surgeon to start as soon as possible to limit CIT
- tPA:
 - Following injection of tPA on back table, the hepatic artery is kept clamped until 10-15 min after reperfusion of the portal vein. The artery was then unclamped to allow excess tPA, if any was present, to back-bleed and the effluent was discarded.

Transplanting hepatitis C (HCV) RNA Positive Donor Organs into HCV RNA Negative Recipients

Patient selection criteria:

1. Liver transplant candidate assessed by Liver Transplant Team to be significantly underserved by the current allocation system.
2. Patient understands the risks and signs the consent to accept HCV RNA positive organ.
3. Patient understands the need for administration of antiviral therapy following liver transplantation.

HCV-positive donor selection criteria:

- a. Age <46 years
- b. No fibrosis or cirrhosis on inspection and ultrastructure
- c. Hepatic steatosis $\leq 30\%$
- d. Hepatitis B NAT negative
- e. No known history of HCV (direct acting antiviral) therapy exposure

Procedures:

1. Data on donor HCV RNA and HCV genotype will be obtained from Gift of Hope once available.
2. HCV RNA will be drawn from recipient on day 5-7, week 2, then week 4.
3. HCV genotype will be obtained once HCV RNA is above 1,000 IU/ml. HCV genotype 1a resistance panel will be obtained if patient has genotype 1a and is being considered for Zepatier or Mavyret therapy.
4. Preauthorization for antiviral therapy will be initiated once HCV RNA, HCV genotype, and resistance panel (if applicable) results are available.
5. Drugs of choice (subject to change with availability of new drugs):
 - a. Epclusa – genotype 1 to 6 with normal renal function
 - b. Mavyret (glecaprevir/pibrentasvir) – genotype 1 to 6, with renal insufficiency, not on cyclosporine
6. Second line drugs – if dictated by insurance formulary
 - a. Harvoni – genotype 1, 4, 5, 6 with normal renal function
 - b. Zepatier – genotype 1, 4 with renal insufficiency
 - c. Vosevi – genotype 1-6
7. Duration of therapy: 12 weeks (16 weeks of Zepatier if NS5A resistance is present)

Steps for Admitting the Abdominal Transplant Patient

1. You will receive a page from the transplant coordinator to notify you of transplant. If liver or pancreas, coordinator will ask you to place an RFA(request for admission). To do this, go to orders only on the EPIC toolbar>enter MRN>enter RFA. If it is a kidney transplant, the coordinator will place the RFA.
2. The nurse coordinator will provide you with recipient information, ETA, OR time and if the donor is high risk. If they do not give you this information, ask. You will need to know if high risk for consenting purposes.
3. Transplant patients should be admitted to 3W, 2nd choice is 3C, and last resort in preop.
4. Once the patient arrives, place admit orders with the following order sets:
 - a. 2096 Liver Transplant Recipient Admission..
 - b. 2101 Kidney Transplant Recipient Admission.
 - c. 2102 Kidney/Pancreas Transplant Recipient Admission.
 - d. If Panc alone use 2102
5. Priority is getting labs drawn first before heading to CXR. You may need to escort the patient to and from radiology if in a time crunch. EKG done while waiting for phlebotomy.
6. If patient is a liver transplant, you will need to obtain VRE rectal swab
7. Complete transplant specific H&P using the transplant template. To access this you must be logged into PVD transplant. See next page for H&P PEARLS
8. Consent the patient. Transplant specific consents must be printed off of EPIC so the most up to date data is represented. To do this, go to EPIC tool bar>UCMC Tools>TR consent and protocol>print off 'Consent for Organ Transplant Surgery' Make sure blood consent box is checked. If donor is high risk, click the check box and ensure they initial it. If it is not high risk, cross the box off. Make sure the patient AND providers have signed, printed, dated and timed. Stickers must be on all pages of the consent.
9. Mark the patient.
- 10. Follow-up all admission workup. Look at your labs, EKG, and CXR. If you have any concerns that could preclude transplant (eg severe hyponatremia, hyperkalemia, leukocytosis, arrhythmias), notify attending immediately so can be addressed or organs can be reallocated.**
11. Kidney transplants will normally go back to the floor after OR. Notify floor charge nurse so they can staff appropriately. Liver and kidney/pancs will need a transfer order for an ICU bed postop.
12. Place preop orders. Order like you normally do through the preop order reconciliation. I recommend doing this after labs are drawn and sent as to not accidentally discontinue them.
 - a. Use preop order set 5083 'Abdominal Transplant Preop Order Set'
 - b. First part is standard preop orders
 - c. Kidneys, kidney/pancs, pancs get preop HSQ

- d. Liver transplants do not get preop HSQ 2/2 coagulopathy, thrombocytopenia
- e. This is where you will choose antibiotics and immunosuppression
 - i. Liver transplant-Zosyn is preferred abx. Click Zosyn and Fluconazole. If PCN allergic, Cipro+Flagyl+Vanco+Fluc. Click Solu-medrol 500mg.
 - ii. Kidney Transplant-Ancef is preferred abx. Click ancef appropriate for weight. If PCN allergic, cipro+clinda. Click Solu-medrol 500mg. Then you must choose between Thymoglobulin OR Basiliximab(Simulect) induction. Ask the attending which they want. If Simulect, click Simulect 20mg. If thymo, click thymo. Calculate IBW and ABW. Then dose 1.5mg/kg IBW, rounded to the nearest 25mg. IF large discrepancy between IBW and ABW split the difference in dosing, not to exceed 150mg. Mix in 500cc bag for OR dose. If you are unsure, ask the transplant pharmacist for assistance.
 - iii. Kidney/Panc-Rocephin is preferred abx. Click Rocephin dose appropriate for weight. If PCN allergic, clinda+cipro. Click Solu-medrol 500mg. Then you must choose between Thymoglobulin OR Basiliximab(Simulect) induction. Ask the attending which they want. If Simulect, click Simulect 20mg. If thymo, click thymo. Calculate IBW and ABW. Then dose 1.5mg/kg IBW, rounded to the nearest 25mg. IF large discrepancy between IBW and ABW split the difference in dosing, not to exceed 150mg. Mix in 500cc bag for OR dose. If you are unsure, ask the transplant pharmacist for assistance.

Transplant H&P PEARLS

Liver/Kidney/Pancreas Transplant

- Recent hospitalizations or infections
- Recently diagnosed cancer
- Previous transplant>When, why was graft lost?
- Document encephalopathy, ascites
- Is intraop CVVH necessary? If so, page on call nephrology.

Common Order Sets

- 2101 Kidney Transplant Admit for Transplant
- 2104 Kidney Transplant Postop Orders
- 2096 Liver Transplant Admit for Transplant
- 2533 Liver Transplant Postop Orders
- 2102 Kidney/Pancreas Transplant Admit for Transplant
- 2116 Kidney/Pancreas Transplant Postop Orders
- 5083 Abdominal Transplant Preop Order Set(Includes immunosuppression and abx)
- 6758 Acute Liver Failure Protocol

Adult Liver Transplant Instructions for OR

Blood bank (2-6827, p3596):

For all cases, prepare:

- 10 units of pRBC
- 2 packs (12 units) of platelets
- 10 units of FFP

Medications to be given during the case:

- Piperacillin/tazobactam 4.5g + fluconazole 400 mg IV at the beginning of the case
If pcn-allergic, give ciprofloxacin 400 mg + metronidazole 500 mg + vanco 20 mg/kg instead of pip/tazo
- Methylprednisolone 500 mg IV during the anhepatic phase

Antibiotic redosing in the OR:

Redose piperacillin/tazobactam 4.5g q3h throughout the case (q6h if eGFR <50)
Redose ciprofloxacin 400 mg q8h throughout the case (do not redose if eGFR <50)
Do not redose vancomycin, metronidazole, or fluconazole

Transplant Time Out:

- Confirm UNOS donor number
- Confirm organ ABO-blood group compatibility
- Confirm vessel compatibility
- Will this case require CVVH?
- Will this case require bypass?
- Confirm availability of CellSaver
- Confirm antibiotic plan
- Confirm immunosuppressive plan
- Evaluate need for furosemide and mannitol during anhepatic phase

Debrief:

- Determine plan for extubation
- Determine plan for post-op ultrasound
- Discuss plan for renal replacement
- Determine if methylprednisolone redosing is warranted
- Determine need for HBV antiviral post-transplant

Upon Arrival to SICU:

For all patients:

- Early extubation if meets weaning criteria
- Obtain a liver ultrasound 6-12 hours post-op or early the next morning

Liver Transplant Kit Content List

The following items should be in every pre-prepared kit:

Qty Item

- 8 Albumin 5% 250 ml bag
- 12 Calcium chloride 1g in 10 ml syringe
- 2 Dextrose 50% 50 ml syringe or bottle
- 2 Furosemide 40 mg in 4 ml vial
- 1 Magnesium sulfate 2g in 50 ml premix bag
- 4 Mannitol 25% 50 ml vial ****WARNING: inspect for crystals prior to administration; if crystals are visible, exchange for a non-crystallized vial; use a filter-type administration set for intravenous infusion****
- 1 Methylprednisolone 500 mg vial
- 1 Norepinephrine 16 mg in 250 ml NS premix bag
- 5 Sodium bicarbonate 8.4% 50 mEq in 50 ml syringe or vial
- 2 Vasopressin 20 units in 1 ml vial
- 1 Verapamil 5 mg in 2 ml vial
- 1 NS 100 ml IV bag (for vasopressin)
- 1 NS 50 ml IV bag (for methylprednisolone)
- 1 Anesthesia billing sheet
- 1 Copy of this document

Pull a bag of insulin R 100 units in NS 100 ml from the OR Omnicell or obtain from the OR pharmacy.

and

One of the following antibiotic regimens should be pulled from the OR Omnicell, as ordered:

Regimen 1:

Qty Item

- 3 Piperacillin/tazobactam 4.5g with sodium chloride 0.9% 50 ml minibag
- 1 Fluconazole 400 mg in NS 200 ml premix

Regimen 2:

Qty Item

- 1 Ciprofloxacin 400 mg in 200 ml D5W premix bag
- 1 Metronidazole 500 mg in 100 ml NS premix bag
- 1 Vancomycin 20 mg/kg IV
- 1 Fluconazole 400 mg in NS 200 ml premix bag

Regimen 3:

Patients undergoing treatment for infection at the time of a liver offer may require an individualized antibiotic regimen. See the orders in EPIC, and send antibiotics/antifungals as ordered for OR administration.

Thromboelastogram-Based Hemostasis Management in Liver Disease and Liver Transplantation

Advanced liver cirrhosis and acute liver failure are both characterized by decreased synthesis of both procoagulants and anticoagulants, leading to a prolongation in the prothrombin time. In addition, cirrhosis also commonly leads to thrombocytopenia, which adds to the bleeding risk. Hence, patients with significant liver dysfunction who have prolonged prothrombin time typically receive fresh frozen plasma and those with thrombocytopenia typically receive platelet transfusion before undergoing invasive procedures to prevent bleeding. However, prothrombin time is an inaccurate measure of the true hemostatic condition in significant liver dysfunction, given the reduced levels of both procoagulants and anticoagulants. Further more, transfusion of blood products in liver patients may also have negative consequences, particularly in the setting of preexisting fluid overload and hypoalbuminemia, both of which predisposes to third-spacing of fluids, often compromising the patient's respiratory status.

Thromboelastogram (TEG) is a rapid global hemostasis assessment that measures the viscoelastic changes that occur during the hemostatic process, reported in real time. TEG has been proven to be an effective guide for transfusion during liver transplantation¹ and for monitoring perioperative changes in coagulation during surgery^{2,3}. More recently, TEG has also been demonstrated to decrease the need for blood product transfusion in cirrhotic patients who underwent invasive procedures⁴. Each component of the TEG correlates with a specific factor in hemostasis, and appropriate intervention for each scenario has been proposed for actively bleeding patients⁵. This protocol seeks to adopt these parameters and interventions to prevent bleeding in patients with significant liver dysfunction who are about to undergo invasive procedures or to reduce or stop active bleeding in liver transplant recipients either intraoperatively or post-operatively (see table below).

Patients to order TEG for:

1. Cirrhotic or acute liver failure patients who have prolonged prothrombin time (INR >1.5) or thrombocytopenia (platelet <100K) and need invasive procedures.
2. Cirrhotic or acute liver failure patients who have prolonged prothrombin time or thrombocytopenia and are actively bleeding
3. Liver transplant recipients who are actively bleeding intraoperatively or post-operatively.

How to order TEG in Epic:

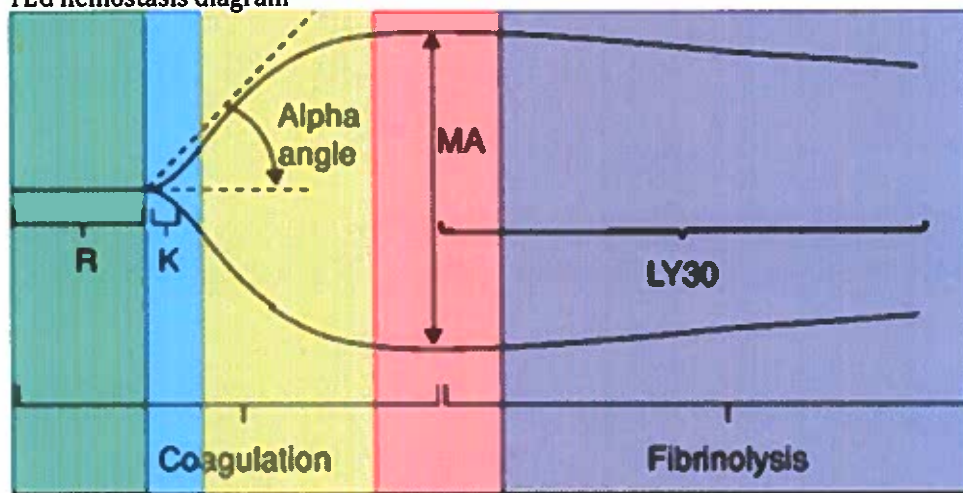
1. TEG1 standard - provides r time, k time, angle, MA, LY-30; available Monday to Friday, 7:30 am to 3 pm via coagulation lab
2. TEG2 heparin - for patients on heparin, provides r time, k time, angle, MA, LY-30; available Monday to Friday, 7:30 am to 3 pm via coagulation lab
3. TEG3 complex - provides r time, k time, angle, MA, FFMA, LY-30; available Monday to Friday, 7:30 am to 3 pm via coagulation lab
4. TEG 6S - provides r time, k time, angle, MA, FFMA; **Intra-operative specimens should be sent ASAP to Blood Bank (pneumatic tube station 400). Specimens from all other locations should be sent to Coagulation Lab (pneumatic tube station 904); Intra-operative ordering already available 24/7, and orders from all other locations anticipated to become available 24/7 by end of June**

References:

1. Salooja N, Perry DJ. Thromboelastography. *Blood Coagul Fibrinolysis* 2001;12:327-337
2. Wang SC, Shieh JF, Chang KY, et al. Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: randomized clinical trial. *Transplant Proc* 2010;42:2590-2593

3. Coakley M, Reddy K, Mackie I, et al. Transfusion triggers in orthotopic liver transplantation: a comparison of the thromboelastometry analyzer, the thromboelastogram and conventional coagulation tests. *J Cardiothorac Vasc Anesth* 2006;20:548-553.
4. De Pietri L, Bianchini M, Montalti R, et al. Thromboelastography-guided blood product use before invasive procedures in cirrhosis with severe coagulopathy: a randomized, controlled trial. *Hepatology* 2016;63:566-573
5. Stensballe J, Ostrowski SR, Johansson PI. Viscoelastic guidance of resuscitation. *Curr Opin Anesthesiol* 2014;27:212-218

TEG hemostasis diagram



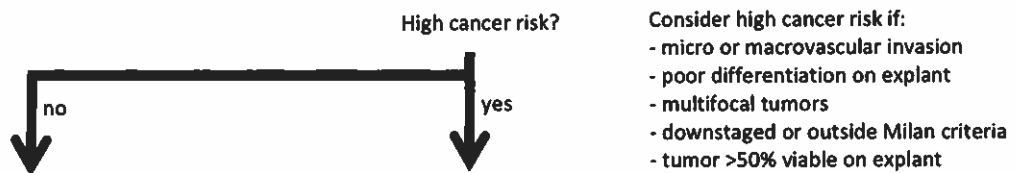
TEG 5000 interpretation for non-heparinized patients

Components	Definition	UCM Normal Values for TEG 5000	Cut-Off Values for correction	Problem with	Management
Kaolin R time	Time to start forming clot	4 - 8 min	>10 min	Coagulation factors	<ul style="list-style-type: none"> R time 10-14 min – give 2 units FFP R time >14 min – give 4 units FFP
Kaolin K time	Time until clot reaches a fixed strength	1.0 – 2.1 min	>3.0	Fibrinogen	Cryoprecipitate
Kaolin Alpha angle	Speed of fibrin accumulation	60 – 73 deg	<52 deg	Fibrinogen	If angle <52 mm, and <ul style="list-style-type: none"> FFMA 7-13 mm, give 2 u cryoprecipitate FFMA <7 mm, give 4 u cryoprecipitate
Kaolin Maximum amplitude (MA)	Highest vertical amplitude of the TEG	57 – 74 mm	<50 mm	Platelets	If FFMA is >13 mm, and <ul style="list-style-type: none"> MA 40-49 mm – give 1 unit platelets MA <40 mm – give 2 units platelets DDAVP in renal insufficiency
Functional fibrinogen maximal amplitude (FFMA)	Measures the fibrinogen that actually contributes to the clot strength after blocking the platelet contribution	13 - 32 mm	<13 mm	Fibrinogen	If MA <50 mm, and <ul style="list-style-type: none"> FFMA 7-12 mm, give 2 units cryoprecipitate FFMA <7 mm, give 4 units cryoprecipitate
Kaolin Lysis at 30 min (LY30)	Percentage of amplitude reduction 30 min after maximum amplitude	0.0 - 5.0%	>6%	Excess fibrinolysis	Give tranexemic acid 10-20 mg/kg bolus or aminocaproic acid 100 mg/kg bolus

TEG 6S interpretation for non-heparinized patients

Components	Definition	UCM Normal Values for TEG 5000	Cut-Off Values for correction	Problem with	Management
Kaolin R time	Time to start forming clot	5.0 - 8.6 min	>10 min	Coagulation factors	<ul style="list-style-type: none"> R time 10-14 min - give 2 units FFP R time >14 min - give 4 units FFP
Kaolin K time	Time until clot reaches a fixed strength	0.8 - 2.6 min	>3.5	Fibrinogen	Cryoprecipitate
Kaolin Alpha angle	Speed of fibrin accumulation	61 - 78 deg	<52 deg	Fibrinogen	If angle <52 deg, and <ul style="list-style-type: none"> FFMA 7-14 mm, give 2 units cryoprecipitate FFMA <7 mm, give 4 units cryoprecipitate
Kaolin Maximum amplitude (MA)	Highest vertical amplitude of the TEG	52 - 71 mm	<45 mm	Platelets	If FFMA is >14 mm, and <ul style="list-style-type: none"> MA 35-44 mm - give 1 unit platelets MA <35 mm - give 2 units platelets DDAVP in renal insufficiency
Functional fibrinogen maximal amplitude (FFMA)	Measures the fibrinogen that actually contributes to the clot strength after blocking the platelet contribution	14 - 32 mm	<14 mm	Fibrinogen	If MA <45 mm, and <ul style="list-style-type: none"> FFMA 7-13 mm, give 2 units cryoprecipitate FFMA <7 mm, give 4 units cryoprecipitate

Immunosuppression for Adult Liver Transplant Recipients						
	ROUTINE PROTOCOL*		RENAL SPARING and CANCER PROTOCOL**			
	Methylpred/ Prednisone	Tacrolimus	Methylpred/ Prednisone	Basiliximab	Tacrolimus	Mycophenolate mofetil (MMF); Everolimus
POD 0	500 mg IV in OR; repeat 500 mg IV x1 on arrival to SICU per OR debrief decision		500 mg IV in OR; repeat 500 mg IV x1 on arrival to SICU per OR debrief decision	20 mg IV x1, on arrival to SICU		Start 1000 mg PO q12h; Reduce to 500 mg q12h if: -- WBC <1.5 -- CMV disease -- Diarrhea
POD 1	200 mg IV x1		200 mg IV x1			
POD 2	120 mg IV x1	Start 0.05 mg/kg PO q12h;	120 mg IV x1		Start 0.03 mg/kg PO q12h;	
POD 3	60 mg PO x1		60 mg PO x1			
POD 4	40 mg PO x1		40 mg PO x1	20 mg IV x1		
5-14d	20 mg PO daily		20 mg PO daily			
15-30d	15 mg PO daily	Dose to 8-10 ng/ml	15 mg PO daily		Dose to 6-8 ng/ml	



1-2 mo	10 mg PO daily		10 mg PO daily			dc MMF**	Start 1 mg PO q12h;
2-3 mo	5 mg PO daily		5 mg PO daily				Dose to 5-8 ng/ml
3-6 mo	dc prednisone	Dose to 6-8 ng/ml	dc prednisone				Dose to 4-6 ng/ml
6-12 mo					Dose to 1-3 ng/ml		
>1 year		Dose to 3-5 ng/ml					

*For AIH and fulminant liver failure, add mycophenolate 1g PO q12h

**For AIH, keep MMF and do not start everolimus

Medication tips:

Tacrolimus, cyclosporine, and everolimus doses should be scheduled for 06:00 and 18:00. Obtain drug trough levels with 4AM labs. For patients unable to take tacrolimus PO: give suspension via tube (PO:susp is 1:1) or give capsule contents sublingually (PO:SL is 2:1). For patients unable to take cyclosporine PO: give suspension via tube (PO:susp is 1:1). Contact transplant pharmacist p4962 if you feel you need to give tacrolimus or cyclosporine intravenously.

Liver Transplant Contact Information		
Transplant Surgery p8767	Talia Baker 312-401-1314	Helen Te p5176 773-316-4996
Liver Fellow on call p2453	Adam Bodzin p8236 856-325-9727	Andrew Aronsohn p3023 773-562-0083
Procurement Coordinator on call p2377	John Fung 216-212-7647	Michael Charlton p8552 385-414-5262
Tx Administrator on call p9771	Michael Millis p8217 773-368-3494	Sonali Paul 857-383-9504
		Anjana Pillai 786-218-0107
Pre-Tx Coordinator: Joan Schulz p7668	Tx Dietitian: Annie Guinane p6591	Gautham Reddy 901-494-6322
	Katie Wherity p4563	Tx Pharmacist: Lisa Potter p4962
Post-Tx Coordinator: Kathy Dasgupta p8010	Tx Social Work: Barrett Gray p3007	Amanda Burress, PA p5701
Intake: 2-4500		Laura Holzinger p6611
		Christine Trotter, APN p6543
	Tx Psychiatry: Daniel Fridberg p5853	
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Infectious Prophylaxis			
Indication	Population	Medication & Dose	Duration
Surgical prophylaxis	Intra-op	Pip-tazo 4.5g IV and fluc 400 mg IV prior to incision PCN allergy: cipro 400 mg IV + metro 500 mg IV + vanco 20 mg/kg IV + fluc 400 mg IV prior to incision	redose pip-tazo q3h, cipro q8h, metro q6h throughout case
	Post-op	Pip-tazo 4.5g IV q8h* PCN allergy: cipro 400 mg IV q12h* + metro 500 mg IV q8h + vanco 15 mg/kg IV q12h* (with PK consult)	X48h after fascial closure
Anti-fungal	Routine (thrush):	Fluconazole 100 mg PO daily If fluconazole is contraindicated: nystatin 5 ml swish/swallow QID	1 month
	High-risk patients (IFI): - Pre-operative renal failure - Serum albumin <2 - >40 units blood product in OR - Choledochojejunostomy - Candida colonization - Early graft failure - Retransplantation - Reoperation after OLT	Fluconazole 400 mg PO daily* If fluconazole is contraindicated: micafungin 50 mg IV daily	2 weeks, then change to thrush prophylaxis
Anti-PJP	All	Bactrim (SMZ/TMP) SS PO daily* Alternates (in order of preference): Pentamidine (Nebupent) 300 mg nebulized monthly Atovaquone (Mepron) 1500 mg PO daily	6 months
Anti-viral	CMV High Risk (D+/R-)**	Ganciclovir 5 mg/kg IV q24h* (see below for renal dosing) or Valganciclovir (Valcyte) 900 mg PO daily* (see below for renal dosing)	3 months
	CMV Mod Risk (R+)	Valganciclovir (Valcyte) 900 mg PO daily* (see below for renal dosing)	3 months
	CMV Low Risk (D-/R-)	Valacyclovir (Valtrex) 500 mg PO BID* (see below for renal dosing)	3 months

*requires dose adjustment for renal impairment

**after stopping prophylaxis, check CMV PCR q2 weeks x2 months

Renal Dosing							
Ganciclovir (IV)		Valganciclovir (PO)		Others		Others	
CrCl (mL/min)	Dose	CrCl (mL/min)	For target 900 mg daily	CrCl (mL/min)	Dose	CrCl (mL/min)	Dose
> 70	5 mg/kg q24h	> 60	900 mg daily	<50	Fluconazole 200 mg daily	<10 or HD	Pip-tazo 3.375g IV q12h
50 - 69	2.5 mg/kg q24h	40 - 59	450 mg daily	<30	Bactrim SS MWF	CRRT	Valacyclovir 500 mg PO daily
25 - 49	1.25 mg/kg q24h	25 - 39	450 mg q48h		Pip-tazo 3.375g IV q8h		Fluc 400 mg daily
10 - 24	0.625 mg/kg q24h	10 - 24	450 mg BIW		Ciprofloxacin 200 mg daily		Pip-tazo 3.375g IV q6h
< 10	0.625 mg/kg q48h	< 10	100 mg TIW after HD (use solution)				Ciprofloxacin 400 mg q12h
HD	0.625 mg/kg after HD	HD					
CRRT	2.5 mg/kg q24h	CRRT	Use IV ganciclovir				

Special Patient Populations			
Patient Population	Medication	Dose	Duration
Any recipient from a HBV cAb pos liver donor	Lamivudine (EpiVir-HBV®)	100 mg PO daily*	Indefinitely *May stop lam in HBsAb positive recipients after complete weaning of steroids if HBsAb titer >10
Any recipient who is HBV sAg pos (regardless of HBV cAb status) Note: Post-transplant antiviral is based on pre-transplant regimen	Entecavir (Baraclude®) OR Tenofovir alafenamide (Vemlidy®)	0.5 mg PO daily* (nucleoside naive) 1 mg PO daily* (lamivudine refractory) OR 25 mg PO daily	Indefinitely OR Indefinitely
Any recipient from a HCV NAT pos liver donor	To be determined per HCV genotype post-transplant;	To be determined per HCV genotype post-transplant	To be determined per HCV genotype post-transplant
Any recipient who is HCV viremic	To be determined per HCV genotype post-transplant;	To be determined per HCV genotype post-transplant;	To be determined per HCV genotype post-transplant;

*requires dose adjustment for renal impairment

Post-transplant lab and visit schedule for outpatients:

If discharged on a Mon or Tues:	Labs and clinic on Wed, Fri, and 2 nd Wed after dc	Labs only on Mon and 2 nd Fri after dc
If discharged on a Wed or Thurs:	Labs and clinic on Fri, Mon, and 2 nd Fri after dc	Labs only on Wed and 2 nd Mon after dc
If discharged on a Fri, Sat, or Sun:	Labs and clinic on Mon, Wed, and 2 nd Mon after dc	Labs only on Fri and 2 nd Wed after dc

Non-routine lab testing:

For all recipients: HIV RNA, HBV DNA, and HCV RNA between 4 and 8 weeks post-transplant
 For recipients from PHS increased risk donors: HIV Ab and RNA; HBV sAb, sAg, cAb and DNA; HCV Ab and RNA at 6 and 12 months post-transplant
 For recipients from HBV cAb+ donors: HIV Ab and RNA; HBV sAb, sAg, cAb and DNA; HCV Ab and RNA at 6 and 12 months post-transplant
 For recipients from HCV RNA+ donors: HCV RNA on day 5-7, week 2, and week 4 post-transplant; HCV genotype once HCV RNA is >1000 IU/ml
 For CMV high-risk recipients: CMV PCR q2 weeks x 2 months after stopping valganciclovir

Postoperative Inpatient Management of the Liver Transplant Recipient

Diagnostics	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7						
Weight	Daily													
Vital signs	Q1h while in ICU, Q4h while on floor													
I/O	Q1h while in ICU, Q4h while on floor													
CBC w/diff, CMP, Mg, Phos, PT/INR	On arrival, then q8h x24h	Daily												
Fibrinogen	On arrival x1													
Lactic acid	On arrival, then q8h x24h													
Tacrolimus									Daily once on tacrolimus					
CVP	Q4h and prn x24h													
PAP	Q4h and prn x24h													
ABG	On arrival, then q8h x24h or until extubated								Daily until extubated					
Type & Screen	Q3 days to remain active													
CXR	On arrival	Daily while PA catheter is in and/or while intubated												
Liver US with dopplers	6-12h post-op or early the next AM	x						x						
Therapeutics	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7						
Immunosuppression	Per protocol													
Antimicrobials	Per protocol - Periop antibiotics continue x48h after fascia closure - Routine prophylaxis starts on POD #1; CMV prophylaxis starts on POD #3													
Analgesics	IV	IV/PO	PO											
Fluid management	IVF NS @ 100 ml/h (adjust per Na or renal function; defer to kidney protocol for a SLK)	IVF Decrease to 75 ml/h	IVF vs diuresis	Consider diuresis										
Thrombosis prophylaxis	SCDs	SCDs	SCDs +/- HSQ 5k BID/Start ASA 81daily once plt >50 & no transfusion in last 24h											
Glucose control	Initiate low-dose insulin algorithm. If blood glucose >250 or if on insulin gtt from OR, use insulin gtt protocol.			Consult endo if needed										
Electrolyte management	Maintain K >3.5 and <5.2; do not replete K if UOP is <30 ml/h or on HD Maintain Phos >2.5 Maintain Mag >1.8													
Transfusions in the first 24h post-op	For fibrinogen <120, give 2 packs cryo For platelets <20, give 1 pack platelets For INR >2.5, give 2 units FFP For HCT <23, give 2 units pRBC (unless bleeding) **if >6 units are transfused, call transplant surgeon** Beyond 24h post-op, any transfusions must be approved by the transplant attending. Routine use of blood products in the absence of the above criteria will be discouraged.													

Milestones	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Deline	All of these by 12-24h post-op: - extubate - dc Swan - dc femoral Aline - dc NG/OG (if roux, discuss w/surgeon before removing)	- dc foley - dc radial Aline - change introducer to TLC					Consider removing TLC	
JP management		Consider removing JPs						
Transfer to floor		X						
Diet	NPO	Clears	ADAT					
Out of bed to chair	X	X	X	X	X	X	x	x
Ambulating		X	X	X	X	X	x	x
PT/OT		X	X	X	X	X	x	x
Chest PT	X	X	X	Evaluate need with Respiratory Therapy, continue if deemed necessary				
Dispo planning		Daily on rounds						
Bedside nursing education		X	X	X	X	X	x	x
Transplant pharmacist education		X Once on floor	Education based timing based on patient/family availability and needs					x
Transplant coordinator education				X	Education based timing based on patient/family availability and needs			x
Transplant nutrition education				X				x
Transplant social work evaluation			X	Daily and as deemed necessary per initial evaluation.				x
Case management evaluation			X	Daily and as deemed necessary per initial evaluation.				x

If a patient has clinical deterioration or change in status, contact the SICU attending (for ICU patients) or transplant service (for floor patients).

Guideline for Alprostadil use after Liver Transplant

Background:

Prostaglandins are released by activated Kupfer cells during organ reperfusion and provide a wide range of cytoprotective actions. The use of alprostadil, a synthetic stable form of PGE₁, can attenuate hepatic ischemia/reperfusion (I/R) injury, subsequently improving liver graft perfusion and function.

A Cochrane review analyzed ten trials in which 652 patients were randomized to prostaglandin therapies.¹ The risk of bias was considered high in most trials. The Cochrane review concluded that:

There was no significant effect of prostaglandins on:

- all-cause mortality (37/298 [12.4%] PG vs 47/312 [15.1%] control; OR 0.84, 95% CI 0.53-1.37; I₂ = 0%)
- primary graft non-function (8/238 [3.4%] PG vs 16/250 [6.4%] ctrl; OR 0.55, 95% CI 0.23-1.33; I₂ = 0%)
- liver re-transplantation (12/161 [7.5%] PG vs 14/171 [8.2%] control; OR 0.99, 95% CI 0.44-2.25; I₂ = 0%)

Prostaglandins seemed to significantly decrease the risk of:

- AKI requiring dialysis (13/158 [8.2%] PG vs 34/171 [9.9%] control; OR 0.37, 95% CI 0.18-0.75; I₂ = 0%).

There was no significant increase in the risk of adverse events with prostaglandins.

A subsequent study by Kornberg et al suggests that treating hepatic I/R injury with alprostadil for at least 72h post-transplant may reduce the risk of early HCC recurrence, particularly in patients exceeding Milan criteria.²

Use at UChicago Medicine:

Use of alprostadil for hepatic I/R injury at UChicago Medicine will be per transplant surgeon discretion, after consideration of donor, graft, and recipient factors. Our dosing is modeled after the Kornberg experience,² with an abbreviated treatment duration. When used, it will be started post-operatively in the SICU and continued for 24 hours. Avoid use in patients with low platelets (<50), increased tendency for perioperative bleeding, or continuous need of catecholamines (i.e. dopamine, norepinephrine, epinephrine).

How to order:

- Product: alprostadil 1000 mcg in 250 ml of D5W or NS.
Manually adjust the alprostadil dose, volume of diluent, and choice of diluent when ordering (all of these can be edited towards the bottom of the order entry screen).
- Dose: 0.0017 mcg/kg/min. Use actual body weight.
- Priority: stat
- Route: IV
- Frequency: continuous for 24 hours
- Administration instructions:
***do not tube**
Attn RN: Start infusion at 0.0017 mcg/kg/min. Increase the rate by 0.0017 mcg/kg/min every 30 minutes to a max rate of 0.0085 mcg/kg/min (i.e. a max of four rate increases). Stop dose escalation and contact ICU provider for hemodynamic instability, platelets <30, or bleeding. Concentration: 4 mcg/ml. Dispose in black container."

References:

- ¹ Cavalcanti AB, et al. Prostaglandins for adult liver transplanted patients (Review). *Cochrane Database of Systematic Reviews* 2011; Issue 11.
- ² Kornberg A, et al. Treating ischaemia-reperfusion injury with prostaglandin E1 reduces the risk of early hepatocellular carcinoma recurrence following liver transplantation. *Aliment Pharmacol Ther* 2015; 42: 1101-1110.

	PO	NG	SL	IV
Tacrolimus	✓	✓ Must use liquid	✓ Use capsules PO:SL 1:0.5-1	✓ Possible but NG preferred PO:IV 5:1
Tacrolimus, extended release	✓	No; consider tacrolimus	No; consider tacrolimus	No; consider tacrolimus
Cyclosporine, modified	✓	✓ Must use liquid	No	No; use cyclosporine, nonmodified
Cyclosporine, nonmodified	Nonformulary; use patient's own or cyclosporine ME	Nonformulary; use patient's own or cyclosporine ME Must use liquid	No	✓ Possible but NG preferred PO:IV 3:1
Mycophenolate mofetil (MMF)	✓	✓ Must use liquid	No	✓ PO:IV 1:1
Mycophenolic acid (MPA)	✓	No; change to MMF MPA:MMF 720:1000	No	No; change to MMF MPA:MMF 720:1000
Azathioprine (Aza)	✓	✓ Crush tablets	No	IV affected by shortage; consider MMF
Sirolimus	✓	✓ Must use liquid	No	No
Everolimus	✓	No	No	No
Prednisone	✓	✓ Crush tablets	No	use methylpred pred:methylpred 5:4

Procedure	Preferred Regimen [§]	Severe Beta-Lactam Allergy [§]	High-Risk for MRSA [†] (See notes section above for patient stratification)		Intraoperative Redosing (Until wound closure)	Post-Operative Redosing
			Without Severe Beta-Lactam Allergy	Severe Beta-Lactam Allergy		
Non-SCIP Hepatectomy/ laparoscopic cholecystectomy	Ampicillin/ sulbactam if < 60kg or 3gm if ≥ 60kg AND Fluconazole 400mg IV	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91- >120kg)	Ampicillin/ sulbactam (1.5 gm if <60kg or 3gm if > 60kg) AND Fluconazole 400mg IV AND Vancomycin* (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg)	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg) AND Fluconazole 400mg	Length of Procedure (intervals given are for GFR≥50mL/min/1.73m2) Ampicillin/sulbactam: 3 hours (1.5gm)‡ Fluconazole: no redosing Ciprofloxacin: 8 hours‡ Metronidazole: 6 hours Vancomycin: 12 hours‡	Maximum 24 hours Ampicillin/sulbactam – q6 hours Ciprofloxacin – q12 hours Fluconazole – Not routinely recommended Metronidazole – q8 hours Vancomycin – Not routinely recommended (maximum 1 dose)
			Fluconazole 400mg	Fluconazole 400mg		
HIGH RISK HepC cirrhosis, cirrhosis of other causes	Ampicillin/ sulbactam if < 60kg or 3gm if ≥ 60kg	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91- >120kg)	Ampicillin/ sulbactam (1.5 gm if <60kg or 3gm if > 60kg) AND Fluconazole 400mg IV AND Vancomycin* (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg)	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg) AND Fluconazole 400mg	Blood Loss > 1.5L Give additional dose of antibiotic after fluid replacement; give the same dose as the initial pre-op dose	Infusion Duration Ampicillin/sulbactam: 10-15 min IV push OR 30 min IVPB Ciprofloxacin: 60 min IVPB only Fluconazole: 120 min (max 200mg/hr) Metronidazole: 60 min IVPB only Vancomycin: 1000 mg: 60 min 1500 mg: 90 min 2000 mg: 120 min
			Fluconazole 400mg	Fluconazole 400mg		
Hepatectomy/ laparoscopic cholecystectomy	Ampicillin/ sulbactam if < 60kg or 3gm if ≥ 60kg	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91- >120kg)	Ampicillin/ sulbactam (1.5 gm if <60kg or 3gm if > 60kg) AND Vancomycin* (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg)	Ciprofloxacin 400mg IV AND Metronidazole (500mg) AND Vancomycin (1gm if 40-70kg, 1.5gm if 71-90kg, 2gm if 91->120kg)		
LOW Risk Non-cirrhotic (fluconazole is not indicated)						

*Rationale for vancomycin use MUST be documented prior to incision (indicate using drop-down list in order)
† If non-severe/non-life-threatening beta-lactam allergy (e.g. rash), may consider ceftioxin instead of ampicillin-sulbactam (Ceftioxin dose 1gm if <60kg or 2gm if > 60kg; 3-5 min IV push or 30min infusion IVPB; intra-operative redosing every 3 hours‡)
‡ For GFR < 50, may consider redosing at double the indicated interval (e.g., 6 hours for ceftazolin, ceftioxin); no redosing needed for severe renal insufficiency (GFR < 10) or ESRD/HD
§ If concern for systemic infection (based on clinical presentation/symptoms) – Empiric antimicrobial therapy should be initiated with ceftazime, vancomycin, and metronidazole (fluconazole should be continued). If severe penicillin/beta-lactam allergy or history of multi-drug resistant infections, discuss empiric antimicrobial choice with ID.

Project WALK: Early Mobilization Program for the Medical-Surgical Patient.

Walking:

- Promotes strength and energy.
- Enhances sleep.
- Aids in recovery from surgery or illness.
- Supports your body's return to normal workings.
- Reduces the chance of a fall, development of a blood clot, or pneumonia.
- Reduces the need for pain medication.



We will work with You to promote Your recovery.

The Healthcare Team will:

- Assess YOUR ability to move in bed and walk on admission to the unit and daily.
- Set walking goals with YOU looking at distance, number of times and YOUR strength.
- Instruct YOU on the use of the Incentive Spirometer with set a goal about the amount of inspiration to obtain.

MAKE A DATE- Set time with YOU to walk or move to chair according to YOUR Mobility Plan.

YOU will be expected to:

- Be an active part of YOUR walking program.
- Monitor YOUR progress - distance walked, and the number of times walked.
- Utilize the Incentive Spirometer 10 times an hour while awake , recording YOUR inspiration volumes.

Day	Day 0- Admission	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Distance	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet
Walked	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet
	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet	_____ feet
Incentive	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol
Spirometer	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol	_____ vol

Table 1a. HCC Regular Screening / Surveillance

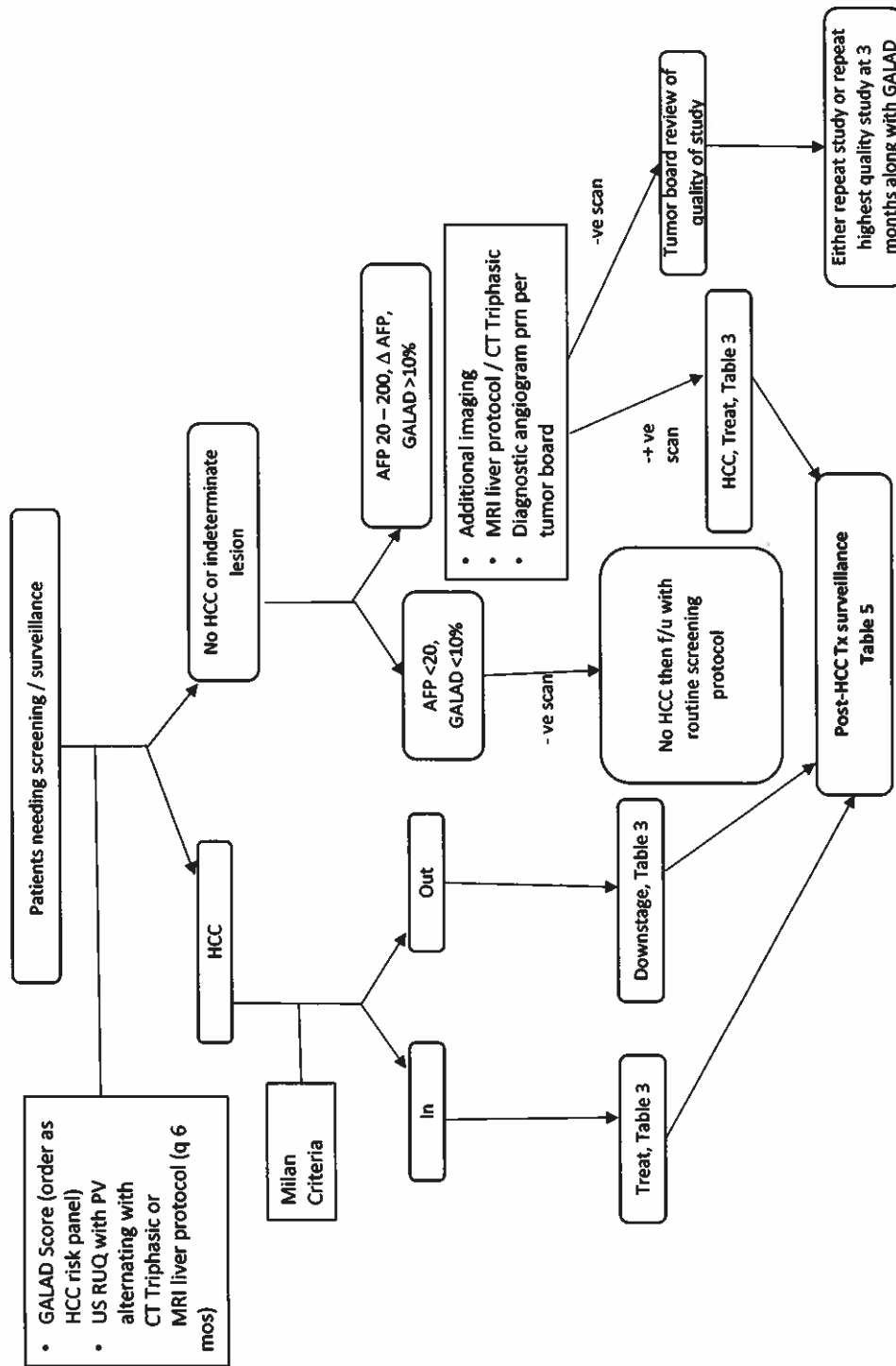


Table 2. HCC treatment algorithm

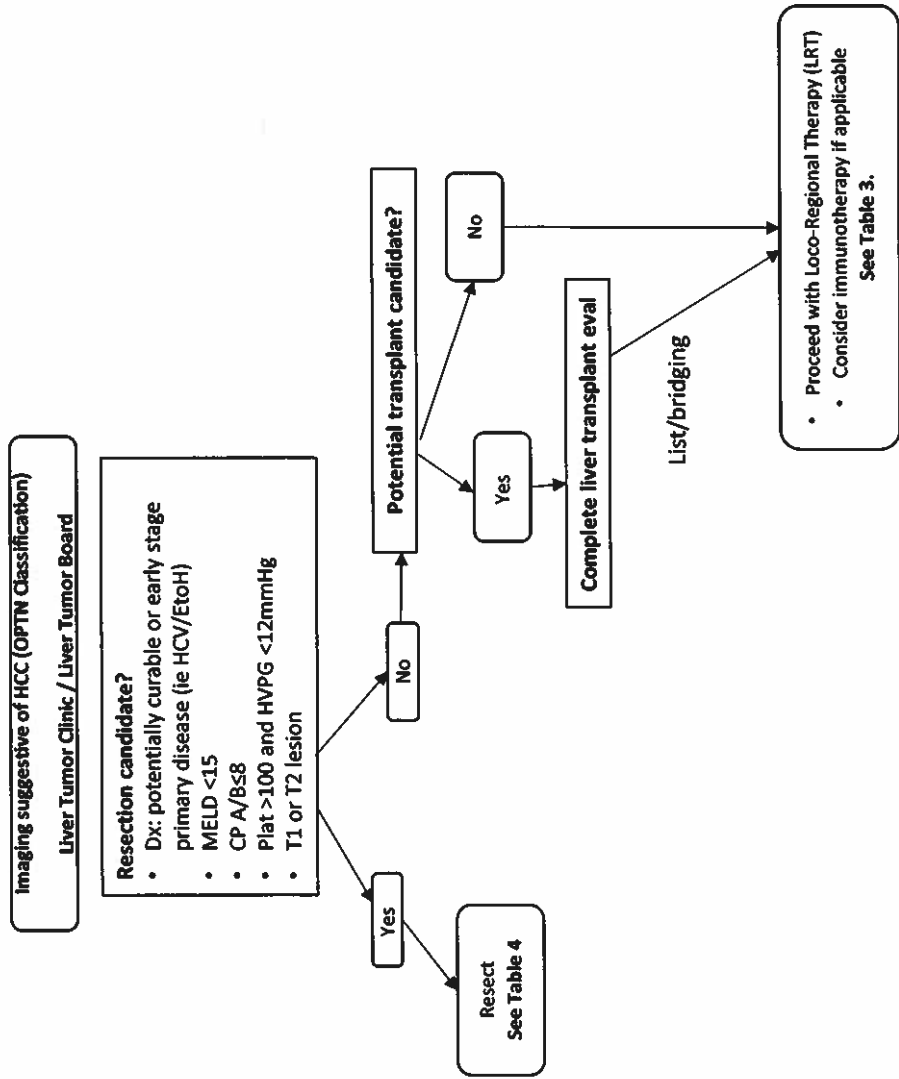


Table 3. HCC Loco-Regional Therapy

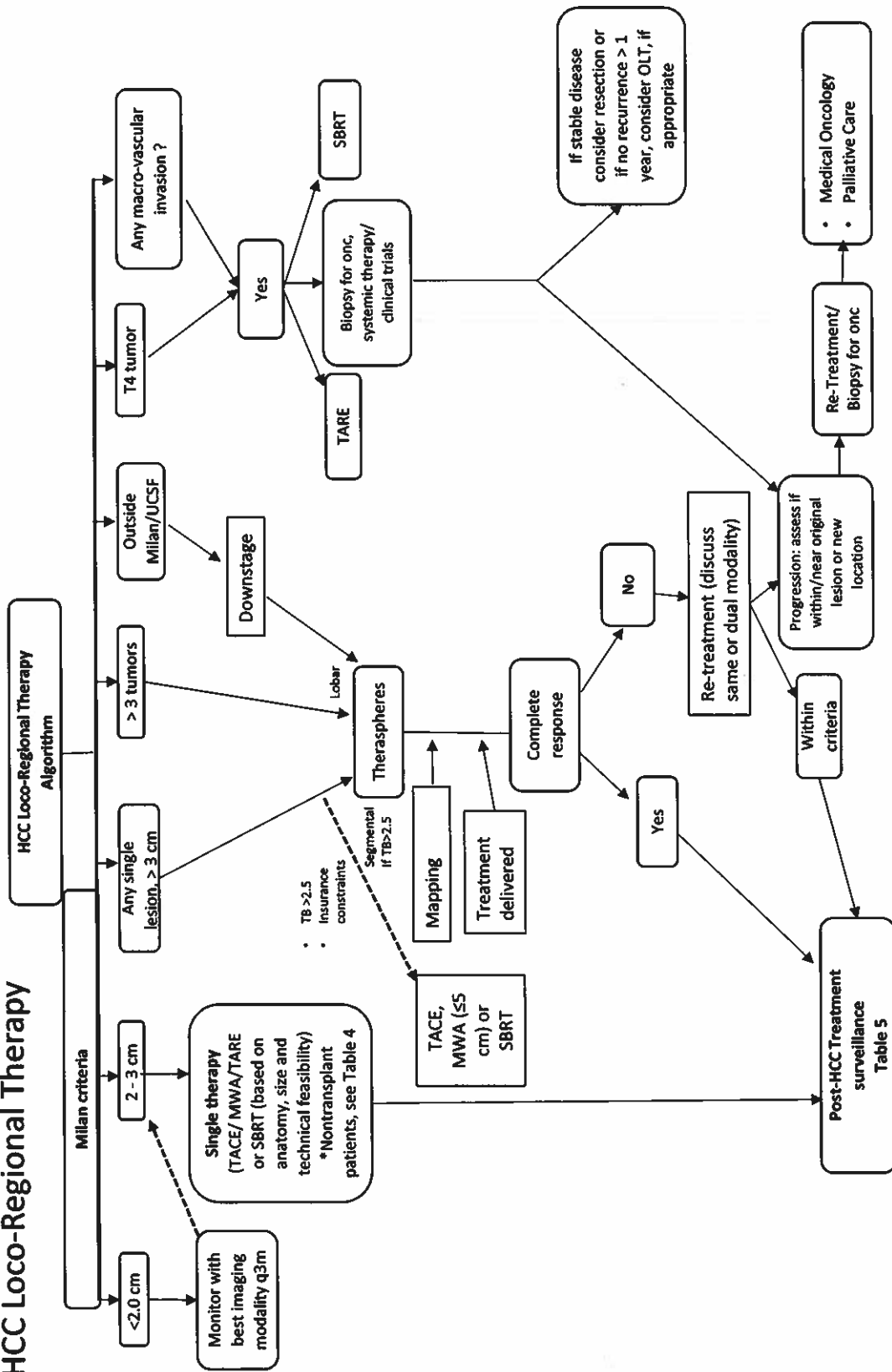


Table 4.
Non-Transplant candidate
HCC treatment algorithm

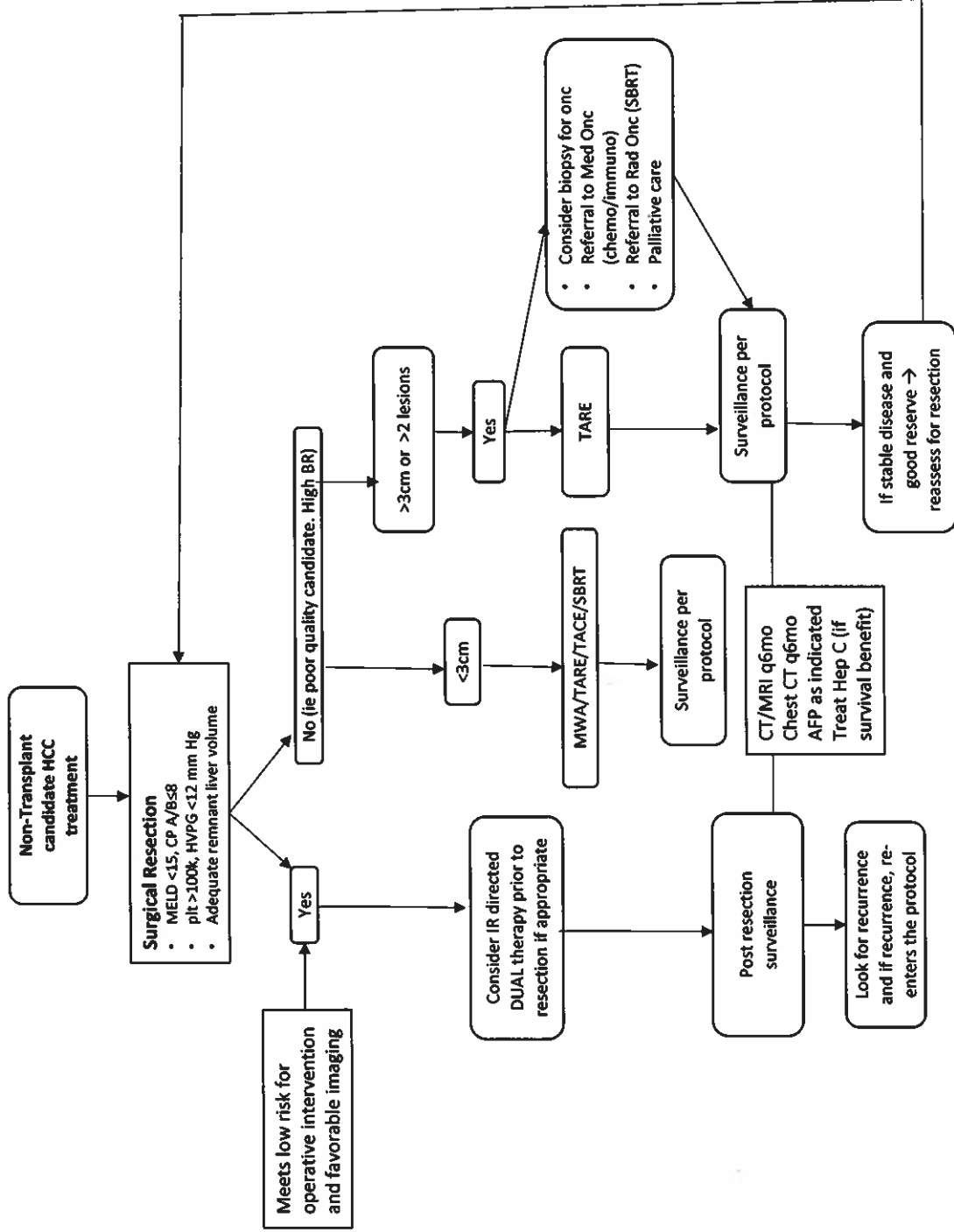


Table 5.
Pre-transplant surveillance protocol post-HCC treatment

- AFP (if elevated pre-treatment) or GALAD score (if appropriate) q6 mo
- Noncon chest CT q 6mo
- MRI/CT liver protocol 4-6 weeks after MWA/SBRT/TACE **OR** 6 weeks and 3 months after TARE
 - For surveillance use the imaging study that yielded the best sensitivity in the prior imaging
 - If no viable tumor, then q3 months MRI/CT liver until OLT
 - If no viable tumor and **not** OLT candidate, q3 months MRI/CT liver for 18 mos then return to q6 mo surveillance
 - Continue monitoring post treatment patients with GALAD score
- +/- Annual bone scan (only if mandated by insurance)
- Liver Tumor Board presentation of all imaging
- Waitlisted patients with new tumor or progression of tumor
 - Within Milan, AFP <400 -> treat per protocol and keep listed
 - Within Milan AFP >400-1000 ->place on hold & treat->wait for mRECIST criteria or 90% AFP response ->re-activate on list
 - **Outside Milan or AFP >1000 ->place on hold & treat ->wait for mRECIST criteria or 90% AFP response from baseline ->then wait 3 months before re-activation on list
- IF PV invasion, wait 1 year of stability
 - **if outside Milan, consider PET (if PET neg. better prognosis)

Table 6.
Post-transplant/resection surveillance protocol for HCC patients

- AFP or GALAD score at 3 mo then q6 mo
- CT liver/pelvis/chest
 - Low risk (within Milan and favorable tumor biology)
 - Q6 mos x 3 years
 - High risk → poorly differentiated, vascular invasion, outside Milan
 - Q3 months x 1 then Q6 mos x 5yrs
- Liver Tumor Board presentation of all concerning imaging

University of Chicago Cholangiocarcinoma (CCA) Protocol Neoadjuvant therapy followed by liver transplantation (LT) for Hilar CCA

Cholangiocarcinoma used to be a contraindication for liver transplantation in the past, due to high recurrence rates at 51-57% and poor patient survival rates of 20-28% (at 3-5 years following OLT). In 1993, the Mayo Clinic adopted a neoadjuvant therapy and liver transplantation protocol for localized, unresectable hilar CCA. The protocol combines modalities of radiotherapy, chemosensitization and liver transplantation in carefully selected patients. By 2010, 120 patients had received liver transplantation under this protocol, and a 5-year survival of 73% was reported for those who received OLT. The 5-year actuarial survival for all patients who began neoadjuvant therapy was 54%.

The University of Chicago Liver Transplant Program will adopt the Mayo CCA protocol to treat patients with localized, unresectable hilar CCA. The protocol will involve:

1. Neoadjuvant chemotherapy prior to chemoradiotherapy will be started, including gemcitabine, platinum, 5FU, and irinotecan containing regimens, if patients meet all other eligibility criteria.
2. External beam radiation therapy (EBRT) consisting of 45 Gy in 30 fractions of 1.5 Gy twice daily over a three week period and either 5-fluorouracil (5-FU) continuous infusion at 200 mg/m²/day or oral capecitabine 825mg/m² BID Monday through Friday during radiation.
3. Within 4 weeks, high dose rate brachytherapy will be delivered to the involved site, giving 9.3 Gy in a single fraction via a nasobiliary tube. *If brachytherapy is not possible, an extra boost of EBRT of 7.5-15 Gy will be administered.*
4. After completion of EBRT, start maintenance Capecitabine 2000 mg/m² daily (2 weeks on, 1 week off) as tolerated while awaiting OLT. This is held during the perioperative period for staging.
5. When MELD score is deemed high enough to garner donor offers, abdominal exploration with routine biopsy of perihilar lymph nodes near the bile duct and hepatic artery plus any other lymph nodes or nodules that are suspicious for tumor.
6. All patients with negative staging laparoscopy remain eligible for OLT.
7. A back-up patient will be called in at the time of organ offer for OLT.

Inclusion criteria:

1. Diagnosis of CCA made by any of the following:
 - a. Endoscopic transcatheter biopsy or brush cytology consistent with CCA
 - b. Malignant appearing hilar stricture plus one or more of the following
 - i. a hilar mass on cross-sectional imaging
 - ii. CA-19.9 > 100 mg/ml in the absence of cholangitis
 - iii. Polysomy by FISH
2. Radial tumor diameter ≤3 cm. There are no exclusion criteria for the longitudinal or ductal extension of the tumor or vascular encasement
3. Macroscopic disease must be proximal to the cystic duct insertion
4. Candidate for liver transplantation

Exclusion criteria:

1. Intrahepatic CCA
2. Uncontrolled infection
3. Prior radiation to the liver
4. Prior biliary resection or attempted resection
5. Intrahepatic metastases
6. Evidence of extrahepatic disease

7. History of other malignancy within 5 years that limits survival
8. Previous percutaneous biopsy (including EUS guided FNA), hilar exploration or attempted surgical resection
9. Vascular invasion (vascular encasement is **not** a contraindication)

Pre-operative evaluation prior to neoadjuvant therapy:

1. Chest CT scan
2. Bone Scan
3. Endoscopic ultrasound with biopsy of regional lymph nodes
4. Routine OLT evaluation

While awaiting OLT:

1. Abdominal MRI or CT every 3 months
2. CT chest every 3 months
3. EUS every 3 months
4. Staging laparotomy when MELD is high enough to start attracting donor offers soon (done with hand assisted laparoscopic approach in patients with no prior abdominal surgeries)
 - a. Excision of peri-arterial lymph node (usually one overlying the take-off of the gastroduodenal artery) and a peri-choledochal lymph node along the distal bile duct regardless of their appearance (these are not accessible by EUS).
 - b. Biopsy any suspicious nodules or other lymph nodes
 - c. Palpate liver carefully for any evidence of intrahepatic metastasis that may have been missed by imaging

Transplantation technique:

1. Use a caval-sparing approach unless there is suspected caudate involvement or atrophy that would threaten the resection margin
2. Avoid hilar dissection and divide the portal vein, hepatic artery, and bile duct as close to the duodenum as possible.
3. Replace the hepatic artery in all cases of deceased donor transplantation due to the on-going radiation injury, which leads to early thrombosis.
4. Excise the bile duct as distally as possible and obtain a frozen section of the margin to rule-out multifocal disease and involvement of distal duct. If the distal bile duct margin shows tumor involvement, perform a pancreaticoduodenectomy.

Post-transplant management and monitoring:

1. IS regimen same as for HCC
2. Routine postOLT care
3. CT or MRI abdomen every 6 months x 3 years, then annually up to 5 years
4. CA 19-9 same as #3
5. High risk explant (multifocal disease, vascular invasion, etc) consider chemotherapy post OLT

Adapted from Mayo protocol

Updated and Instituted 9/28/2017

Approved by Liver Multidisciplinary Committee

Special thank you to the entire liver team who worked to make this handbook possible.

Sincerely,

Lisa Potter, PharmD & Christine Trotter, ACNP

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Model for End-stage Liver Disease (MELD)

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All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

Literature review current through: May 2018. | **This topic last updated:** Sep 29, 2016.

INTRODUCTION — Prognostic models are useful for estimating disease severity and survival, and can serve as helpful medical decision-making tools with respect to guiding patient care. These models are developed using statistical methodologies that involve determining the effects of variables of interest (eg, demographic data, clinical data, and laboratory values) on specific outcomes such as death.

Several prognostic models are currently used in healthcare settings. Some focus on generalized health status such as the Acute Physiology and Chronic Health Evaluation System (APACHE III) [1], while others are disease specific. Examples of the latter in the field of hepatology include models for predicting survival in patients with primary biliary cholangitis, primary sclerosing cholangitis, and alcoholic liver disease [2-5]. Two models that are used commonly in the care of patients with cirrhosis are the Child-Turcotte-Pugh score and the Model for End-stage Liver Disease (MELD) score [6-10].

This topic will review the development, use, impact, refinements, and limitations of the MELD score, particularly with regard to its use in allocating organs for liver transplantation. Other issues related to the selection of patients for liver transplantation are discussed separately. (See "[Liver transplantation in adults: Patient selection and pretransplantation evaluation](#)".)

MELD OVERVIEW — The Model for End-stage Liver Disease (MELD) is a prospectively developed and validated chronic liver disease severity scoring system that uses a patient's laboratory values for serum bilirubin, serum creatinine, and the international normalized ratio (INR) for prothrombin time to predict three-month survival ([calculator 1](#) and [calculator 2](#)). In patients with cirrhosis, an increasing MELD score is associated with increasing severity of hepatic dysfunction and increased three-month mortality risk ([figure 1](#)) [11]. Given its accuracy in predicting short-term survival among patients with cirrhosis, MELD was adopted by the United Network for Organ Sharing (UNOS) in 2002 for prioritization of patients awaiting liver transplantation in the United States. (See '[Adoption of MELD for organ allocation](#)' below and "[Liver transplantation in adults: Patient selection and pretransplantation evaluation](#)", [section on 'Cirrhosis'](#).)

Development of the MELD score — MELD was originally developed to predict three-month mortality following transjugular intrahepatic portosystemic shunt (TIPS) placement and was derived using data from a population of 231 patients with cirrhosis who underwent elective TIPS placement. The model was subsequently validated in an independent cohort of patients from the Netherlands undergoing TIPS placement [8]. The original model included serum bilirubin, serum creatinine, INR, and etiology of the liver disease (cholestatic or alcoholic versus other etiologies).

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variceal bleeding, and spontaneous bacterial peritonitis) in the MELD score does not substantially improve its predictive accuracy [9]. However, this does not imply that these portal hypertensive complications are not associated with decreased survival, but rather that these complications are more likely to be associated with advanced liver disease as determined by the MELD score.

Since survival following TIPS is primarily determined by the severity of the underlying liver disease, and since MELD is an accurate predictor of survival after TIPS, it was hypothesized that the MELD score might be useful as a prognostic indicator in a broader range of patients with advanced liver disease who were not undergoing TIPS placement. Subsequent studies demonstrated that the MELD score was useful in predicting mortality in several groups of patients, including patients on the waiting list for liver transplantation, hospitalized patients with hepatic decompensation, ambulatory patients with non-cholestatic liver disease, patients with primary biliary cholangitis, and a historic cohort of unselected patients with cirrhosis seen at Mayo Clinic Rochester at a time when liver transplantation was not available [9,13,14].

Calculating the MELD score — Several online tools are available for calculating the MELD score ([calculator 1](#) and [calculator 2](#)) [15]. The MELD equation that has been used by for prioritizing allocation of deceased donor livers for transplantation is demonstrated below:

$$\text{MELD} = 3.8 \cdot \log_e(\text{serum bilirubin [mg/dL]}) + 11.2 \cdot \log_e(\text{INR}) + 9.6 \cdot \log_e(\text{serum creatinine [mg/dL]}) + 6.4$$

With this model, scores can range from negative values to infinity. However, to avoid confusion, UNOS modified the MELD scoring system to eliminate negative values by setting to 1.0 any measured laboratory values that were less than 1.0. Thus, patients with the combination of an INR of ≤ 1 , serum creatinine ≤ 1 mg/dL, and serum bilirubin ≤ 1 mg/dL will receive the minimum score of 6 MELD points. In addition, UNOS set an upper limit for the MELD score at 40 points.

In an effort to avoid an unfair advantage for patients with intrinsic renal disease, the maximum serum creatinine level was set to 4.0 mg/dL, which is also the value that is automatically assigned to patients who have received hemodialysis at least twice, or continuous venovenous hemodialysis for 24 hours, in the preceding week. There is currently no modification in the score for patients receiving anticoagulation.

MELDNa — In January 2016, Organ Procurement and Transplantation Network Policy 9.1 (MELD Score) was updated to include serum sodium as a factor in the calculation of the MELD score [16]. [The MELDNa score](#) can be calculated online.

Hyponatremia is a common problem in patients with advanced cirrhosis, and the severity of the hyponatremia is a marker of the severity of the cirrhosis. Serum sodium is a reflection of the vasodilatory state in cirrhosis and predicts waitlist mortality independent of the MELD score [17]. There is a linear increase in mortality by 5 percent for each mmol decrease in serum sodium between 125 and 140 mmol/L [18]. Multiple studies have shown that the addition of serum sodium concentration improves the predictive accuracy of the MELD score in hyponatremic patients with low MELD scores who are awaiting liver transplantation [18-25]. Addition of serum sodium to the MELD model elevates the transplant priority for about 12 percent of listed patients [17]. Severe hyponatremia (<125 mmol/L) may be a better predictor of mortality than MELDNa score amongst patients with refractory ascites [26]. (See "[Hyponatremia in patients with cirrhosis](#)", section on 'Predictor of adverse prognosis'.)

Patients with low MELD score and hyponatremia benefit the most from the MELDNa based allocation system. For example, a patient with MELD score of 6 and serum sodium of 125 mmol/L or less gets an additional 13

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(GFR), serum sodium is no longer independently predictive of mortality [27].

APPLICATIONS OF THE MELD SCORE — The primary use of the Model for End-stage Liver Disease (MELD) score is in prioritizing patients on the waitlist for deceased donor liver transplantation based on liver disease severity and short-term mortality risk. However, as described above, the MELD score also predicts mortality following transjugular intrahepatic portosystemic shunt (TIPS) placement and has been demonstrated to have predictive value for outcomes in patients with cirrhosis undergoing [non-transplantation surgical procedures](#) [28]. Several other applications of the MELD score have been demonstrated and include, but are not limited to, predicting mortality in [acute alcoholic hepatitis](#) [28] and in acute variceal hemorrhage [29,30]. (See '[Development of the MELD score](#)' above and '[MELD applications beyond organ allocation](#)' below.)

Organ allocation — In 2002, the MELD score was adopted by the United Network for Organ Sharing (UNOS) for use in deceased donor liver allocation for adults with cirrhosis. MELD has also been adopted, or is under consideration for being adopted, by multiple countries and regions worldwide [31]. In the United States, adoption of MELD, which serves as a marker of liver disease severity and mortality risk among patients awaiting liver transplantation, has been associated with decreased mortality among patients on the liver transplant waiting list [32]. (See '[Adoption of MELD for organ allocation](#)' below.)

It is important to note that under the current deceased donor liver allocation system, adult patients with acute liver failure (UNOS status 1A) are exempt from the MELD-based prioritization process. However, outside of the context of the UNOS allocation policy for status 1A patients, the MELD score may have some prognostic value in selected patients with acute liver failure [33-35]. (See '[MELD applications beyond organ allocation](#)' below.)

Organ allocation prior to MELD — In the 1990s, as the number of patients listed for liver transplantation increased and the number of available deceased donor livers remained stable, the number of patients dying while awaiting transplantation rose linearly. The time spent on the waiting list became an important, albeit unintended, deciding factor in the deceased donor liver allocation process. However, it was demonstrated that time spent on the liver transplantation waiting list did not correlate with the risk of death while awaiting transplantation [36]. Due to increasing concerns regarding this disparity in liver allocation, the Department of Health and Human Services issued a mandate in 1998 that deceased donor livers for transplantation be prioritized in a more equitable manner, emphasizing the concept of transplanting the "sickest first," and de-emphasizing the amount of time spent on the transplantation waiting list [37,38].

In response to this mandate, UNOS initially adopted the Child-Turcotte-Pugh (CTP) scoring system for its liver transplantation prioritization system ([table 1](#)) ([calculator 3](#) and [calculator 4](#)). However, it soon became apparent that the CTP score was not sufficient to resolve the dominance of waiting time as a deciding factor.

The failure of the CTP score was due to several factors:

- The allocation system adopted by UNOS defined only three categories of disease severity in patients with cirrhosis (status 2A, 2B, and 3), with the minimal listing criterion for liver transplantation being a CTP score of at least 7. Patients with a CTP score of 7 to 9 were designated as status 3, while those with a CTP score of at least 10 were status 2B. Patients deemed to be at risk of dying within seven days were made status 2A. However, since there were only three categories, each category contained numerous patients and waiting time continued to be a major factor in the allocation process. Furthermore, determining whether a patient would die within seven days (ie, designated as status 2A) was not based on any validated criteria.

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- The CTP score is limited in its discriminatory capacity due to both a "ceiling" and a "floor" effect. A patient with a serum bilirubin level of 4 mg/dL, for example, is assigned the same number of points as a patient with a bilirubin of 15 mg/dL, even though the degree of elevation in serum bilirubin level is known to be an important prognostic indicator in patients with cirrhosis.

Adoption of MELD for organ allocation — During the liver transplantation community's search for a more equitable allocation system, the MELD score emerged as a more objective model for prioritizing patients based on liver disease severity. The MELD score was adopted by UNOS in 2002 for use in deceased donor liver allocation for adults with cirrhosis.

The utility of the MELD score for predicting three-month mortality among patients awaiting liver transplantation was demonstrated in a study that included 3437 adult liver transplantation candidates who were listed between 1999 and 2001 [13]. Of these, 412 died during the three-month follow-up period. Waiting list mortality was directly proportional to the MELD score at the time of listing, with mortality being 1.9 percent for patients with MELD scores less than 9, and 71 percent for patients with MELD scores ≥ 40 (figure 1).

The use of MELD to predict whether undergoing liver transplantation would provide a survival benefit compared with continued medical management has been investigated in several studies. It has been demonstrated that survival benefit increases with increasing MELD score and that at lower MELD scores, recipient mortality risk during the first post-transplantation year is higher than for candidates who remain on the waiting list [39-41].

Prioritization for liver transplantation based on MELD score — Patients awaiting liver transplantation are ranked according to their MELD score and stratified by blood type. Patients have their MELD scores updated and forwarded regularly to UNOS by the listing transplant center according to UNOS directives [42]. As a general rule, patients who are severely ill (higher MELD scores) will have their MELD scores updated more frequently than patients with less severe liver disease. Patients with a MELD score ≥ 25 , for example, have their scores updated every seven days. Patients may have their MELD score updated more often if they experience a decline in health status (manifested by a rise in their calculated MELD score). Due to the dynamic nature of cirrhosis, the MELD score may either increase or decrease while patients await liver transplantation. (See "[Liver transplantation in adults: Patient selection and pretransplantation evaluation](#)", section on 'Cirrhosis'.)

Time spent on the liver transplantation waiting list at a given MELD score is used to break ties among patients with the same blood type. If a patient's MELD score increases (indicating worsening of liver disease severity), the waiting time clock is set to zero and restarted at the higher score. However, according to current UNOS policy, if a patient's MELD score goes down, the time accumulated at the higher MELD score is maintained and added to the time accumulated at the lower score.

Standard MELD exceptions in liver transplantation — There are some conditions associated with chronic liver disease that may result in impaired survival, but that are not directly accounted for in the MELD scoring system [43]. Some of these conditions have been designated by the liver transplant community as "standard MELD exceptions." Patients who meet specific disease-related criteria for standard MELD exceptions may be eligible for an upgrade in MELD points, with subsequent automatic upgrades every three months provided that the patients continue to meet the specific disease-related criteria. These standard MELD exceptions were developed in order to more accurately represent the patient's mortality risk while awaiting liver transplantation. (See "[Hepatocellular carcinoma](#)" below and "[Other standard MELD exceptions](#)" below.)

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- Portopulmonary hypertension
- Familial amyloid polyneuropathy
- Primary hyperoxaluria
- Cystic fibrosis
- Hilar cholangiocarcinoma (provided the liver transplant center has a UNOS approved protocol detailing the work-up and management of patients with cholangiocarcinoma undergoing transplantation)
- Hepatic artery thrombosis (occurring within the 14 days after liver transplantation, but not meeting criteria for status 1A)

Hepatocellular carcinoma — HCC is the most common standard MELD exception. Whether patients receive exception points (or are candidates for transplant listing at all) depends on the extent of their HCC. Giving additional MELD points to patients with HCC initially led to a substantial increase in the proportion of listed patients with HCC [45]. Subsequently, the HCC exception point policy was modified to more accurately reflect the mortality risk due to HCC, and to not unduly favor patients with HCC relative to patients listed with their biologic MELD score. The decision to give exception points to patients with HCC was based on two observations:

- Patients with HCC who meet criteria for liver transplantation have a post-liver transplantation survival that is not worse than other patients undergoing liver transplantation. (See "[Liver transplantation for hepatocellular carcinoma](#)".)
- Many patients with HCC do not demonstrate the degree of hepatic synthetic dysfunction necessary to give them a competitive calculated MELD score, and thus would be given too low a priority based on their calculated MELD score alone. A low calculated MELD score in a patient with HCC would translate into increased waiting time, with a concomitant increased risk of tumor growth during the waiting period, resulting in increased morbidity and mortality.

When being considered for liver transplantation and MELD exception point allocation, patients with HCC are categorized using the American Liver Tumor Study Group (ALTSG) modification of the tumor node metastasis (TNM) staging system for HCC ([table 2](#)):

- Stage I: One nodule <2.0 cm; patients may be listed for liver transplantation, but they do not receive exception points.
- Stage II: One nodule between 2 and 5 cm or two to three nodules, none >3 cm. Patients may be listed for liver transplant at their calculated MELD scores for the first six months, provided that their HCC remains under control [46]. At six months, candidates receive a MELD exception score of 28. For every subsequent three months spent on the waiting list, patients receive additional points corresponding to an estimated increased mortality of 10 percent. All MELD HCC exception scores are capped at 34.
- Stage III: One nodule >5 cm or two to three nodules with at least one >3 cm. Patients may be considered for liver transplant listing on a case-by-case basis, but they do not receive the standard MELD HCC exception points.

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Since it is generally not desirable to biopsy hepatic lesions suspected of being HCC in liver transplant candidates, detailed imaging criteria for both computed tomography (CT) and magnetic resonance imaging (MRI) scans have been developed and are used by UNOS to support the diagnosis of HCC. (See "[Liver transplantation for hepatocellular carcinoma](#)", section on 'Requirements for listing and management while on the wait list'.)

Other standard MELD exceptions — The standard MELD exceptions other than HCC include the following [44,47,48]:

- Portopulmonary hypertension, characterized by an elevated pulmonary artery pressure. However, since a mean pulmonary artery pressure >35 mmHg is associated with poorer outcomes after liver transplantation, in order to receive MELD exception points for portopulmonary hypertension, the mean pulmonary artery pressure must be maintained <35 mmHg with treatment. (See "[Portopulmonary hypertension](#)".)
- Hepatopulmonary syndrome, characterized by a PaO₂ <60 mmHg on room air.
- Familial amyloid polyneuropathy, characterized by the identification of the transthyretin (TTR) gene mutation (Val30Met versus non-Val30Met) by DNA analysis or mass spectrometry in a biopsy sample and confirmation of amyloid deposition in an involved organ.
- Primary hyperoxaluria with evidence of alanine glyoxylate aminotransferase deficiency. These patients must be listed for combined liver-kidney transplantation.
- Cystic fibrosis, characterized by a forced expiratory volume in one second (FEV1) <40 percent.
- Hilar cholangiocarcinoma, provided the transplant center listing the patient has a written and UNOS approved protocol detailing the work-up and management of patients with cholangiocarcinoma undergoing transplantation.
- Hepatic artery thrombosis (occurring within 14 days of liver transplantation, but not meeting criteria for status 1A).

Petitioning for additional MELD points — As a general rule, patients listed with the standard MELD exceptions (with the exception of hepatic artery thrombosis occurring within 14 days of transplant, but not meeting status 1A criteria) receive an increase in their MELD exception score every three months while on the waiting list that corresponds to an estimated 10 percent increase mortality risk, provided they continue to meet the disease-related listing criteria.

Patients may also have complicating medical conditions that are related to their liver disease, but that do not qualify for standard MELD exception points. Transplant centers may petition their Regional Review Board (RRB) for additional points for listed patients with complicating medical issues related to their liver disease if the patient's medical providers believe that the patient's biologic MELD score does not adequately reflect the patient's true liver-related morbidity and mortality.

Some examples of complicating medical issues that may prompt a petition to the RRB include, but are not limited to:

- Recurrent cholangitis in patients with primary sclerosing cholangitis who are on antibiotic suppressive therapy

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... permission may be considered by the committee and either approved or denied depending on the basis for the request and the objective data supporting the need for additional MELD points.

Impact of the MELD liver allocation system — The introduction of the MELD score has, overall, improved liver allocation, though there have been other effects that were not anticipated. The impact of the adoption of the MELD score for organ allocation was examined in a study using data from UNOS [49]. Outcomes of deceased donor liver transplantation were compared between the pre-MELD era (era 1: February 27, 2001 to February 26, 2002) and the post-MELD era (era 2: February 27, 2002 to February 26, 2003).

Compared with the pre-MELD era, the post-MELD era was associated with:

- A 12 percent reduction in new patients added to the liver transplant waiting list (particularly patients with low MELD scores because accrual of waiting time was no longer advantageous in the MELD system)
- A higher mean MELD score at the time of transplantation (24 in the post-MELD era versus 18 in the pre-MELD era)
- A 10 percent increase in the number of deceased donor liver transplantations performed
- A 3.5 percent decrease in the number of deaths on the liver transplantation waiting list

In 2005, Argentina adopted MELD for organ allocation. Compared with the five years prior to the adoption of MELD, during the five years after the adoption of MELD, there were decreases in both waiting list mortality (29 versus 22 percent) and dropout rates (39 versus 29 percent) [50]. The number of deaths decreased from 273 per 1000 patient-years at risk in 2005 to 173 per 1000 patient-years at risk in 2010.

There had been initial concern that adoption of the MELD scoring system might result in poorer post-liver transplant outcomes if livers were being allocated to patients who were "too sick" (those with high MELD scores). However, there was no significant change in early (three-month) patient or graft survival in Era 2 (post-MELD) in the United States compared with Era 1 (pre-MELD) [49]. Similarly, there was no change in one-year post-transplant survival after the adoption of MELD in the Argentinian study [50]. These data demonstrate that the MELD allocation system has been successful in de-emphasizing waiting time as a major factor in prioritizing patients for liver transplantation. In addition, adoption of the MELD scoring system has been associated with increased transplantation rates without concomitant increased mortality rates.

Adoption of MELD has also been associated with other effects, some of which were unanticipated:

- In the post-MELD era, a person's race was no longer associated with the likelihood of receiving a liver transplant, risk of death on the liver transplant waiting list, or risk of being removed from the waiting list due to being too ill [51].
- There was an increase in the number of combined liver-kidney transplants being performed because of the emphasis of MELD on renal function [52].
- More high-risk deceased donor livers (ie, livers from older donors or donation after cardiac death [DCD] livers) were being steered toward patients with lower MELD scores [53,54]. In the pre-MELD era, high-risk donor livers were typically used for patients in most urgent medical need of liver transplantation. However, it should also be noted that since the adoption of the MELD system for liver allocation, there has also been a national initiative to increase the use of high-risk donor livers in order to increase the number of available

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- Women in the post-MELD era are more likely than men to die or become too ill for transplant, whereas in the pre-MELD era the likelihoods for men and women were similar [51]. The precise reasons for this are not completely clear, but studies suggest that women may be somewhat disadvantaged in the MELD system due to their generally smaller body mass and, therefore, lower creatinine levels [56,57]. It is also likely that donor liver allocation to women is impacted by factors outside the purview of the MELD score, including matching of organ size to recipient body size [58].

MELD applications beyond organ allocation — The MELD scoring system has prognostic value in a variety of other clinical settings and populations of patients with liver disease [5,14,29,30,33,34,59-65], including:

- **Selecting patients for TIPS placement** — The MELD score was developed initially to predict three-month survival among patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) placement [8]. Using the MELD score, as modified by UNOS, the best outcomes with TIPS occur among patients with a MELD score less than 14.

As a general rule, TIPS should be avoided if possible in patients with a MELD score greater than 24, unless the procedure is being used as salvage therapy to control active variceal bleeding [66,67]. When deciding whether to carry out TIPS placement in patients with MELD scores between 15 and 24, clinical judgment and extensive discussion with the patient, family members, and interventional radiology regarding the risks of hepatic decompensation are required.

Patients with MELD scores greater than 24 who are reasonable liver transplant candidates are probably best served by foregoing TIPS placement and waiting for liver transplantation [68]. However, the projected waiting time for a deceased donor liver to become available can be quite prolonged. As a result, clinical circumstances may arise that necessitate consideration of TIPS to control complications from portal hypertension in patients with high MELD scores. Such patients should ideally be evaluated for liver transplantation before TIPS in case they develop irreversible hepatic decompensation after the procedure.

- **Alcoholic hepatitis** – The Discriminant Function (DF) has traditionally been used to predict survival in patients with alcoholic hepatitis ([calculator 5](#)) [5]. However, the DF may be somewhat limited in its applicability as it relies primarily on measurement of the prothrombin time, which is subject to variability among different laboratories. Several studies have evaluated the MELD score as a prognostic index in alcoholic hepatitis, and a simple [online tool](#) is available in which the MELD score has been calibrated to predict 90-day mortality among patients with alcoholic hepatitis [69]. (See "[Prognosis and management of alcoholic fatty liver disease and alcoholic cirrhosis](#)".)
- **Hepatorenal syndrome** – A study of 105 consecutive patients with hepatorenal syndrome suggested that the MELD score may be a useful predictor of survival among patients with type 2 hepatorenal syndrome [59]. A MELD score of ≥ 20 was associated with significantly shorter transplantation-free survival compared with those patients with lower MELD scores (median survival of 3 versus 11 months, respectively). (See "[Hepatorenal syndrome](#)".)
- **Acute liver failure (UNOS status 1A)** – MELD is the scoring system used by UNOS for prioritizing organ allocation in adult patients with cirrhosis awaiting transplantation; however, the allocation process for patients with acute liver failure, designated as UNOS status 1A, is not based on the MELD score.

Although MELD is not currently used in clinical practice for UNOS status 1A patients, the accuracy of MELD in this patient population has been evaluated. In a study that included 720 adult status 1A liver

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The MELD score has also been specifically assessed for its prognostic value in acetaminophen-induced hepatotoxicity [34]. In one study, a higher MELD score was predictive of the development of acute liver failure and hepatic encephalopathy, but once acute liver failure developed, the MELD score was not a more accurate predictor of survival than either the King's College Criteria or the international normalized ratio (INR) alone [34].

Similarly, in a study of patients with acute liver failure due to hepatitis A virus infection, MELD was only moderately accurate in predicting mortality risk (c-statistic 0.7) [61]. In a study utilizing UNOS data, it was demonstrated that patients who were designated status 1A actually had a mortality rate that was similar to that in patients with cirrhosis who had biologic MELD scores ranging from 36 to 40. Furthermore, the study demonstrated that status 1A patients were actually at lower mortality risk compared with patients with cirrhosis with biologic MELD scores >40. These investigators called into question the current policy of prioritizing status 1A patients above all other liver transplant candidates [35]. Therefore, the relationship between MELD and survival in patients with acute liver failure is complex, and although some studies suggest that MELD may have some prognostic value in acute liver failure, there are likely other parameters that are important mortality predictors in this unique patient population. (See "[Acute liver failure in adults: Etiology, clinical manifestations, and diagnosis](#)" and "[Acetaminophen \(paracetamol\) poisoning in adults: Treatment](#)".)

- **Acute variceal hemorrhage** – Several studies have investigated the prognostic value of MELD in predicting mortality among patients presenting with acute variceal hemorrhage [29,30,63,64]. The studies suggest that higher MELD scores are associated with increased mortality rates. As an example, in a study of 178 patients with cirrhosis and acute variceal bleeding, a MELD score <11 was associated with a <5 percent mortality rate within six weeks, whereas a MELD score ≥19 was associated with a 20 percent mortality rate [30].
- **Assessment of surgical mortality risk in liver disease** – Patients with cirrhosis are at increased risk of perioperative morbidity and mortality, and the CTP score has traditionally been used to risk stratify these patients prior to surgical intervention. More recently, the MELD score has been evaluated with respect to its ability to predict perioperative mortality in patients with cirrhosis undergoing various surgical procedures.

An [online tool](#) is available for determining the risk of postoperative mortality for several types of major surgery, including gastrointestinal, orthopedic, and cardiac surgery [28].

LIMITATIONS OF THE MELD SCORE — The MELD score is vulnerable to variations in laboratory measurements. For example, despite being normalized for the sensitivity of thromboplastin, the international normalized ratio (INR) can vary across laboratories if thromboplastin derived from rabbit brain is used rather than recombinant thromboplastin, potentially leading to important differences in prioritization of patients according to MELD [70-72]. (See "[Tests of the liver's biosynthetic capacity \(eg, albumin, coagulation factors, prothrombin time\)](#)".)

The MELD score may also be influenced by the method by which serum creatinine is measured. Variability in serum creatinine measurement using different assays is particularly problematic in the presence of an elevated serum bilirubin concentration, although this can be circumvented by using an enzymatic method to measure serum creatinine, particularly when the total bilirubin level is >25 mg/dL [73,74].

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allocation process. These models require further vetting and assessment of the impact on waitlist mortality and transplantation outcomes before being considered for formal adoption.

Reweighting of MELD components — A study of the United Network for Organ Sharing (UNOS) data from 2001 to 2006 used all available laboratory values for the MELD components in waitlisted liver transplantation candidates and described an updated MELD formula in which the coefficients for the MELD components were significantly different from the coefficients in the original MELD model [75]. The updated MELD formula assigned lower weights to serum creatinine and international normalized ratio (INR) and a higher weight to serum bilirubin. The updated model performed better than the existing MELD score in predicting waitlist mortality.

Refitting of MELD — Another study addressing optimization of the MELD scoring system for organ allocation was conducted using UNOS data from adult patients added to the liver transplant waiting list between 2005 and 2008. The investigators developed and independently validated new models that updated the coefficients for the MELD components and implemented new upper and lower bounds for creatinine (0.8 and 3.0 mg/dL, respectively) and for INR (1.0 and 3.0, respectively) [17]. The revised models were generated with and without serum sodium in the model (RefitMELDNa and RefitMELD, respectively). Both models performed better than the existing MELD score, MELDNa, and the reweighted MELD score in predicting mortality on the liver transplant waiting list.

SUMMARY AND RECOMMENDATIONS

- The Model for End-stage Liver Disease (MELD) score is a prospectively developed and validated cirrhosis severity scoring system that uses a patient's laboratory values for serum bilirubin, serum creatinine, and the international normalized ratio (INR) to predict three-month survival ([calculator 1](#) and [calculator 2](#)). In patients with cirrhosis, an increasing MELD score is associated with increasing severity of hepatic dysfunction and increasing three-month mortality risk ([figure 1](#)). (See '[MELD overview](#)' above.)
- [The MELDNa score](#) include serum sodium as a factor in the calculation of the MELD score and is used by the United Network for Organ Sharing (UNOS) for prioritizing allocation of deceased donor livers for transplantation.
- Patients awaiting liver transplantation are ranked according to their MELD score and stratified by blood type. Patients have their MELD scores updated and forwarded regularly to UNOS by the listing transplant center. The MELD score may either increase or decrease while patients await liver transplantation. Within a given geographic region, time spent on the waiting list at a given MELD score is used to break ties among patients with the same blood type. (See '[Prioritization for liver transplantation based on MELD score](#)' above.)
- There are some conditions associated with chronic liver disease that may result in impaired survival, but that are not directly accounted for in the MELD scoring system. Some of these conditions have been designated as "standard MELD exceptions." Patients who meet specific disease-related criteria may be eligible for standard MELD exceptions and, as such, may receive an upgrade in MELD points. Standard MELD exceptions were developed by the liver transplantation community in an effort to more accurately represent certain groups of patients' mortality risk while awaiting liver transplantation. (See '[Standard MELD exceptions in liver transplantation](#)' above.)

Standard MELD exceptions include:

- Hepatocellular carcinoma

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- Primary hyperoxaluria
- Cystic fibrosis
- Hilar cholangiocarcinoma (provided the transplantation center has a UNOS-approved protocol detailing the work-up and management of patients with cholangiocarcinoma undergoing transplantation)
- Hepatic artery thrombosis (occurring within 14 days of liver transplant, but not meeting criteria for status 1A)

Patients may also have complicating medical conditions that are related to their liver disease, but that do not qualify as standard MELD exceptions. Transplantation centers can petition their Regional Review Board for additional points for listed patients with complicating medical issues related to their liver disease if the providers believe that the patient's biologic MELD score does not adequately reflect the patient's true liver-related morbidity and mortality.

- The MELD scoring system has prognostic value in an array of other clinical settings and populations of patients with liver disease beyond its application in the deceased donor liver allocation process. (See '[MELD applications beyond organ allocation](#)' above.)

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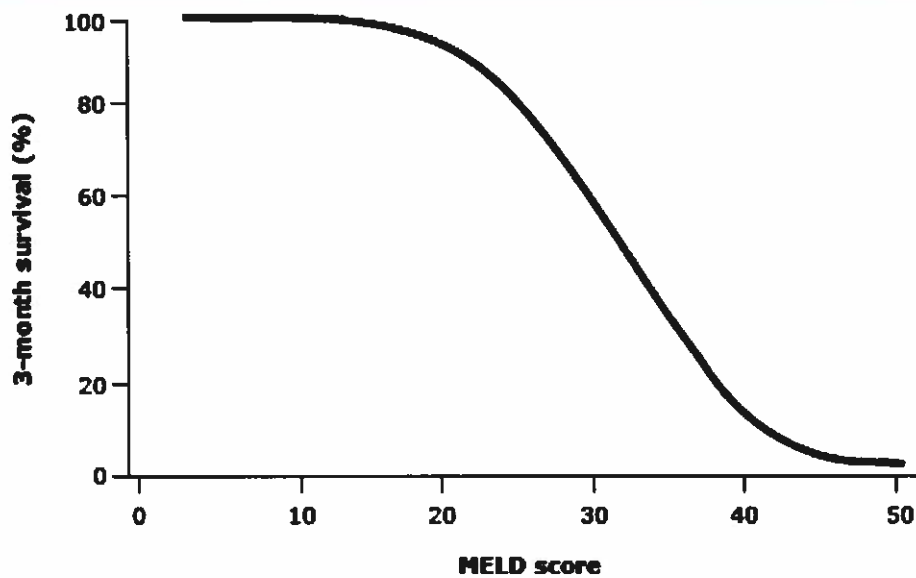
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in patients with cirrhosis



MELD: Model for End-Stage Liver Disease.

Adapted from: Wiesner, R, Edwards, E, Freeman, R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology* 2003; 124:91.

Graphic 77732 Version 4.0

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	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease); 7 to 9 is class B (significant functional compromise); and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

INR: international normalized ratio.

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T1	One nodule, ≤ 1.9 cm
T2	One nodule, 2 to 5 cm; two or three nodules, all ≤ 3 cm
T3	One nodule, > 5 cm; two or three nodules, at least one > 3 cm
T4a	Four or more nodules of any size
T4b	T2, T3, or T4a, plus gross involvement of intrahepatic portal vein or hepatic vein, as indicated by CT, MRI, or ultrasonography
N1	Involvement of regional (porta hepatis) lymph nodes
M1	Metastatic disease including extrahepatic portal or hepatic vein involvement
Stage grouping	
Stage I	T1
Stage II	T2
Stage III	T3
Stage IVA1	T4a
Stage IVA2	T4b
Stage IVB	Any N1 or M1

TNM: tumor, node, metastasis; CT: computed tomography; MRI: magnetic resonance imaging.

Graphic 53242 Version 2.0

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Liver transplantation: Donor selection

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INTRODUCTION — The shortage of available donor organs is the major limiting factor in liver transplantation. Optimal deceased donors are generally young, previously healthy persons who develop a fatal brain injury due to causes such as head trauma, intracerebral hemorrhage, or anoxia. The relative paucity of donor organs has led transplant centers to consider organs from marginal donors.

This topic will review the selection process for deceased donors and examine donor characteristics associated with recipient outcomes. Patient selection for liver transplantation, living donor liver transplantation, and ethical issues in liver transplantation are discussed elsewhere.

- (See "[Liver transplantation in adults: Patient selection and pretransplantation evaluation](#)".)
- (See "[Living donor liver transplantation](#)".)
- (See "[Ethical issues in liver transplantation](#)".)

DONOR EVALUATION

Donation after brain death — The United Network for Organ Sharing (UNOS) provides minimum guidelines for organ procurement. The initial evaluation is typically performed by the local organ procurement organization (OPO). The OPO representative verifies that the prospective donor meets the criteria for brain death. Consent for donation is obtained from the potential donor's next of kin. ABO blood type, height, weight, and chest circumference are obtained because recipient matching is based upon blood type and donor organ size.

Potential donors with contraindications to donation are excluded. These include non-hepatic malignancy (other than primary brain tumor without ventriculoperitoneal shunt). Previously, anti-human immunodeficiency virus (HIV) seropositivity was an absolute contraindication to donation in the United States. The ban was in part due to concern that transplanting HIV-positive organs into patients with HIV that was well controlled could result in the transfer of resistant HIV to the recipient. However, in 2013, a law was passed that ended a ban on transplanting organs from donors with HIV into HIV-positive recipients because of better HIV therapy as well as high waiting list mortality rates for patients with HIV [1]. Although septicemia is usually considered a contraindication to donation, organs from bacteremic donors have been used successfully. A large retrospective study, for example, showed similar 30-day graft and patient survival in recipients of organs from bacteremic and non-bacteremic donors [2].

The OPO representative obtains a medical history, evaluates for a history of substance or alcohol abuse, and performs a physical examination. Laboratory testing generally includes ABO blood type, complete blood count

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acid testing (NAT) for HIV and HCV in all or selected high risk donors to shorten the window period between acquisition of infection and detection by ELISA in order to reduce the risk of transmission to the recipient [3]. Ultrasound imaging or liver biopsy is performed if needed.

The local OPO is responsible for donor maintenance until the time of procurement. Vital signs, intake, and output are monitored. Fluids and vasopressors are given as needed to achieve hemodynamic stability. Antibiotics are provided if necessary.

Living donors — This topic is discussed in detail elsewhere. (See "[Living donor liver transplantation](#)", section on '[Donor selection](#)'.)

DONOR FACTORS IMPACTING RECIPIENT OUTCOME — Multiple donor and transplant-related characteristics associated with recipient outcomes have been evaluated [4-13]. Comparisons among these studies can be difficult since variable clinical endpoints have been measured, recipients had different forms of underlying liver disease, and because donors are often selected based upon recipient characteristics. Clinical endpoints frequently include the following measures:

- Initial graft function
- Primary nonfunction (PNF, ie, graft failure in the immediate postoperative period)
- Graft survival and
- Patient survival

Donor factors that have been associated with adverse outcomes include advanced donor age, donor sex or donor-recipient sex mismatch, moderate to marked hepatic steatosis, and donor hypernatremia.

Strategies used to increase available donor livers may affect outcomes. These strategies include adult living donor liver transplantation, donation after cardiac death, the use of hepatitis C virus (HCV)-positive donors for HCV-infected recipients, and hepatitis B surface antigen (HBsAg)-positive donors for hepatitis B virus (HBV)-positive and anti-hepatitis B core antigen (HBc)-positive recipients. (See "[Liver transplantation for chronic hepatitis B virus infection](#)", section on '[De novo HBV infection/reactivation](#)' and "[Living donor liver transplantation](#)".).

Although donor characteristics and technical factors will be discussed individually, a combination of risk factors may interact to affect outcomes in individual patients.

Older age — The use of livers from older donors is now a common practice [14]. However, livers from older donors can have more initial dysfunction due to ischemic or preservation injury and in recipients with hepatitis C, there is an association of donor age with the development of severe recurrent hepatitis C. Delayed non-function may occur, necessitating retransplantation. Use of organs felt to be of good quality on careful inspection [15] and minimizing cold ischemia time [16,17] may help to maximize outcomes when livers are used from older donors.

Several studies have evaluated the relationship between donor age and recipient outcomes [4,6-8,15,16,18-21]. An illustrative report included 772 patients who underwent liver transplantation at three centers [15]. Older donors were defined as those aged 50 years and above. Laboratory parameters including alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, and prothrombin time were higher in recipients with older donors during the first week after transplantation. More importantly, graft survival was

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worsening outcomes has varied. Other studies suggest that acceptable outcomes can be achieved with selected older donors [7,8,16,22,23]. Limiting cold ischemia time and degree of steatosis were hypothesized to be important in optimizing the results of transplantation from older donors.

The use of livers from older donors is a particular concern for hepatitis C infected recipients. A single center study of 124 liver transplants showed that donor age >60 years was associated with the development of severe recurrent hepatitis C and provided an optimal age cutoff to predict an increased risk of HCV-related graft loss [24].

Hepatic steatosis — Donor livers that appear fatty on inspection are biopsied for histological determination of fat content. Severe macrovesicular steatosis is associated with primary nonfunction [12,25-30]. Outcomes are more variable when organs with moderate steatosis are used. Illustrative studies have shown the following:

- One study, which analyzed 158 donor liver biopsies, found that moderate fatty change (defined as 30 to 60 percent fat content) was associated with the development of early graft dysfunction [27].
- Another report that categorized donor steatosis as mild (<30 percent), moderate (30 to 60 percent), and massive (>60 percent) found an increased frequency of early graft dysfunction and PNF when donor organs had moderate or massive steatosis [28]. Compared with patients who received livers with mild steatosis, graft survival at one month was slightly lower in those who received livers with moderate steatosis and substantially reduced in those given grafts with massive steatosis.
- A report of 225 consecutive transplants showed that while ≥ 30 percent donor steatosis was associated with early graft dysfunction, five-year recipient survival was similar between patients who received grafts with <30 or >30 percent steatosis [31].
- A retrospective review of the United Network for Organ Sharing Standard Transplant Analysis and Research files examined 5051 liver transplants [32]. At one year, 864 (17 percent) of the grafts had failed. The study found that on multivariable analysis, donor livers with greater than 30 percent macrovesicular steatosis had an increased risk of graft loss (relative risk 1.71). Many transplant centers try to avoid using organs with more than 40 percent fatty infiltration and refuse organs with more than 50 percent fat content [33].

Hypernatremia — Worse outcomes have been reported in liver transplant recipients who receive grafts from donors with hypernatremia. Donor hypernatremia may be a surrogate marker for other factors affecting graft function, including prolonged donor intensive care stay, excessive saline infusion, and negative water balance resulting from aggressive treatment of cerebral edema, and reduced antidiuretic hormone secretion after brain death. In two reports, the rate of graft loss within one month of transplantation was increased when the donor plasma sodium level exceeded 155 mmol/L [34,35]. Other investigators observed a direct relationship between donor serum sodium levels and degree of early graft dysfunction [36]. Most respondents to a survey of the South-Eastern Organ Procurement Foundation liver transplant centers indicated that the maximum donor serum sodium level that they would accept was 160 to 170 mEq/L [33].

Hemodynamic instability — Hepatic blood flow decreases with periods of hypotension and the use of high doses of vasopressors predisposing to ischemic liver injury. Early graft dysfunction was observed when donors had hypotension refractory to dopamine levels exceeding 15 mcg/kg/min [37]. However, the use of high doses of dopamine was not associated with graft dysfunction when the donor's blood pressure was maintained above 90 mmHg.

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given to a male recipient may be particularly problematic. As an example, a retrospective evaluation of 994 liver transplants performed over 10 years showed significantly lower graft and patient survival for transplantation of female donors into male recipients compared with other donor-recipient combinations (approximately 56 versus 75 percent two-year graft survival) [39].

A further study of 462 liver transplants with 1.1 to 2.6 years of follow-up found that graft survival was superior with male donors relative to female donors when controlling for other factors [38]. The poorest results were observed with the use of female donors over age 60. A study of pediatric liver transplant patients also documented superior one and five-year graft and patient survival for male-male donor-recipient pairs compared to males who received livers from female donors [40]. The organ allocation system does not take the donor's or recipient's sex into account in distributing livers since other considerations are more important.

ABO compatibility — Livers are routinely matched by ABO blood type (ABO identical), although mismatched organs have been used in extreme circumstances. Mismatched organs may either be ABO compatible (eg, an organ from a donor who is type O going to a recipient who is type B) or ABO incompatible (eg, an organ from a donor who is type A going to a recipient who is type B). A retrospective study of 234 liver transplants found that two-year graft survival was 30 percent in 17 ABO-incompatible emergency transplants compared with 76 percent in 55 ABO-compatible emergency transplants and 80 percent in 162 ABO-compatible elective transplants [42]. Compared with ABO-compatible transplants, humoral rejection, acute cellular rejection, arterial thrombosis, and biliary complications were more common in ABO-incompatible recipients. These data suggest that ABO incompatibility (and not a need for emergency transplantation) was the major reason for graft loss, although the urgent nature of the transplant and severe illness likely had a role as well. Registry data from Europe showed that the risk of mortality was increased nearly two times in recipients of ABO-incompatible livers [43]. However, good outcomes have been reported among recipients with blood type O who receive an organ from a donor with blood type A2 with overall and graft survival rates that are similar to those seen when a recipient with blood type O receives an ABO-compatible organ [44].

Many centers use ABO-incompatible livers in emergency situations such as fulminant hepatic failure when an ABO-identical or compatible organ is unavailable, with the understanding that retransplantation will be required in some patients. In such cases, perioperative plasmapheresis, intensive induction immunosuppression, and prostaglandin E1 administration may reduce the development of severe acute rejection [45,46].

There have also been successful elective transplantations of ABO-incompatible organs from living donors. In a series of 22 recipients of ABO-incompatible organs, overall patient and graft survival were 100 percent after a mean follow-up of 10 months (range 3 to 21 months) [47]. All of the patients received [rituximab](#) two weeks prior to transplantation and also underwent plasma exchange with blood group AB fresh frozen plasma every other day prior to transplantation. Plasma exchange transfusion was continued until the IgM and IgG isoagglutinin titers that corresponded to the donor ABO blood group were $\leq 1:8$. During the first two weeks following transplantation, plasma exchange transfusion was repeated if the titers were $> 1:32$.

TECHNICAL FACTORS

Cold ischemia time — Prolonged cold ischemia time (ie, greater than 12 hours) may impact donor organ viability and graft survival. Donor livers are typically preserved in University of Wisconsin storage solution cooled to 0 to 4° C after harvesting. Cold preservation leads to liver injury over time, and the duration of cold ischemia time (CIT) affects recipient outcomes.

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transplantation [49]. Data from a large European registry indicated that the risk of recipient mortality was stable for CIT up to 12 hours and increased with longer preservation times [43]. In multivariate analysis, there was a negative interaction between CIT exceeding 12 hours and recipient age greater than or equal to 60 years, and CIT exceeding 12 hours and status as a previous transplant recipient with graft failure.

Other studies found that CIT exceeding 12 hours was associated with an increased rate of biliary complications, such as intrahepatic strictures [50]. Most centers try to limit CIT to less than 12 hours, particularly in the presence of other donor or recipient characteristics that can adversely affect transplant outcomes.

RISK ASSESSMENT INDICIES

Donor risk index — Data from over 20,000 liver transplants were used to develop a predictive model comprised of donor factors known at the time an organ is offered to quantify the risk of graft failure, and this model is known as the donor risk index [51]. The parameters most strongly associated with graft loss include increasing donor age, donation after cardiac death, and use of split/partial grafts. Other risk factors include African American donors, shorter donors, death due to cerebrovascular accident, and causes of brain death other than trauma or anoxia.

Eurotransplant donor risk assessment — Analysis of 4701 deceased donors from Eurotransplant and the European Transplant Registry identified risk factors for graft loss in first time recipients who received a deceased donor liver [52]. Cold ischemia time, highest serum sodium level, cause of donor death, gamma-glutamyl transferase (GGT) level, and female donor sex were predictors of graft loss at three months. In addition, cold ischemia time, GGT, and cause of donor death were associated with 12-month graft loss. The data were used to construct nomograms to allow for rapid assessment of the complex interaction among risk factors in a given donor. When the donor risk index was applied to the dataset, there was limited agreement with the Eurotransplant nomogram ($\kappa = 0.23$). The area under the receiver operating characteristic curve for both predictors was relatively low, indicating the difficulty in defining criteria for extended donors.

APPROACHES TO EXPAND DONOR LIVER SUPPLY

Donation after cardiac death — Patients with an irreversible, catastrophic illness may serve as non-heart-beating donors after withdrawal of care in a controlled hospital setting and after achieving set criteria for cardiac death [53,54]. Such donation is referred to as "donation after cardiac death" (DCD). In the United States, life support is usually withdrawn in the operating room. The patient is observed until the time of death, which is declared by a clinician who is not part of the transplant team. An additional one to five-minute waiting period is mandated before organ retrieval is initiated with femoral artery cannulation and infusion of cold University of Wisconsin storage solution. Warm ischemia time includes the interval between withdrawal from life support and infusion of University of Wisconsin solution [53].

Successful outcomes have been reported with mean warm ischemia times of 16.4 + 10.9 minutes to 19 + 9 minutes [53-55]. One group suggested that they would accept warm ischemia times of up to one hour for livers [53]. Studies comparing recipients of organs from DCD donors with standard brain-dead deceased donors have been variable, with some showing similar outcomes, while other suggest decreased graft and patient survival following receipt of a DCD donor organ [53-58]. However, many of the studies are limited by the fact that they were not randomized, potentially leading to disparate outcomes that were not the result of the type of donor organ.

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year graft loss (27 versus 18 percent) and higher three-year mortality (19 versus 14 percent).

- Another retrospective series compared 87 liver transplantations from DCD donors with 1157 liver transplantations from brain-dead deceased donors [56]. Patient survival was significantly lower in the DCD group at 1, 4, 10, and 15 years (84 versus 91 percent, 68 versus 81 percent, 54 versus 67 percent, and 54 versus 58 percent, respectively). In addition, graft survival was also lower in the DCD group.
- A third retrospective series with 200 liver transplantations from DCD donors and 1828 liver transplantations from brain-dead deceased donors did not find any differences in graft or patient survival between the groups at one, three, or five years [57].

Donor factors associated with graft failure include hepatitis B core antibody positivity, a mean arterial pressure lower than 60 mmHg for more than 20 minutes after the withdrawal of life support, and longer cold ischemia times (>6 hours in one study) [57,59]. Recipient factors associated with graft failure include hepatitis C virus infection, the presence of malignancy, previous liver transplantation, a body mass index greater than 30, and non-Caucasian race [57,59].

Perhaps most concerning is the association between the use of DCD donors and the development of biliary complications. A retrospective analysis of 20 patients who received DCD donor found that 60 percent had biliary complications, including 55 percent with serious biliary abnormalities [60]. A second retrospective series found that biliary complications were significantly more likely when DCD donors were used compared with standard, brain-dead deceased donors (47 versus 26 percent) [56]. However, a lower rate of biliary complications was noted in a third retrospective series with 200 patients [57]. Biliary complications included ischemic cholangiopathy (12 percent), bile leaks (4 percent), extrahepatic biliary strictures (6 percent), and combined bile leaks and extrahepatic biliary strictures (6 percent).

Although there may be an increased risk of graft loss and biliary complications, judicious use of DCD donors could provide a substantial number of needed organs. According to some estimates, this practice could expand the organ supply by up to 1000 livers per year [54].

Modified donor harvesting technique — A small randomized trial compared the impact of a modified double perfusion (MDP) liver harvesting technique to single aortic perfusion on graft survival in suboptimal livers. The MDP technique consisted of aortic and portal cooling with clamping of the splenomesenteric vein inflow. Use of the MDP technique was associated with a lower rate of PNF and higher six-month patient and graft survival [61].

Hepatitis C-positive donors — Transplantation of livers from hepatitis C virus-positive (HCV+) donors into HCV+ recipients initially raised concerns that aggressive recurrent liver disease would result from introduction of new viral strains into the recipient. However, studies with up to five years of follow-up, along with the advent of interferon-free direct-acting antiviral treatments for HCV have reduced those concerns [62-64], and the use of HCV-positive livers has increased from 7 percent in 2010 to 17 percent in 2015 [65].

Outcomes in recipients of HCV+ grafts are discussed separately. (See "[Recurrence of hepatitis C virus infection following liver transplantation](#)".)

Hepatitis B-positive donors — Transplantation of organs from donors with serologic markers for past HBV infection has the potential to increase the donor pool, particularly in regions where HBV carriers are frequent (such as the Mediterranean region and Asia). It is generally recommended that grafts from hepatitis B core antibody (HBcAb)-positive donors should be offered to hepatitis B surface antigen (HBsAg)-positive recipients,

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The use of HBcAb-positive livers was examined in a study of 1437 patients with cirrhosis due to various causes who underwent liver transplantation [70]. HBcAb-positive grafts were transplanted into 219 recipients, 66 (30 percent) of whom were HBsAg-positive. Patients who received livers from HBcAb-positive donors were at increased risk for graft loss compared with those who received livers from HBcAb-negative donors (adjusted hazard ratio [HR] 1.56, 95% CI 1.18-2.04). The risk was higher among recipients who were HBsAg-negative than among those who were HBsAg-positive (HR 1.59 versus 1.36). However, since the study was observational, there is a risk of selection bias (eg, patients who were more acutely ill may have been more likely to receive HBcAb-positive grafts).

More controversial is the use of livers from donors who are HBsAg-positive. Transplantation of such grafts has been described [71,72] but should probably not be offered to patients who are HBsAg-negative or to recipients who have concurrent HDV infection since such patients may develop severe HDV related disease after transplant [73].

Machine liver perfusion — Both hypothermic machine perfusion and normothermic ex-vivo liver perfusion (NEVLP) are being studied as techniques to expand the donor pool by limiting the deleterious effects of cold ischemia on extended criteria grafts such as DCD and steatotic livers [74-76].

A phase 1 study provided proof of concept for the use of an ex-vivo circuit to maintain liver allografts in a physiologic state by perfusion with blood containing oxygen and nutrients at a temperature of 37°C during transportation and storage [74]. NEVLP allows for assessment of graft function including metabolic and perfusion parameters and bile flow, which have the potential to predict graft viability in an effort to minimize primary graft non-function with use of extended criteria donor livers [75].

SPLIT-LIVER TRANSPLANTATION — Splitting livers into right and left lobes for transplantation has been investigated as a way to increase the supply of donor organs. Studies have looked at allocating the split organ to an adult and a pediatric recipient or to two adults.

A working group appointed by the American Society of Transplant Surgeons and the American Society of Transplantation has advocated the institution of a national policy for splitting appropriate donor livers into left lateral and extended right grafts for transplantation into a pediatric and an adult recipient, respectively [77]. Many suitable livers are reduced in size for pediatric transplantation, and are not split with an adult recipient. According to the analysis of the working group, approximately 20 percent of donors could be split, increasing the total number of liver transplant recipients in the United States by up to 1000 annually. Outcomes of in situ liver splitting for adult/child pairs have been comparable to whole graft transplantation.

In a study of 106 split liver transplantations, adult 1-, 5-, and 10-year survival rates were 93, 77, and 73 percent, respectively, with graft survival rates of 89, 76, and 65 percent, respectively [78]. For children, 1-, 5-, and 10-year survival rates were 84, 75, and 69 percent, respectively, with graft survival rates of 77, 63, and 57 percent, respectively.

Splitting the organ between two adults was examined in a retrospective study of 42 patients who received split liver transplantations [79]. One lobe of the liver went to the patient on the waiting list with the same blood type and the highest Model for End-stage Liver Disease score, provided the graft-recipient weight ratio (GRWR) for one of the lobes was at least 0.8 percent. The second lobe went to a recipient with the same blood type in whom the GRWR was 0.8 percent or more. The three-month, one-year, three-year, and five-year survival rates were 76,

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risk or mortality on the liver transplant waiting list without impacting patient or graft survival. In an 18-year study of over 2000 liver transplant recipients from a single transplant program, there was no significant difference in rates of one- three- and five-year patient survival for patients receiving marginal liver grafts compared with those receiving standard grafts during the second nine year period [80]. Marginal liver grafts included those with any of the following characteristics:

- Liver donor age >70 years (see '[Older age](#)' above)
- Livers discarded regionally and shared nationally
- Livers from hepatitis C positive donors (see '[Hepatitis C-positive donors](#)' above)
- Livers with cold ischemia time >12 hours (see '[Cold ischemia time](#)' above)
- Livers from donation after cardiac death donors (see '[Donation after cardiac death](#)' above)
- Livers with >30 percent steatosis (see '[Hepatic steatosis](#)' above)
- Livers split between two recipients (see '[Split-liver transplantation](#)' above)

The mortality rate for patients who were waitlisted at the transplant program using marginal liver grafts was lower compared with the national waitlist mortality rate (19 versus 24 percent).

SUMMARY AND RECOMMENDATIONS

- The United Network for Organ Sharing provides minimum guidelines for organ procurement. The initial evaluation is typically performed by the local organ procurement organization (OPO). The OPO representative verifies that the prospective donor meets the criteria for brain death. Consent for donation is obtained from the potential donor's next of kin. (See '[Donation after brain death](#)' above.)
- Donor characteristics that are associated with an adverse effect on graft function and/or graft survival include "donation after cardiac death", advanced donor age, moderate to marked hepatic steatosis, and donor hypernatremia. (See '[Donor factors impacting recipient outcome](#)' above.)
- The number and severity of donor risk factors is considered in evaluating prospective donors and risk assessment indices have been developed. (See '[Risk assessment indices](#)' above.)
- A shortage of donor livers has led to alternative approaches such as the use of donation after cardiac death donors and transplantation of hepatitis C virus (HCV)-positive livers into HCV-positive recipients to increase the donor organ supply. (See '[Approaches to expand donor liver supply](#)' above.)
- Judicious use of marginal or extended criteria liver grafts may lower the risk of mortality on the liver transplant waiting list without impacting patient survival or graft function or survival. (See '[Marginal liver graft outcomes](#)' above.)

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