

## **Liver Transplantation**

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### **What is a Liver Transplant?**

A liver transplant involves removing the patient's own diseased ("native") liver at surgery and replacing it with a liver from another person. This is commonly referred to in the medical literature as Orthotopic Liver Transplant (OLT). Generally, the patient ("recipient") receives a whole liver but on occasion may receive only a portion of the donor liver.

### **Who needs a Liver Transplant?**

Liver transplantation is indicated in children and adults, whose livers are failing due to liver disease, have primary liver tumors, or systemic diseases where liver replacement will be potentially curative. The causes of liver failure vary by the patient's age group. In children, a common reason for liver transplantation is biliary atresia, a disease in which the bile ducts, which are the plumbing system of the liver, do not develop properly. Although reconstructive surgery done in the first few months of life can prevent worsening liver disease, some affected children still experience deep jaundice and other evidence of liver failure. In adults, the most frequent causes of liver disease leading to the need for liver transplantation include hepatitis C virus (HCV), and a number of other conditions including hepatitis B virus, Non Alcoholic Fatty Liver Disease, Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis. Hepatoblastoma (in children) and hepatocellular carcinoma (in adults) are two important tumors where liver transplantation may be indicated if surgical removal of the affected part of the liver is not feasible. A careful workup is done to make sure the tumor has not spread outside the liver before proceeding with liver transplant. Well selected patients with hepatocellular carcinoma can do extremely well with this approach, occasionally in combination with other treatments such as chemotherapy delivered directly into the liver to shrink the tumor while the patient awaits liver transplantation. An uncommon but important indication for liver transplantation is acute ("fulminant") liver failure in which a person with no previous history of liver disease rapidly goes into liver failure. Important causes of this condition include drug overdose (either accidental or suicidal), from medications such as acetaminophen, or acute viral hepatitis A or B. Sometimes the actual cause is not known. These patients require prompt referral to a liver transplantation center before they develop severe brain swelling resulting in deep coma and death.



## **Does Every Patient with Cirrhosis Need a Liver Transplant?**

Fortunately, many patients with cirrhosis remain stable (“compensated”) for years. Symptoms such as fluid retention in the abdomen (“ascites”), confusion (“hepatic encephalopathy”) or more dramatic problems such as bleeding from large veins (“varices”) in the esophagus or stomach are major events that indicate the liver condition is deteriorating and that referral for liver transplant evaluation is required. Another important indication for liver transplantation is the discovery of a tumor in the liver of a patient with cirrhosis. In adults, most patients with hepatocellular carcinoma have cirrhosis and thus an important part of the management of patients with cirrhosis is screening for tumors at an early stage as they may do well with resection of the tumor surgically, ablation by injecting the tumor with alcohol, radiofrequency ablation or possibly liver transplantation. Careful and regular followup with a physician experienced in the management of liver disease is key to look for these complications and monitor the patient’s liver function on a regular basis. It is prudent for a patient with cirrhosis even if it is well compensated to be seen at least twice a year for a checkup including screening for hepatocellular carcinoma. The type of specialist a stable cirrhotic patient sees is usually a gastroenterologist although at referral centers care of patients with liver disease is often under the direction of a hepatologist who is a physician who focuses on liver disease. Generally patients felt to require liver transplantation are referred by their treating physician to a transplant center. However it also possible for an individual patient to seek care at a transplant center by using an online resource such as the United Network for Organ Sharing which lists transplant programs by State and also provides information on patient outcomes for each center. To determine which center, if there is more than one local option, is the best fit for an individual patient it may be possible to gain additional insights through other resources such as local patient support groups. After referral a patient and family need to enquire about how long the evaluation process takes, how to communicate with the center and when to call the center among others. Generally patients are assigned to a particular nurse coordinator who is their immediate contact with the transplant center.

## **How do Patients get Placed on a Waiting List for Liver Transplant?**

When a patient is seen at a liver transplant center, they undergo a rigorous evaluation to assess not only how severe their liver disease is, but also whether they have any other medical conditions which might impact their ability to undergo this major surgery. Thus, patients see a medical liver specialist (“hepatologist”) and a transplant surgeon as well as other specialists such as a cardiologist and infectious disease expert. In addition, a social worker and psychiatrist meet with the patient and their family to ensure that appropriate support and motivation to proceed with liver transplant is present. If the patient has a prior history of drug or alcohol problems, a plan needs to be in place prior to transplant to avoid relapse afterwards. Typically, the transplant center asks the patient in whom alcohol or drugs have been an issue to provide documentation of involvement in a relapse



prevention program as a condition for acceptance for transplant with the specifics varying by patient and center. Additional workup usually involves x-rays of the liver and adjacent organs, some form of cardiac stress test, a number of blood tests including blood group, hepatitis markers and an HIV test, and additional medical consultations. Once all these tests and consultations have been completed, the patient's eligibility for liver transplant is discussed by specialists, nurse coordinators, and other healthcare providers including social workers who have been involved in the patient's evaluation by the program. A decision is then made whether the patient requires liver transplant, whether additional tests are necessary first or if the patient has a contraindication to transplant such as bad heart disease. Following this discussion, the patient is then placed on the waiting list ("listed") for transplant if that is the group decision and becomes eligible to receive a donor organ when appropriate.

### **What are Contraindications to Liver Transplant?**

Liver transplantation may not be possible in some patients because of other severe medical problems such as bad heart or lung disease which would make the surgery very risky and the chance of a good long-term outcome unlikely. Extensive liver cancer would also reduce the chance for a good long-term outcome and thus transplant is not performed in this situation. Some primary liver tumors such as cholangiocarcinoma which grows from the bile ducts do poorly with liver transplant based on a high rate of tumor recurrence after an otherwise successful operation. However, good results have been achieved within protocols conducted at selected centers which combine radiation therapy with transplant for cholangiocarcinoma in highly selected patients. Similarly infection with HIV, the virus that causes AIDS was regarded as a complete contraindication to any form of transplantation prior to the introduction of Highly Effective Antiretroviral Therapy in the mid-1990's. Now, carefully selected HIV infected patients without AIDS are accepted by some programs for liver transplantation. Finally, a number of patients with severe obesity may not be candidates for liver transplantation based on the difficulty in performing the surgery and the potential for reduced long-term success rates. With continued advances in medicine, at least some contraindications to liver transplant may no longer exclude individual patients.

### **Where do Donor Organs Come From?**

Most organs for liver transplant come from deceased donors. Deceased donors are individuals who have suffered brain death following a massive brain injury such as severe head trauma or major stroke, which means that even though many of their bodily functions continue, they have no prospect of returning to consciousness. A careful examination by an experienced brain specialist with appropriate x-rays and other investigations such as testing for brain waves is needed to confirm the diagnosis of brain death. The organs to be used for transplantation into the recipient or recipients are



removed (“procured”) by a team of surgeons and then shipped on ice in a special preservative solution to the center where the recipient is waiting. Several different recipients may receive organs from the same donor (i.e. kidneys, heart, lungs and liver).

Less commonly, it may be possible to use the same donor liver for two different recipients by dividing (“splitting”) it into two unequal parts. The larger portion is used for an adult recipient while the smaller one is used for a child or a small sized adult. More commonly, another approach is for a healthy adult to donate a portion of his/her liver for either another adult or a child. The amount of donor liver necessary for the surgery depends on the size of the potential recipient with a fully grown adult requiring the largest amount (usually most of the right liver lobe). The donor operation is very complex in live donor transplant as not only must the portion of the liver removed have intact blood vessels and bile ducts, but the part left behind must function well enough so that the donor will not develop liver failure. Generally, living donors are relatives or have some other significant relationship with the potential recipient, have the same blood type, are in excellent general health, and have liver anatomy that will allow safe removal of part of their liver.

### **How are Deceased Donor Organs Allocated?**

Once a patient has been accepted for liver transplant, he/she is added to the waiting list at his/her transplant center which, in turn, submits key information to the national system known as the United Network for Organ Sharing (UNOS). UNOS helps to organize the collection and distribution of deceased donor organs in collaboration with local Organ Procurement Organizations (“OPOs”). Patients are listed by height, body weight and blood group with UNOS and organs are then allocated by the severity of their liver disease. Historically, a number of systems have been used by UNOS in an effort to ensure allocation of organs is fair. The current system is based on the Model for End Stage Liver Disease (MELD). MELD is based on a few simple, blood tests including creatinine, bilirubin and INR. A formula is available that allows calculation of a number (MELD Score) to determine the patient’s place on the waiting list. Additional points are awarded for certain conditions such as primary hepatocellular carcinoma to ensure that transplant occurs in a timely fashion. As the patient’s liver tests worsen, the MELD score usually increases. A similar formula exists for pediatric patients (“PELD”) which also factors in growth retardation which is an important complication of severe liver disease in children. For both adults and children, the system is designed to direct organs to the sickest patients awaiting liver transplantation and reduce deaths on the waiting list. Unfortunately, with the continuing shortage of deceased donor organs, a number of patients will continue to be at risk for dying of complications related to liver disease while awaiting liver transplant.



## **What does the Surgery Involve?**

Liver transplant surgery is very complicated in large part because the diseased native liver can be very difficult to remove from the recipient. Once this is accomplished, however, the donor liver is placed in the recipient's abdomen. The major blood vessels are reconnected in the new liver as well as the bile ducts. Anti-rejection medications are started in the operating room and the patient is then transferred to ICU for careful monitoring. Typically, patients are transferred out to a regular floor within a few days. During this time, the correct dose of anti-rejection medications is established. The two major anti-rejection medications used are either cyclosporine or tacrolimus. Additional anti-rejection medication may be given if rejection occurs or if toxicity is suspected with the major drugs. Patients are usually discharged from hospital within two to three weeks of the transplant.

## **What does the Long-Term Follow-up after Liver Transplant Involve?**

Patients are seen frequently in the first weeks and months following transplant. Key aspects of care include confirmation of wound healing, removal of sutures, and regular blood tests including liver function tests (LFTs) and creatinine to monitor kidney function which can be affected by the anti-rejection medications. If the LFTs become abnormal, further investigation with a liver biopsy (to rule out rejection) and/or endoscopic cholangiography (to rule out bile duct obstruction) may be necessary. Rejection occurs most commonly in the first weeks and months after transplant but generally responds well to increased doses of corticosteroids. With time, the amount of anti-rejection medication can be slowly reduced to avoid side-effects such as high blood pressure and diabetes mellitus. After the first three to six months, another concern can be recurrence of the original liver disease in the new liver most frequently HCV. Thus, successful care of the liver transplant recipient requires attention to a number of medical issues. Despite all these concerns, liver transplant recipients can anticipate an improved quality of life and life expectancy compared to not undergoing the procedure at all.

