

Introduction

The first human liver transplant was performed in 1963 by a surgical team led by Dr. Thomas Starzl of Denver, Colorado, United States. Dr. Starzl performed several additional transplants over the next few years before the first short-term success was achieved in 1967 with the first one-year survival posttransplantation. Despite the development of viable surgical techniques, liver transplantation remained experimental through the 1970s, with one year patient survival in the vicinity of 25% (*Umeshita K et al., 2003*).

The introduction of cyclosporine by Sir Roy Calne markedly improved patient outcomes, and the 1980s saw recognition of liver transplantation as a standard clinical treatment for both adult and pediatric patients with appropriate indications. Liver transplantation is now performed at over one hundred centres in the USA, as well as numerous centres in Europe and elsewhere. One year patient survival is 85-90%, and outcomes continue to improve, although liver transplantation remains a formidable procedure with frequent complications. Unfortunately, the supply of liver allografts from non-living donors is far short of the number of potential recipients, a reality that has spurred the development of living donor liver transplantation ((*Tuttle-Newhall JE et al., 2005*).

Liver transplantation is potentially applicable to any acute or chronic condition resulting in irreversible liver dysfunction, provided that the recipient does not have other conditions that will preclude a successful transplant. Metastatic cancer outside liver, active drug or alcohol abuse and active septic infections are absolute contraindications. While infection with HIV was once considered an absolute contraindication, this has been changing recently. Advanced age and serious heart, pulmonary or other disease may also prevent transplantation. Most liver transplants

are performed for chronic liver diseases that lead to irreversible scarring of the liver, or cirrhosis (*Adam R et al., 2005*).

Before transplantation liver support therapy might be indicated (bridging-to-transplantation). Artificial liver support like liver dialysis or bioartificial liver support concepts are currently under preclinical and clinical evaluation. Virtually all liver transplants are done in an orthotopic fashion that is the native liver is removed and the new liver is placed in the same anatomic location. The transplant operation can be conceptualized as consisting of the hepatectomy (liver removal) phase, the anhepatic (no liver) phase, and the postimplantation phase. The operation is done through a large incision in the upper abdomen. The hepatectomy involves division of all ligamentous attachments to the liver, as well as the common bile duct, hepatic artery, and portal vein. Usually, the retrohepatic portion of the inferior vena cava is removed along with the liver, although an alternative technique preserves the recipient's vena cava ("piggyback") technique (*Reddy S et al., 2004*).

The donor's blood in the liver will be replaced by an ice-cold organ storage solution, such as UW (University of Wisconsin) or HTK (Histidine-Tryptophan Ketoglutarate) until the allograft liver is implanted. Implantation involves anastomoses (connections) of the inferior vena cava, portal vein, and hepatic artery. After blood flow is restored to the new liver, the biliary (bile duct) anastomosis is constructed, either to the recipient's own bile duct or to the small intestine. The surgery usually takes between five and six hours, but may be longer or shorter due to the difficulty of the operation and the experience of the surgeon (*Tuttle-Newhall JE et al., 2005*).

The large majority of liver transplants use the entire liver from a non-living donor for the transplant, particularly for adult recipients. A major advance in paediatric liver transplantation was the development of reduced size liver transplantation, in which a portion of an adult liver is used for an infant or small

child. Further developments in this area included split liver transplantation, in which one liver is used for transplants for two recipients, and living donor liver transplantation, in which a portion of healthy person's liver is removed and used as the allograft. Living donor liver transplantation for pediatric recipients involves removal of approximately 20% of the liver (Couinaud segments 2 and 3) (**Martinez OM and Rosen HR. 2005**).

Living donor liver transplantation (LDLT) has emerged in recent decades as a critical surgical option for patients with end stage liver disease, such as cirrhosis and/or hepatocellular carcinoma often attributable to one or more of the following: long-term alcohol abuse, long-term untreated Hepatitis C infection, long-term untreated Hepatitis B infection. The concept of LDLT is based on (1) the remarkable regenerative capacities of the human liver and (2) the widespread shortage of cadaveric livers for patients awaiting transplant. In LDLT, a piece of healthy liver is surgically removed from a living person and transplanted into a recipient, immediately after the recipient's diseased liver has been entirely removed (**Vohra V. 2006**).

Historically, LDLT began as a means for parents of children with severe liver disease to donate a portion of their healthy liver to replace their child's entire damaged liver. The first report of successful LDLT was by Dr. Silvano Raia at the Universidade de São Paulo Medical School in 1986. Surgeons eventually realized that adult-to-adult LDLT was also possible, and now the practice is common in a few reputable medical institutes. It is considered more technically demanding than even standard, cadaveric donor liver transplantation, and also poses the ethical problems underlying the indication of a major surgical operation (hepatectomy) on a healthy human being (**Strong RW. 2006**).

Like all other allografts, a liver transplant will be rejected by the recipient unless immunosuppressive drugs are used. The immunosuppressive regimens for all solid organ transplants are fairly similar, and a variety of agents are now available. Most liver transplant recipients receive corticosteroids plus either tacrolimus or Cyclosporin or Mycophenolate Mofetil (*Krahn LE and DiMartinli A. 2005*).

Liver transplantation is unique in that the risk of chronic rejection also decreases over time; although recipients need to take immunosuppressive medication for the rest of their lives. It is theorized that the liver may play a yet-unknown role in the maturation of certain cells pertaining to the immune system. There is at least one study by Dr. Starzl's team at the University of Pittsburgh which consisted of bone marrow biopsies taken from such patients which demonstrate genotypic chimerism in the bone marrow of liver transplant recipients (*Nadalin S and Malago M. 2007*).

Prognosis is quite good. 1-year survival (in Finland) is 83%, 5-year survival is 76% and 10-year survival is 66%. Majority of deaths happen during the first three months after transplantation (*Fan ST. 2006*).