

Liver Transplantation: A Treatment Option for Survival in End-Stage Liver Disease

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Abstract

The liver is the largest internal organ in the body. A healthy liver is necessary for survival that can regenerate most of its own cells when these are damaged. It is an essential organ in digestion, and also undertakes several metabolic processes, such as bile production; bilirubin synthesis; and protein, lipid, fats, and carbohydrate metabolism. Liver transplantation (LT) is a surgery of liver that removes a whole liver or just part of a liver which no longer functions properly with therapies and medications, and replaces it with a healthy liver from a deceased donor or a portion of a healthy liver from a living donor. It is a well-recognized life-saving treatment option for people when liver cannot regenerate and the damage becomes about life-threatening due to liver cirrhosis, decompensated disease, liver cancer, acute liver failure, and hepatocellular carcinoma (HCC). The liver transplanted person needs a long-time follow up treatment with medications to prevent the body from rejecting of the new liver.

Keywords: liver transplantation, liver cirrhosis, donor, immunosuppression, rejection, MELD

1. Introduction

The liver is the largest internal organ of the body that is located within the peritoneal cavity, and is in the right upper quadrant of the abdomen. At present liver resection is practicing worldwide widely to minimize morbidity and reduce mortality (Sumadewi, 2023). Liver transplantation (LT) is a life-saving treatment option of a diseased liver through the replacement with a healthy liver from a deceased donor or a portion of a healthy liver from a living donor (Lucas, 2021). It is a treatment option for people who have significant complications due to end-stage chronic liver disease. It is a life-saving intervention for an increasing number of patients with end-stage liver disease when the liver no longer works as it should (Varma et al., 2011).

The LT can be orthotopic (same place) or heterotopic (other place), and can be performed in patients of all ages. At present orthotopic liver transplantation (OLT) is considered the gold standard treatment for end-stage liver disease, acute liver failure, and liver-based metabolic disorders. The first experimental attempt of hepatocyte liver transplantation (HLT) was developed in 1976 to treat the hyperbilirubinemic Gunn rat (Iansante et al., 2017). A healthy adult living-donor can donate a portion of his/her liver to someone with end-stage liver disease. Following the LT, the liver of the donor will regenerate within a few months (Freeman et al., 2005).

The surgical procedure of LT is very complex process. For a successful LT it is required a careful harvest of the donor organ and meticulous implantation into the recipient. The total procedures of LT must be done by highly trained transplant physicians and supporting medical team (Reddy et al., 2013). The LT offers live-saving therapy for patients with end-stage liver disease that is often caused by liver cirrhosis, such as liver cancer, liver failure; whose condition cannot be controlled with other treatments. It is the second most common solid organ transplantation after kidney transplantation worldwide (Mahillo et al., 2013).

The LT centers match donors with recipients based on compatible liver size and blood type. In 2011, more than 5,800 adult LTs were performed in the USA. It is estimated that in 2018 more than 32,000 LTs were conducted globally, and among them 8,200 were in the USA (Statistics Portal, 2018). More than 10,000 LTs are performed each year in Europe, and about 119,803 LTs took place across Europe between 1988 and 2015 (Blachier et al., 2013). In 2021, there were about 34,694 LTs performed globally that is an increase of 6.5% from 2020 and a 20% increase from 2015 (Terrault et al., 2023). In the USA, about 41,734 LTs were performed between 1992 and 2001 (Marcellin & Kutala, 2018). From 1988 to 2022, more than 200,000 LTs were performed in the USA, and only in 2022 there were 9,528, of which 526 were performed in patients under the age of 18 years (Lucey et al., 2023).

There are enormous improvements in surgical techniques, patient management, effective therapy, and immunosuppressive drugs in the last 60 years of LT (Maciel et al., 2021). After LT more than nine out of ten people are still alive after one year, around eight in every ten people live at least five years, with many people living for up to 20 years or more. However, donor organ shortage and lifelong need for immunosuppression are the main restrictions to LT (Adam et al., 2018).

2. Literature Review

The literature review section is an introductory unit of research, which exhibits the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). Roberto Ferreira Meirelles Júnior and his coauthors have found that a major challenge in LT field is the insufficient number of donors compared with the growing demand of transplant candidates. They have emphasized that appropriated donor and receptor selection, allocation and organ preservation topics should contribute to improve the number and outcomes in LT (Meirelles et al., 2015). Astrid Marot and his coauthors have found that 14% of carefully selected patients with clinically severe alcoholic hepatitis (AH) not responding to medical therapy have alcohol relapse after LT (Marot et al., 2018).

Emrah Otan and his coworkers have aimed to evaluate the outcomes of living donor liver transplantation (LDLT) patients in whom neurological complications developed early during postoperative follow-up in the intensive care unit (ICU). They have observed that over the last two decades, postoperative management and new immunosuppressive regimens have been developed. The survival of orthotopic liver transplantation (OLT) recipients has improved (Otan et al., 2015). Altan Alim and his coauthors have wanted to identify the indications, survival, and complications of LT in congenital metabolic diseases. They have also described demographic information of patients, liver graft types, and donor information (Alim et al., 2022).

Nadim Mahmud has reviewed the general indications and contraindication to LT, and has provided an overview of the transplant evaluation process. He believes that LT may be life-saving for patients with acute liver failure or end-stage liver disease. It is therefore critical for healthcare providers caring for patients with liver disease to be familiar with the general indications for transplantation and to know when it is appropriate or inappropriate to refer for transplant evaluation (Mahmud, 2020). Norah A. Terrault and her coworkers have shown that LT offers live-saving therapy for patients with complications of cirrhosis and stage T2 hepatocellular carcinoma. They have also presented a status report on the most pressing topics in LT and future challenges (Terrault et al., 2023).

Nicole Bianchin Maciel and her coworkers have shown that immunosuppressive drugs have important role in transplant of solid grafts to avoid episodes of acute and chronic rejection and to improve graft survival and patient survival (Maciel et al., 2021). Rosana Guerrero-Domínguez and her coauthors have found that renal failure is one of the most common and major complications among 17-95% LT recipients that is associated with prolonged hospital stay in the intensive care unit, the need for postoperative dialysis, infectious complications, acute rejection, and increased mortality (Guerrero-Domínguez et al., 2014).

3. Research Methodology of the Study

To rationalize the selection of a research methodology, a researcher must understand its philosophical origins and unique characteristics (Rieger, 2019). Methodology is a guideline for the accomplishment of a good research (Kothari, 2008). Therefore, research methodology is the specific procedures that are used to identify, select, process, and analyze materials related to the topics (Somekh & Lewin, 2005). To prepare this paper, I have used the secondary data sources that are related to liver transplantation (Mohajan, 2017, 2018, 2020). I have consulted the published journal articles, books and handbooks of famous authors, websites, etc. to complete the paper (Mohajan, 2024a-q).

4. Objective of the Study

Main objective of this article is to discuss the pre- and post- complications of liver transplantation. At present acute and chronic liver diseases are increasing due to virus infection, pharmacological drug consumption, poor diet and lifestyle, alcoholism, cancer metastasis, and some other factors (LeCluyse et al., 2012). Liver transplantation (LT) is the only therapeutic option for patients with life-limiting liver disease in the form of acute

liver failure and end-stage chronic liver disease (Mahmud, 2020). Other minor objectives of the study are as follows:

- to show the overview and basic physiology of liver,
- to focus on historical background of LT, and
- to show the liver transplantation complications and success.

5. Overview of Liver

The liver is the largest and the most complex internal organ of the body. It is located within the peritoneal cavity, and is in the right upper quadrant of the abdomen. It is a wedge or cone shaped with the base on the right and the apex to the left (Ramachandran & Kumar, 2019). It is dark pinkish-brown peritoneal organ, in an average adult human weighs 1.5 to 2kg, which is roughly 2-3% of the total body weight. An average liver volume in healthy adult people is 1,225cm³ (± 217) (Juza & Pauli, 2014). The liver consists of two lobes: i) the right lobe (larger), ii) the left lobe (smaller) that are divided by the plane of middle hepatic vein (Bismuth, 1982).

6. Basic Physiology of Liver

The liver is the largest internal organ in the body that accomplishes many complex functions. It is the powerhouse of the body for metabolism and a center for numerous physiological processes (Mohajan, 2024a,b). It performs a group of essential functions of the body, such as vascular, immunological, metabolic, and secretory and excretory functions (Alamri, 2018). The functions of liver in brief are blood detoxification and purification; synthesis of plasma proteins; storage of glycogen, vitamins (e.g., A, D, E, C), minerals (e.g., iron and copper); production and excretion of bile and urea; detoxification of drugs and toxins; the metabolism of carbohydrates, fats and proteins; filtration of bacteria, degradation of endotoxins and lactate metabolism, etc. (Jastrow, 1908). The liver is the only organ that has the extraordinary property of self-regeneration (Ozougwu, 2014).

The liver has a dual blood supply: the portal vein provides 75% and the hepatic artery provides 25% of the blood supply. Each vessel provides 50% of oxygen delivery. After LT sufficient blood flow through the hepatic artery is essential for the viability of a new liver graft. In every minute about 1500ml of blood flows through the liver that is about 25% of the cardiac output, which is more than any other organ (Abbasoglu et al., 1998).

7. Historical Background of LT

In 1955, Stuart Welch performed a heterotopic LT in the canine species. In 1956, Jack Cannon is credited with the first animal orthotopic LT although the species was not disclosed. The first attempts at LT were performed on dogs in 1954 by Italian professor of surgery Vittorio Staudacher (1913-2005) (Busuttil et al., 2012). The first attempted human LT was performed in 1st March 1963 in the world by American physician, researcher, and expert on organ transplants Thomas Earl Starzl (1926-2017) who has often been referred to as “the father of modern transplantation.” The patient was a three years old boy with biliary atresia who underwent LT, but he died due to coagulation disorder and uncontrolled bleeding (Starzl et al., 1963). In 1967, he transplanted liver of a 19 months old girl with hepatoblastoma who was able to survive for over one year before dying of metastatic disease. In the first five LTs no patient survived more than 23 days (Zarrinpar & Busuttil, 2013). In 1979, survival after liver transplantation improved significantly to a 1-year survival rate of over 70% due to the development of cyclosporine (Starzl et al., 1989). Since the first successful human LT reported by Thomas Starzl in 1963, the LT has evolved rapidly and more than 100,000 procedures performed to date, and survival rates have improved significantly up to 71% at 10 years after LT (Adam et al., 2012).

8. Total LT Activities

The major indications for LT are irreversible hepatic failure irrespective of the etiology of the liver disease. Not all the patients who face irreversible liver failure ultimately will undergo for a LT. It is necessary to the explanation of the indicators of liver failure, the timing of transplant evaluation, pre- and post- transplant management, and the potential benefit of LT (O’Leary et al., 2008).

8.1 Sign and Causes of LT

If the patients have evidence of fulminant hepatic failure, life-threatening systemic complications, cirrhosis with complications, such as hepatic encephalopathy, ascites, hepatocellular carcinoma, cryptogenic cirrhosis, hepatorenal syndrome, and bleeding caused by portal hypertension, are considered for LT (O’Leary et al., 2008). The symptoms of liver failure are jaundice, a condition that causes yellowing of the skin and the whites of the eyes, fatigue, weakness, loss of appetite, nausea, weight loss, muscle loss, itching, bruising, or bleeding easily because blood does not clot, bleeding in the stomach, vomiting blood, passing black stools ascites, the buildup of fluid in the abdomen, forgetfulness, confusion (Khan et al., 2006).

People with either acute or chronic liver failure may need a LT for survival. The most common reasons for LT are chronic viral hepatitis by any virus (mainly hepatitis B virus (HBV) and hepatitis C virus (HCV)),

autoimmune hepatitis, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), secondary biliary cirrhosis (SBC), alcoholic liver disease, non-alcoholic fatty liver disease, hepatocellular carcinoma (HCC), liver cancer, and liver failure. One of the most common reasons is cirrhosis caused by long-term alcohol abuse. In children, biliary atresia is the most common cause for LT (Starzl et al., 1989).

8.2 Liver Donor

The LT is a life-saving surgery of the patients with acute and chronic liver diseases, where the donors play important roles. The donor will be a family member or non-family member with blood matching who can provide support before, during, and after surgery (Hashikura et al., 1994). The voluntary and benevolent donor must be 18-60 years. S/he must be in excellent physical and emotional health, cannot have any history of cancer with normal liver function (Otan et al., 2015). First successful living donor liver transplant (LDLT) was performed on a child in 1990 in Australia, and the LDLT was his mother (Strong et al., 1990). Most of the time, a liver is donated from someone who has died that is now known as a deceased donor. When an organ donor dies, the liver is removed by a surgeon and replace to the transplant recipient as quickly as possible. Livers for transplant must be matched for body size and blood type (Amara et al., 2022). The children need a small portion of the left lobe of liver of the adult donor. On the other hand, adult to adult living donor transplantation is achieved by using the entire right lobe of liver of the donor (Broelsch et al., 1991).

The liver donation operation is a major surgery that requires a 5-10-day hospitalization and 2-3-month period of recovery (Llovet et al., 2018). The donor surgery has a very low risk of death, the liver of donor regenerates to its original size within a few months. Both livers of donor and receiver will grow back to normal size within a few weeks after surgery (Kim & Testa, 2016). Not all candidates are suited for liver donation. The blood vessels to the liver and bile ducts in the liver of the donor must be suitable for transplantation. The LT centers match donors with recipients based on compatible liver size and blood type. Usually, older patients with cardiac or respiratory complications are not allowed for liver donation (Wiesner et al., 2003). The demand for organs is increasing day by day, in parallel the usable deceased and live donors are also expanding gradually (Terrault et al., 2023). In 2020, more than 90% of LT deceased donors, and only 4.3% of living donors were in the Western world. But, in many Asian countries most transplants are from living donors LT (Kwong et al., 2022).

8.3 LT Assessment

A LT is a complex process that requires hundreds of steps before, during and after LT. The LT evaluation are reviewed in details by a patient selection committee consists of transplant surgeons, hepatologists, house-staffs (junior physicians), anesthesiologists, psychologists, transplant coordinators, advanced practice nurses, social workers, dietitians, pharmacists, research coordinators, pastoral counselors, and a finance office representative (O'Leary et al., 2008). Some people wait a long-time for their LT, while others need an urgent LT. The LT donors are scarce worldwide; liver allocation prioritizes patients, who likely will die soonest without transplantation (Goudsmit et al., 2023). The patient needs many tests before the surgery to decrease the potential risks of heart attack, stroke, and death (Schlegel et al., 2023). Many people have positive emotions, such as hope, joy, and gratitude, and some have difficult emotions, such as fear, sadness, anxiety, irritability, anger, and grief, fear of dying during the transplant journey (Levenson & Olbrisch, 1993).

A LT is considered when a person might die from liver disease within the next 1-3 years. The three scoring systems are used for urgent LT: i) the Model for End-stage Liver Disease (MELD) scoring system when the patient's age is 12 and older, ii) The Child-Turcotte-Pugh (CTP) classification has been used to assess surgical risk in LT (Pugh et al., 1973), and iii) the Pediatric End-stage Liver Disease (PELD) scoring system when the patient's age is less than 12. These scores have been validated to predict the survival time in most patients with chronic liver disease (Wiesner et al., 2003). The MELD/PELD scores are numerical scales based on the patient's risk of dying while waiting for LT. Both of them are dependent on bilirubin, international normalized ratio (INR) albumin, creatinine, growth failure, and age listed (Freeman et al., 2005). The MELD-Na orders transplant candidates from less ill (MELD 6) to extremely ill (MELD 40). Usually, the LT may be approved the patients with decompensated cirrhosis or MELD \geq 15 (Martin et al., 2014).

The LT is a major surgery that lasts 6-8 hours, and has major risks. After surgery, a patient is taken to the intensive care unit (ICU) where s/he is placed on a mechanical ventilator that supports breathing for average two days, and then transfer to the medical floor (Lukey et al., 2023). Frequent tests are conducted to assess the functioning of the new liver. After 10 to 14 days the patient can leave the hospital, and needs follow up treatment as outpatient for continued monitoring of the new liver. Nutrition recommendations will be different for each individual according to the dietitian (Adam et al., 2018).

Some complications from liver surgery are infection, bleeding, clotting of the artery to the liver, blocked blood vessels to the new liver, leakage of bile or blocked in bile ducts, inactiveness in immune system, poor function of the new liver, inactivity of new liver for a short-time right after surgery, and post-transplant lymphoproliferative

disease (PTLD) (Hernandez et al., 1998). Renal dysfunction is common after LT.

8.4 Post LT Situation

Most of the LT persons are able to return to a normal and healthy lifestyle, and can enjoy an improved quality of life. They are able to start normal exercise after their recuperation, and women are able to conceive and have normal post-transplant pregnancies and deliveries. Proper nutrition maintenance is necessary after LT to control the changes in the body (Lewis & Howdle, 2003). If autoantibodies develop after LT then various complications arise, such as chronic hepatitis, severe graft dysfunction, chronic rejection, loss of graft, and death (Dubel et al., 1998). The LT patients need multiple visits to the hospital for evaluation rest of life. Some LT patients may experience feelings of stress, anxiety, guilt, confusion, irritability, trouble in sleeping, and depression. Sometimes there is an increased risk for developing certain types of cancers, such as post-transplant lymphoma (Rothenhäusler et al., 2002).

After LT the patient must take antirejection or immunosuppressive medicines that weaken the immune system response for the rest of life (Thuluvath et al., 2007). Calcineurin-inhibiting immunosuppressive medications are the mainstay of post-transplant immunosuppression. Medicines prednisone, tacrolimus, azathioprine, mycophenolate mofetil, cyclosporine, and sirolimus are used to prevent organ rejection after LT that help to prevent rejection of the new liver. The side-effects of immunosuppressive medications can be very hard on the body (DiMartini et al., 2008). These medications can increase blood pressure, cholesterol, blood sugar, kidney problems, and weight gain that have a chance of developing heart disease, stroke, and diabetes. Heart disease is the leading cause of death with post-transplant patients after the first three months (Berlakovich et al., 2000). Some of the more annoying side-effects after LT are hair loss, insomnia, diarrhea, nausea, headaches, swelling, and neuropathy (Paugam et al., 2009). Recurrence of fatty liver disease and obesity after LT is a problem because it leads to metabolic syndrome with higher risk for stroke and heart attacks (Rothenhäusler et al., 2002).

The LT has several disadvantages, such as the risks of complications related to surgery, the high cost of the procedure, and the need for lifelong immunosuppression (Iansante et al., 2017). The immune-mediated rejection is determined through the lab findings, such as elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), etc. Sometimes abnormal liver function values, such as prothrombin time, ammonia level, bilirubin level, albumin concentration, and abnormal blood glucose can increase (Jain et al., 2000). Immune system helps the people to fight against infections that are done by recognizing from non-self. Anything it sees as non-self is attacked by the immune system and destroyed. The new liver naturally is recognized as non-self and is attacked by the immune system, and this process is called rejection (Lucey et al., 2023). Some patients are not allowed for LT, those who have severe cardiopulmonary disease, uncontrolled sepsis, active extrahepatic malignancy, acquired immune deficiency syndrome (AIDS), and who are in brain death (Osorio et al., 1994).

9. Conclusions

In this study, I have found that liver is an essential organ of human to sustain life. It is the only organ in the body that can regenerate itself. It plays an important role in metabolism through the preservation and regulation of the levels of lipid and glucose in the body as well as energy metabolism. No artificial device is available to support or replace a damage live. Therefore, LT is an effective and established life-saving procedure for the patients with end-stage liver disease. Recently, despite a significant progress has been made in the area of LT, organ scarcity remains a significant constraint, and also the recipients continue to face long-term immunosuppression complications. I have observed that LT is a comparatively safe and successful life-saving treatment option that can be applied in patients with acute and chronic liver disease.

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