



Liver Transplant: A New Opportunity

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Abstract: Introduction: The human liver is a large brown/reddish abdominal organ weighing approximately 1800 g in men and 1400 g in women, it performs more than 500 vital functions. Liver regeneration is an extraordinary biological phenomenon of adaptation and response. Objective: To carry out art history based on national and international medical literature on liver transplantation in humans. Discussion: liver transplantation remains the only definitive treatment for patients with end-stage hepatic failure and has demonstrated considerable success, especially in high-volume centers in

developing countries, and achieving numerous factors can influence long-term survival; considering immunosuppressive treatment, with an overall survival at five years exceeding 75 to 80 %, With a cadaveric donor or by hepatectomy with a living donor, which is one of the most technically demanding procedures in hepatobiliary surgery and liver transplantation itself. Conclusions: liver transplantation is today an opportunity to preserve the life of the terminal patient, evoking hope with a high possibility of having a good quality of life. In Mexico, liver transplantation is carried out with very good results.

Keywords: Liver, Transplant, Donor, Liver transplant, Hepatectomy, Living donor, Liver Regeneration

INTRODUCTION

The human liver is a large abdominal organ of brown/reddish color and weighing approximately 1800 g in men and 1400 g in women, it is divided by the falciform ligament, which forms the smaller left lobe as well as the greater right lobe. [1] In 1957, French surgeon Claude Couinaud formalized the classification of the liver by dividing it into eight independent functional segments. Each segment has its own portal pedicle, arterial pedicle and bile duct. [2] The blood supply is high, with 80% coming from the portal vein, which originates in the spleen and intestine, and the remaining 20% from the hepatic artery, which is oxygenated blood. Venous blood flow out of the liver, through the three suprahepatic veins that divide the organ into the anterior and posterior segments. [3] The function of the liver is vital, as it performs multiple functions that contribute to detoxification, digestion, metabolism, immunity and vitamin storage, among other functions, and its regenerative action is one of its strongholds. Since it performs more than 500 vital functions [4]

It is common knowledge that hepatocentrism predominated, which was a medical doctrine that considered the liver the center of the human being. It originated in ancient populations (Mesopotamian civilization) and persisted through the years in Western countries until the seventeenth century. Empedocles (c. 490-c. 430 BCE) determined that fire was present primarily in yellow bile, which was said to reside in the liver. [5] And the liver was believed to be the origin of blood, as Galen (c. 129-216), describes this organ as warm and moist, the "source of veins and the main instrument of blood production" considering it the seat of the human soul.[6]

The ancient Greeks did not recognize liver regeneration because their anatomical and physiological knowledge was based only on observation, focusing exclusively on the surface appearance of the liver. Ironically, Greek mythology describes the story of Prometheus, the Greek god whose immortal liver was consumed day after day by Zeus' eagle. The regeneration of the organ is discovered by scientists in the 19th century through advanced knowledge of anatomy and microscopic studies. [7, 8] The organ can recover completely even if up to 70-75% of its mass is lost or removed, the first official scientific description of liver regeneration was made in 1879, and cellular and molecular processes were deciphered in the mid-twentieth century. [9] The rapid restoration of liver volume and function after hepatectomy greater than > 70% or severe hepatocellular damage, and its strict regulation at the onset and cessation of regeneration, is a unique property of the liver, which has been an enigma in medical science for years. [10]

The regulatory mode of autonomic liver regeneration is a question of medicine as it is strict between the liver volume and the body surface area of the subject, expressed as hepatic index (liver weight/total weight x 100 ~ 2.5%), then described as a "hepatostatic" regulation. [11] From the above statement, it has been verified that transplantation in a clinical and experimental manner, where the grafts are small and the recipients are large and vice versa, is confirmed to be a great adaptation of the donor liver volume to the largest/medium/smallest body surface of the recipient. [12, 13] The liver and brain are the organs with the greatest capacity to maintain their integrity, both morphologically and their functionality, and thus respond to aggressions that alter or vary the internal environment of the human body. This characteristic is present in other "biological systems": physiological homeostasis, with specific tissue development, an assertive cell cycle, and great ecological resistance, to a circadian rhythm and even suffering from cancer. [14, 15] Hepatic regeneration is one of the most extraordinary biological phenomena of adaptation and response to maintain internal homeostasis. In recent decades, there has been a great deal of intense research due to its applications or therapeutic implications. [9, 16]

The history of organ transplants compared to the time of the planet's existence and their successful development is very short. The oldest precedent of transplantation has its origin in India, where the surgeon Sushruta, in the eighth century BC, practiced tissue transplants in various ways in several patients. In addition, it can be said that in the years 140-208 AD. The legendary Chinese surgeon Hua Tuo performs exchanges of diseased organs for healthy organs in humans, in the form of a transplant, however, outside of the eras of antiquity already described, unlike in the Middle Ages there was no evidence of any fact in the area. It was not until the Renaissance in 1767 that a Scottish surgeon, John Hunter, published the success of his research on experimental implants. [17] The Swiss biologist and naturalist Charles Bonnet (1720-1793) experimented with annelids by checking grafts and observing regeneration phenomena like plant grafts. [18] Later, in France, Henri Louis Duhamel du Monceau made plant and animal grafts, studying processes of scarring and vascularization (a technique for joining blood vessels). The term "animal grafting" first appeared in his writings in 1746. One of his published works « Recherches sur les causes de la multiplication des espèces des fruit». [19]

In 1869 the surgeon Jacques Louis Reverdin obtained the first epidermal grafts in man, who carried out the first human transplant and then surgeons in the USA practiced it and later in Europe. [20] The first human corneal transplant was in 1905 by physician Eduard Zirm, and since 1961, more than 1,800,000 people have regained their sight from corneal transplants. [21] However, the success of organ transplantation in the nineteenth century was to be able to restore circulation, to know the anatomy of the organs and their physiology. Alexis Carrel (1875-1944), a French surgeon, demonstrated the possibility of solid organ transplantation, at least in dogs. He was able to develop cell culture techniques, described a method to anastomose arteries and veins, and created a pump capable of keeping whole organs alive and oxygenated. [22]

The surgical possibility of performing a transplant was one answer, but there was still another phenomenon to be resolved: the body's immune system did not tolerate the grafting of tissue or the transplanted foreign organ. In 1933 Yury Voronoy performed the first kidney transplant with a cadaveric donor, presenting rejection, attributing it to an immunological process. The first successful kidney transplant between identical twins was performed in 1953 by surgeons Joseph Murray and John P. Merrill. [23] The use of

immunosuppression using irradiation and steroids was attempted, which gradually evolved over the decades to include azathioprine and cyclosporine. [24, 25] Cyclosporine was included as the immunosuppression therapy and became the dominant gold standard until the 1990s. Otherwise, Starzl used tacrolimus for the first time in 1989, and with a greater potential compared to cyclosporine, and today it displaces it accurately in this area of immunosuppression. [26, 27] The first successful liver transplant in the world, performed in an animal model, took place in 1955, and the first human liver transplant was reported in 1968 in the United States. [28]

OBJECTIVE

To carry out art history based on an exhaustive search of the national and international medical literature on liver transplantation in human beings, its antecedents, its applicability, its processes, publications that provide knowledge in depth of the subject, in anticipation of documentary, professional and analytical research.

DISCUSSION

Organ transplantation involves removing an organ from one person (the donor) and placing it in another (the recipient). This procedure is performed in patients with terminal organ failure, or by brain death or circulatory death; The process comprises five phases, which can overlap, and which are listed below:

- "Phase I: Identification of potential organ donors and referral to an organ procurement organization.
- Phase II: Declaration of death and obtaining consent for organ donation.
- Phase III: Donor evaluation.
- Phase IV: Donor management.
- Phase V: Organ procurement." [29, 30]

The brain-dead donor is associated with hemodynamic, metabolic, and immunological dysregulation that could affect graft tissue quality, villi damage, and increased levels of fatty acid-transporting protein. [31]

Organ preservation remains a critical challenge in transplantation, primarily due to hypothermia-induced oxidative stress and metabolic dysfunction. A cell-free, mitochondria-enriched preservation strategy, by adding newly isolated mitochondria from human mesenchymal stem cells to standard preservation solutions, as a cell-free mitochondrial strategy to improve organ preservation under healthy conditions. of hypothermia. [32]

Acute cell rejection is antibody-mediated rejection or chronic allograft failure and graft-versus-host disease; these are the main causes of graft loss and death in recipients, usually accompanied by infections that exacerbate inflammatory lesions in the allograft. [33] Acute rejection of intestinal transplantation is the leading cause of graft loss and an important predisposing factor to chronic rejection, occurring more frequently in isolated transplants and particularly with splenectomy. [34] In addition, it should be known or the same concern that should be indispensable, in which transplantation from a living donor is

for the well-being and safety of the donor. To ensure this, only individuals with a low operative risk should be considered as potential candidates. And without neglecting the HLA compatibility report, ABO compatibility and lymphocytotoxic cross-match, which should be taken into consideration. [35] Graft-versus-host disease results from immune responses exerted by immune cells capable of the allograft to recipient organs, and an incidence of 20% to 50% of patients after transplantation is documented. In severe cases, it is fatal, classified as acute and chronic. [36] Acute occurs during the first 100 days after transplantation or at any time by donor T cells and manifests in the skin, gastrointestinal system, and liver. Chronic disease, on the other hand, is a disease that occurs after the first 100 days of transplantation and is very similar to an autoimmune disease. [37] Antibody-mediated transplant graft rejection is of multiple and varied cause, which may be due to:

1. Donor-specific antibodies
2. Acute tissue lesion, with focal fibrin thrombin in the capillaries of the lamina propria, C4d deposition
3. Anti-human leukocyte antigen antibodies
4. Other [38]

Hepatic steatosis is a disease associated with chronic metabolic dysfunction, is more common worldwide and represents an important and growing public health challenge, which evolves into steatohepatitis associated with metabolic dysfunction or even advanced fibrosis, cirrhosis, hepatocellular carcinoma and liver transplantation itself. [39] It is estimated that one-quarter of the world's population suffers from steatotic liver disease associated with metabolic dysfunction, which is increasing rapidly due to the global epidemic of type 2 diabetes mellitus and obesity. The incidence of hepatitis B and C has decreased thanks to advances in prevention and treatment; however, the overall burden of hepatocellular carcinoma continues to increase. [40] On the other hand, there are significant health disparities in alcohol-associated liver disease, largely driven by social determinants of health, with primary outcomes including incidence of mortality, cirrhosis, major adverse hepatic events, type 2 diabetes mellitus, any type of cancer, and major adverse cardiovascular events. [41] Thus, steatohepatitis associated with metabolic dysfunction is one of the main indications for liver transplantation, and the stage of fibrosis is the best predictor of clinical outcomes. [42] Current treatment of severe alcoholic hepatitis is based on corticosteroid therapy and alcohol withdrawal. Since liver transplantation saves lives in patients with alcoholic hepatitis at high risk of premature death, refractory alcoholic hepatitis has become a new indication for liver transplantation in patients. Well-defined selection criteria are needed for candidate selection and accurate tools to predict relapses into alcohol consumption after liver transplantation. [43]

Liver transplants for acute alcohol-associated hepatitis have increased rapidly over the past decade consistent with increased demand and satisfactory patient and graft survival, but little is known about the actual long-term outcomes of this population, who are undergoing isolated orthotopic liver transplantation for alcohol-associated acute hepatitis in the era of the real safety net after liver transplantation. [44] In the United States, hospitals are assigned to a designated organ procurement organization, responsible for managing deceased donors in the designated donation service area. Hospitals may apply for exemptions to work with different organ procurement, upon proper justification. [45] It should be noted that liver transplantation of donated organs has been studied to renin, which was raised up to 100 times above normal and was strongly correlated with sodium in

the end-stage liver disease model. Renin was not associated with early allograft dysfunction, but it was strongly associated with acute renal failure. [46] Progressive liver dysfunction and failed trans jugular intervention led to an urgent transplant. Given the expected intraoperative cardiopulmonary instability and surgical complexity, the use of double-cannula vessel - venous extracorporeal membrane oxygenation was initiated prior to clamping of diffuse hepatic vein thrombosis and inferior vena cava stenosis. A classic hepatectomy with a portacava vessel shunt was performed. [47]

Primary sclerosing cholangitis is a chronic inflammatory disease that affects the intrahepatic and/or extrahepatic bile ducts. It can lead to biliary stasis, strictures, fibrosis, and liver cirrhosis, which often require liver transplantation, in its anatomical subtypes (intrahepatic, hilar, and distal). [48]

The most common etiologies of liver disease among liver transplant recipients were hepatitis B virus, cryptogenic cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis. In contrast, in the United States, the leading causes of liver disease among liver transplant recipients, particularly those without hepatocellular carcinoma, were nonalcoholic steatohepatitis a priority and alcohol-related liver disease to a lesser degree. [49, 50]

In pediatric patients where referral for liver transplantation depends on the clinical circumstances of the child: emergency in case of acute liver failure or acute decompensation, urgency in case of progressive disease or anticipation, however, increase life expectancy and/or quality of life, their indications are those that may be end-stage liver disease with significant synthetic dysfunction (acute or chronic), intractable portal hypertension, refractory ascites, coagulopathy, encephalopathy, variceal hemorrhage, recurrent episodes of life-threatening cholangitis, spontaneous bacterial peritonitis, refractory pruritus, disfiguring xanthomas, growth retardation despite maximum nutritional support, unresectable liver tumors, etc... [51]

Long-term immunosuppressive therapy after solid organ transplantation, such as liver transplantation, should be considered ideally maintained with treatments with stable pharmacokinetic profiles to improve quality of life and survival, and reduce graft rejection and loss. [52] Recipient age was significantly associated with survival; younger recipients had better outcomes, consistent with previous research. Coinciding with a meta-analysis by Mohan. [53, 54]

Many liver transplant recipient patients do not properly take their immunosuppressive therapy as prescribed, which can be a major cause of graft rejection. [55, 56] However, liver transplantation remains the only definitive treatment for patients with end-stage hepatic impairment and has demonstrated considerable success, especially in high-volume centers in developing countries, and achieving numerous factors may influence long-term survival. [57]

According to data from the European Liver Transplant Registry, the 1-, 10-, and 18-year survival rates for liver transplantation were 83% to 88%, 68% to 72%, and 48% to 55%, respectively. In a meta-analysis of 117 liver transplant survival studies, survival rates at 1, 2, 3, 5, and 10 years were estimated to be 85%, 80%, 75%, 73%, and 71%, respectively. [58] Older age, whether in donors or recipients, particularly beyond the 50-60 year thresholds, was associated with lower post-transplant survival. Since aging affects the function of different organs and decreases their effectiveness, it is therefore more than evident.

Particularly in patients aged 60 years, it was associated with lower post-transplant survival. [59]

The risk of death in transplant recipients decreased significantly in the last decade compared to the previous decade, so that the risk of death in patients who received a transplant after 2010 decreased by approximately 44%, and this decrease was statistically significant. [60] This is explained by advances in surgical techniques and post-transplant care, such as access to more effective and less complex medications, the development of less invasive procedures, and the growing expertise of transplant teams in surgery. Evaluating liver retransplantation remains the only treatment for graft failure. [61]

Orthotopic liver transplantation has improved dramatically in recent years, as the overall success of this intervention is the refinement and standardization of the surgical procedure. The complete transplant procedure is made up of four main stages: [62]

1. Donor hepatectomy.
2. Hepatectomy of the recipient.
3. Graft implantation with 4 vascular anastomoses, followed by hemostasis.
4. Bile duct reconstruction.

Liver transplantation is the major surgical aggression to which a patient can be subjected, already quite weakened by the long evolution of a chronic liver disease. The success of the procedure is undoubtedly due to the formation of a multidisciplinary team, the refinement of the surgical technique of procurement, resection, and implantation, the concomitant development of better anesthetic techniques, and immunosuppression. [63] Biliary complications are an important source of graft dysfunction both early and late, since the genesis of late biliary stenoses is not associated with vascular etiology. High rates of acute cell rejection, hepatic artery thrombosis, infections, higher body mass index in the recipient and age of the donor, prolonged warm ischemia, and retransplantation. These are the complications that have been reported. [64] Technically, liver transplantation is the most complex of all transplants. The surgical technique has been well established for many years and has not changed much. [65]

In 1992, Belghiti developed the modified piggy-back technique in which a side-by-side cavocaval anastomosis is performed on the anterior aspect of the recipient's right inferior cava to minimize outflow obstruction. [66] Wu also reported another technique, which has the advantages of simplifying hepatectomy steps and separation, and the vena cava anastomosis is wide, thus avoiding obstruction of the outflow tract. However, it requires complete blockage of the inferior vena cava, and the period is prolonged in time without liver function during the procedure, which can cause intraoperative hemodynamic instability and renal dysfunction. [67] In general, the selection of surgical techniques depends on the patient's conditions, different surgical techniques have specific advantages and disadvantages, and that appropriate surgical technique, based on the patient's condition to ensure hemodynamic stability during the operation, is of paramount importance in improving prognosis. [68]

In addition, mild, strong, and bidirectional blood group incompatibility was associated with an increased risk of mortality, and this increase was statistically significant in the univariate analysis, with no significant difference between the ABO-incompatible and

ABO-compatible groups. [69] That is why transplant patients with primary sclerosing cholangitis, primary biliary cirrhosis, autoimmune hepatitis, hepatitis B, Budd-Chiari syndrome, or cryptogenic liver disease (**see Figure 1**), which due to its chronicity is believed to have better adaptability to the graft, better long-term survival compared to those with acute liver failure is the opposite situation. [70] It is therefore confirmatory that long-term immunosuppressive therapy following solid organ transplantation, such as liver transplantation, is ideally maintained with treatments with stable pharmacokinetic profiles to improve quality of life and survival, and to reduce graft rejection and loss. [71]

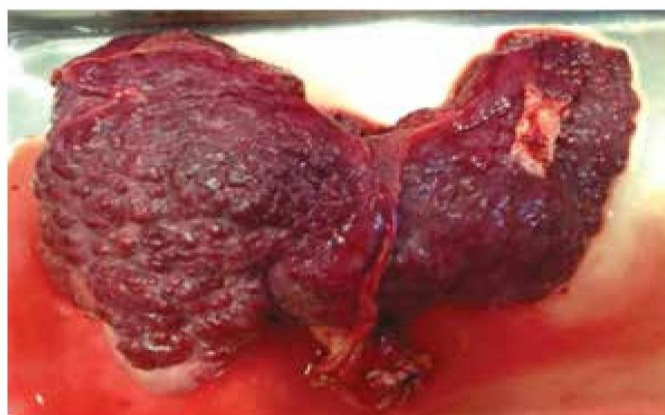


Figure 1

After hepatectomy of the recipient, diffuse liver damage is observed with macroscopic changes in relation to macro and micronodular cirrhosis. Image taken from the reference: Diliz-Pérez HS, Rossano-García A, García-Covarrubias L, Córdova-Gallardo CJ, Bautista-Olayo R, Montalvo-Javé EE, et al. Reporte del primer caso de trasplante hepático ortotópico en el Hospital General de México "Dr. Eduardo Liceaga". Rev Med Hosp Gen Mex. 2013; 76:34-40. [72]

In a survival scenario, the only curative treatment in an advanced stage of cirrhosis/liver failure is liver transplantation. Today, after the improvement in surgical technique and immunosuppression, the overall five-year survival exceeds 75%. In Mexico, liver cirrhosis is documented in 2023 as the fourth cause of death. [73] It should be noted that in Latin America liver transplants are few, since of the 33 countries that perform it only 18 do so, which compared to developed countries the transplant rate of this organ is well below the standard, except for Brazil. Mexico is today the one that transplants the least worldwide, occupying the dishonorable third place, with a rate of 1.8 cases per million inhabitants. [74] According to CENATRA, which is the "National Transplant Center" in Mexico, it reports that from 1991 to 2011, 1,107 liver transplants were counted with 59 centers already authorized. The number of liver transplants carried out has increased, but it continues to be deficient for the population that needs it. [75] In 2025, 262 liver transplants were performed in the country and, as of April 26, 2026, 82 procedures were counted. [76] Survival of 87.6% for the patient, and 82.4% for the graft at one year and 72% and 66% for the graft at five years have been successfully documented. It is a priority to choose patients who are candidates for transplantation. Since 2002, the MELD (Model for End-Stage Liver Disease) system was implemented, which is based on four prognostic

variables: bilirubin level, serum creatinine, international normalized index, and the cause of liver disease. [77, 78] The lack of organs for disposal continues to be the main limitation in the country.

That is why an alternate door with liver transplantation is elucidated, which is that of a living donor, which consists of removing half of the donor's liver, this surgical technique has twice the complexity of the classic technique of a cadaveric donor; See Figure 2., since the liver can grow back and regain its normal size shortly after surgery in which a part is removed for donation. See Figure 3. [79] In 2022, about 9,500 liver transplants were carried out in the U.S. Between and, about 600 were with livers from living donors. [80]

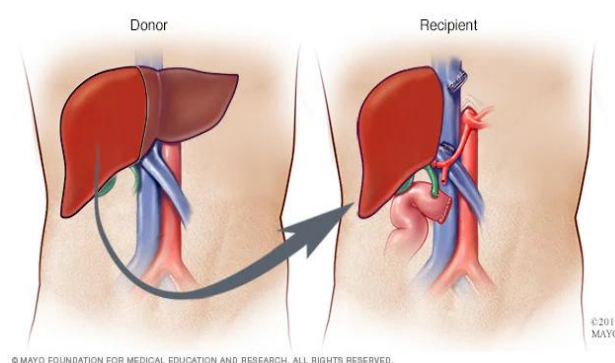


Figure 2

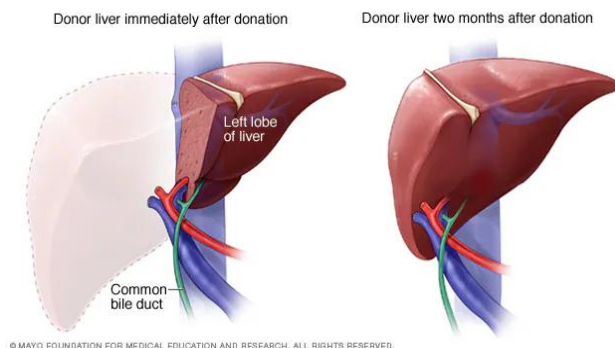


Figure 3

Figures 2 and 3: Images extracted from the reference: Liver transplant. Newsletter: Mayo Clinic Health Letter — Digital edition. Reviewed on 08/19/2026 at: <https://www.mayoclinic.org/es/tests-procedures/liver-transplant/about/pac-20384842#dialogId33021011>

In many Asian countries, a shortage of deceased donors means that living-donor liver transplantation. So he chooses to carry them out despite various factors; such as the fact that there were no significant differences in recurrence-free survival or overall survival between ABOi LDLT and ABOc, which supports ABOi LDLT as an oncologically acceptable option. With the Milan criteria in liver cancer. [81, 82] Living-donor hepatectomy remains one of the most technically demanding procedures in hepatobiliary surgery and liver

transplantation, so robotic donor hepatectomy is still considered to be concentrated in only a limited number of programs. [83]

The donor's liver volume should be estimated and a volumetric analysis of the liver segments that are important for both the selection and evaluation of the donor should be performed. There are several formulas, but computed tomography is the most used method for preoperative liver volumetry. With a margin of error of 5% to 15%. Donors underwent right hepatectomy, left hepatectomy, left lateral hepatectomy, or reduced left lateral hepatectomy. [84] Postoperative adaptation among living liver donors, as they experienced physical adjustment difficulties due to discrepancies between their preoperative expectations regarding pain, speed of recovery, and complications, with psychosocial burdens related to surgical scarring and increased life satisfaction after transplantation. [85] In living liver transplant donors, the complication rate for left lobectomy was 4.0%, while for right lobectomy it was 13.0%, due to biliary leakage and hemorrhage. [86] Pig-to-non-human primate models remain the primary source of survival, physiological and immunological data that are not yet obtainable in humans, particularly xenotransplantation, it is only a basis for research in the future. However, a species-specific physiological incompatibility is confirmed. [87]

On the other hand, in the frenetic search and research, new surgical techniques have been innovated, where bidirectional portal vein reconstruction technique with double patch (see figure 4) simultaneously optimizes the geometry of the portal vein of the graft and the recipient in liver transplantation from a living donor with type C anatomy. [88]

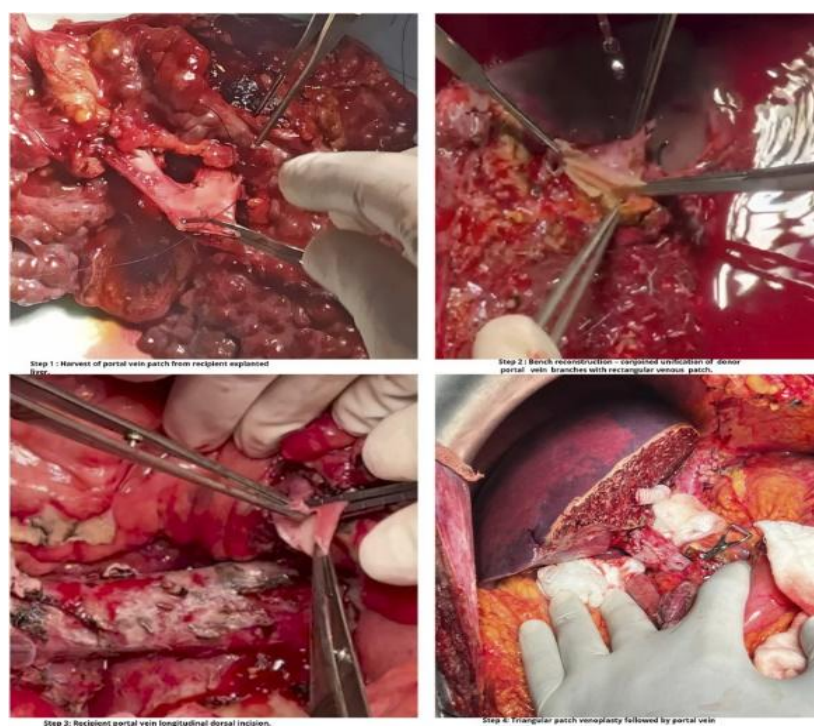


Figure 4

Surgical steps of pulmonary vein reconstruction with bidirectional double patch. Image taken from the reference: Shams-Ud-Din, Acharya B, Dogar AW, Arsalan M, Umar M,

Abbas SH. Bidirectional portal vein reconstruction for type C anatomy in living donor liver transplant. *Transpl Int.* 2026 Jul 13; 39:16600. doi: 10.3389/ti.2026.16600. [88]

Portal vein reconstruction was successfully completed in all patients without interposition grafts. There was no early portal vein thrombosis or clinically significant stenosis. All recipients showed satisfactory graft function and portal vein patency was maintained during the 6 months of follow-up, with Doppler flow. [89] In many cases, anatomical difficulties occur during surgery, limiting the ability to anticipate and mitigate surgical risks, and is therefore essential to improve preoperative evaluation and optimize outcomes of comprehensive characterization of hepatic, portal venous, hepatic venous, and biliary arterial anatomy in living liver donors. [90] Finally, survival rates are evaluated by identifying key clinical, surgical, and laboratory parameters associated with post-transplant mortality in a high-volume center that primarily performs living-donor liver transplants. Three modifiable or monitorable factors are highlighted as key predictors of reduced survival in pediatric liver transplant recipients: [91]

1. The low weight of the transplant.
2. High graft weight/recipient weight ratio
3. Early postoperative thrombocytopenia

In addition, the psychological factors that affect living organ donors are considered, showing that sex was the only demographic variable that was significantly correlated with depression, anxiety and stress, which shows that female donors are the ones who experience it the most, at 37%, 33% and 40% respectively. So, interventions to increase the psychological resilience of potential organ donors and demonstrate that psychological support. [92] It has been investigated that living donor transplantation is performed in 99% right hepatectomy. There were no donor deaths, Clavien-Dindo grade IV complications, or biliary complications. With an overall morbidity rate of 28.9%. Liver failure after hepatectomy occurred in 22% of donors. However, mortality and a slow but complete recovery of donors are not reported, which is why constant preparation of the surgeon should be planned in order to increase access to liver transplantation from living donors. [93]

CONCLUSIONS

Liver transplantation is today an opportunity to preserve the life of the terminal patient due to fulminant liver failure, evoking hope with a high possibility of having a good quality of life. In Mexico, liver transplantation is carried out stoically and despite the precarious resources/supplies, but with very good results. It is decisive to project being able to turn the exponential number of liver transplants in Mexico into a challenge and/or an area of opportunity, as well as the increase in the option with living donors. The surgeon together with the multidisciplinary team could give an option of a new life and that is viable to the patient with acute or chronic liver failure, which is fatal and fatal.

Conflict of Interest

The authors stated that they had no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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