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Living Donor Liver Transplantation

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Abstract

Living donor liver transplantation was introduced for the purposes of increasing the number of donors, reducing mortality and morbidity rates, and improving long-term survival of the recipients. The procedure for living donor liver transplantation is the same as for cadaveric liver transplantation. The suitability of potential donors is established following exhaustive evaluations of the donor's liver and overall health.

In adult transplantation cases, living donor liver transplantation outcomes are as good as in cadaveric transplants, but donor morbidity continues to be significant as are biliary complications, whereas outcomes in pediatric liver transplants from living donors are more successful than those from cadaveric liver grafts.

Living donor liver transplantation is a valid alternative to cadaveric transplantation that can offer improvement of survival rates in the future if we manage to select suitable candidates and overcome a few technical difficulties. **(Trends in Transplant. 2010;4:138-44)**

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Key words

Liver transplantation. Living donor. Pediatric liver transplatation. Adult liver transplatation. Trends in liver transplantation.

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Introduction

The main objective of living donor liver transplantation (LDLT) is to increase the number of organs available for transplantation. Although the potential risks to the donor's life are low, they very much govern the performance of this type of transplantation. Nevertheless, the mortality rate for patients on the waiting list for a donor justifies the use of this procedure. This document details the outcomes of discussions held at the consensus meeting of the Spanish groups, whose objective was to detect problems and provide possible solutions.

Donation process

Trends in living donor transplantation

Over the past few years, advances in liver transplantation have allowed the survival rate after one year to rise to nearly 95%. Although Spain has one of the highest transplant rates in the world, availability of cadaveric organs for transplantation is not sufficient at this time to cover existing needs. Waiting list mortality has hovered around 7-8% for the last few years; the probability of undergoing transplantation was 51% in 2008.

While in recent years a slight increase in living donor kidney transplantations has been observed[1], in LDLT the trend has been in the opposite direction[2]. One of the reasons for this decline has been the fact that application of the model for end stage liver disease (MELD) causes the urgency for donations to decrease as patients with a higher risk of death are identified.

Other reasons are donor mortality and morbidity rates, the risk of worse outcomes in recipients according to their etiology or the seriousness of their illness, the potential donor evaluation process itself, which means only between 9 and 17% are accepted for donation, as well as issues related to the donors' quality of life following transplantation.

At this time, LDLT continues to be a complex procedure that involves morbidity and mortality risks for donors as well as risks for recipients due to the need for complex vascular and biliary reconstruction. Nevertheless, the general opinion is that this type of transplantation is justified due to the fact that the waiting list mortality rate still remains too high[3]. In addition, the prevalence of hepatocellular carcinoma (HCC) means it is impossible to cover all of the need for liver transplants so that HCC should be considered as an indication criterion for LDLT.

Improvement of LDLT requires proper identification of appropriate candidates, such as MELD exceptions or those with HCC, reduction of donor morbidity and mortality and improvement in their quality of life following the donation, compensation for financial loss and, lastly, the introduction of more aggressive options such as programs for cross-matching donor and recipient or programs for use from donors with blood group incompatibility.

The majority of LDLT that take place in Spain are being performed in pediatric recipients[4]. So far, more than 2,000 implantations of left lateral segment grafts, which is an option that parents frequently request, have been performed worldwide. Selection of potential recipients is based on pediatric end-stage liver disease criteria that predict mortality within three months of being included on the waiting list. This modification of the adult "score" does not appear to identify all of the children in urgent need of transplantation. Those in exceptional situations or serious cases account for approximately 50% of those who receive a transplant. In addition, children over the age of 12 compete with adults, which

makes giving them priority more difficult. The solution would be to systematically prioritize pediatric patients, giving status as a child whenever necessary and making it an obligation for this pediatric grouping to make division of the graft a priority so as to be able to transplant into both an adult and a child at the same time. The graft will thus have been assigned to two patients and there would be no predominance of one group over the other which, in the majority of cases, is a source of conflict. To maintain the offer of a living donation is also a duty for those parents or relatives who are willing to make a donation.

In some cases, LDLT has been proven to have survival outcomes that are equivalent[5] or superior to full grafts. However, and in spite of being associated with a somewhat greater survival rate, the risk of graft loss is somewhat higher for divided or split grafts than for full ones.

Incentives for live donations

In order to encourage living donations, the objective must be to reduce to the minimum the negative impact that transplantation has on the donor, as much physically as psychologically or even financially.

One of the main drawbacks is the scar, which can be resolved through the use of laparoscopic surgery[6,7]. Economic obstacles for the donor could be solved through the creation of protection mechanisms that would guarantee employment maintenance or provide access to long-term care insurance.

The majority of hospitals are not candid with patients on the waiting list about the possibility of opting for a LDLT. To improve on this situation in the future, informing patients on the waiting list about this option should be mandatory, as should advising them about referral centers when need be.

Table 1. Characteristics of the ideal live donor

- Age: 18-55 years
- BMI: < 30 kg/m^2
- No cardiopulmonary, renal or metabolic disease
- Residual liver volume (LLL): > 40%
- Graft (RLL): > 0,8% recipient weight
- Steatosis < 20%
- Favorable anatomical suitability
- Donor/recipient must be ABO-compatible
- Significant relationship with the recipient
- Independence and competence of the donor

Donor evaluation

The key to LDLT lies mainly in the consideration of the risk to the donor, which should be minimal, and the benefit for the recipient. The donor must weigh the risk of possible mortality, aftereffects, and social, economic, and work aspects. The importance of these factors may vary according to survival of the recipient. The risk of minor complications for the donor is about 27%, that for potentially serious complications that are successfully resolved is 26%, about 2% for life-threatening conditions, and 0.8% for death[8].

Extensive evaluation of the donors is key to achieving good short- and long-term outcomes. The risk of complications in the donor is currently about 37%, about half of which are minor while the remainder are considered to be potentially serious, according to the Clavien classification system. Therefore, one of the most pressing objectives is to try and reduce this number by means of thorough prior testing and a meticulous surgical technique to ensure the highest standard of quality of life for the donor following the operation.

Table 1 shows the factors that determine the selection of donors and table 2 shows the protocols for the selection of potential donors.

Table 2. Phases in the process of donor evaluation

Preliminary general health evaluation	First informed consent form Detailed medical history Physical examination Blood tests, blood group, hepatitis serology
Psychological evaluation	Mental stability Voluntary nature and willingness Relationship between donor and recipient Informing the donor sufficiently about the surgical procedure
Anatomy	Cholangio-MRI CT angiography All-in-one MeVis®
Overall risks of the surgical procedure	Lab tests: biochemical, lipid profile, iron, ferritin, transferrin, α1-antitrypsin, ceruloplasmin, immunoglobulin levels, thyroid function tests, tumor markers, coagulation factors Hyper-coagulation profile* Chest X-Ray Lung function test Stress test-ECG Echocardiogram
Liver biopsy†	Presence of steatosis (contraindicated: if > 20% or if 10-20% and RLVBWR < 0,8) Discovery of other histologic findings: (portal and sinusoidal fibrosis; NASH; portal inflammation and necroinflammatory changes)
Preparation for surgery	Autologous blood donation Second psychological evaluation Evaluation by hepatologist Assessment by anesthetist Final consent Ethics committee Civil registry

RLVBWR: remnant liver volume body weight ratio; NASH: nonalcoholic steatohepatitis.
*If donor has a history of deep vein thrombosis.
†in patients with abnormal liver function test results, radiologic abnormalities (steatosis and others), BMI > 30 kg/m^2, or relatives of recipients with primary biliary cirrhosis, primary sclerosing cholangitis or autoimmune disease.

The donor must be informed of the risks and drawbacks associated with transplantation before giving consent.

Despite all this, a comprehensive preoperative evaluation does not guarantee the absence of postoperative morbidity in the donor. The mortality risk for donors is five times greater in LDLT than in living kidney donation[9,10]. Progressive experience and improvements in donor selection may reduce mortality and morbidity rates in the future, although they are not expected to ever be as low as in living donor kidney transplantation.

The need for total transparency regarding outcomes for donors and awareness that morbidity and mortality rates will never be zero justify the need for establishing a prospective donor morbidity registry and establishing a standard system for recording complications in donors. In the meantime, surgery complications should be recorded following the Clavien classification system or one of the recent adaptations based on it[11].

Follow-up of donors is essential and should be made, at the very least, for the first three years following surgery, at a rate of once every three months during the first year and at 12-month intervals after that. It is recommended that the tests to be required should include complete lab tests and volume calculations using magnetic resonance imaging. It is necessary to have a long time of follow-up

of all donors because we don't know what the long-term complications could be. The majority of programs consider that during the first year, follow-up should be performed every three months.

Evaluation of the liver

The liver is an organ that has surgically important vascular variations, both venous and arterial, in addition to the biliary tract, which makes evaluating it very complex. Current imaging technology is extremely efficient and allows the anatomic distribution of all of its structures, including the biliary tract, to be described with great exactitude. Helical computed tomography with multiplanar reconstruction and magnetic resonance imaging allow the visualization of all of these structures in a single exploration. In addition, the possibility of including a reconstruction of the liver through use of a special program (MeVis®) allows three-dimensional images to be obtained that further increase safety in surgical planning. Even so, imaging during the surgical intervention itself must be used to guarantee the anatomical orientation suggested by the preoperative evaluation. In a major surgical procedure, such as that performed on the donor, where meticulous dissection of the hilum of the liver is required, there is no room for guesswork and each step of the process must be performed with the maximum possible safety and knowledge of the possible consequences.

Selection of candidates for liver transplantation

The ideal candidate for LDLT is a person who would benefit from receiving a cadaveric liver, but who has a low probability of receiving one for transplantation because of the seriousness of their disease, and in addition, is someone who has not previously suffered from significant deterioration in quality of life.

At present, the MELD system is able to identify and prioritize those patients with the highest probability of pretransplant death. That is why LDLT currently targets all those patients who are not correctly identified and therefore not prioritized.

From our point of view, HCC represents a leading indication for LDLT, both for patients who meet the Milan criteria and for those who exceed these criteria but are known to have a relatively good prognosis (Barcelona criteria, Kyoto criteria, etc.)[12], or those who respond following chemoembolization or radiofrequency ablation and survive for at least three months within the Milan criteria.

Donor operation in adult-to-adult and adult-to-child living donor liver transplantation

Donor surgery in adult-to-adult procedures

In the majority of cases, the surgical technique for the adult donor consists of a right hepatectomy including segments V-VIII, and in which the middle hepatic vein remains with the donor.

Donor surgery in adult-to-pediatric recipient procedures

The surgical technique for the adult donor normally includes resection of liver segments II and III. Anatomical variability is significantly lower, especially where the bile duct, which is unique in 90% of cases, is concerned. This makes the surgery easier to perform and minimizes the need for banked-blood.

Recipient operation in adult-to-adult and adult-to-child living donor liver transplantation

Recipient surgery in adult-to-adult procedures

Vascular reconstruction depends on achieving the best possible venous drainage, which means not only performing anastomosis of the right hepatic vein, but also reconstructing all of the veins, whether they be accessory veins of the right lobe or tributaries of the middle hepatic vein, for which cryopreserved grafts are frequently necessary. Although the artery is small (only 3-5 mm in diameter) its reconstruction rarely causes problems. Continuous hemodynamic monitoring is needed to ensure adequate arterial flow. Last of all come the bile ducts, which have a diameter between 2 and 4 mm and are the "Achilles heel" of this type of transplantation. The ideal is to perform a systematic duct-to-duct biliary reconstruction, and when this is not possible, to perform a hepaticojejunostomy.

Recipient surgery in adult-to-pediatric recipient procedures

Surgical techniques in pediatric living donor transplantation depend largely on the patient's original disease. Vascular reconstruction is essentially the same as in adults, although in this case the size of the liver is always larger than required so that it is not necessary to maneuver to ensure venous drainage. On the contrary, because of its association with congenital anomalies, insufficient portal flow must be ruled out (due to hypoplasia of the portal vein). On the other hand, the size of the bile ducts, which is frequently insufficient, make it necessary to always perform a hepaticojejunostomy, something that is absolutely necessary in cases of biliary atresia.

Results

Adults

As has already been mentioned, the objective of LDLT is to increase the number of donors, reduce mortality and morbidity rates among donors, and improve the long-term survival of recipients.

Outcomes for LDLT have improved in the last few years. Although survival rates are now comparable to those from cadaveric donors, the incidence of biliary complications affects long-term outcomes. Nevertheless, according to follow-ups for periods of more than five years in the USA as well as in Europe, the presence of these complications does not appear to affect long-term outcomes.

The current trend in Western countries towards progressive reduction of this type of transplantation is not due to poor outcomes, but rather to sporadic cases of donor death, which have led to the closing of LDLT programs at hospitals where these have occurred. There have been a variety causes, from those due to the absence of an appropriate level of care to those where the pressure on the medical staff has had an impact on care delivery.

A total of 232 adult and 91 pediatric LDLT were performed in Europe during 2007. Both patient and graft survival rates are better in LDLT. Since MELD scores in LDLT patients are lower than in patients receiving cadaveric transplants, there is a need for caution when comparing figures.

The experience in Spain is small, although at present the absence of donor mortality associated with good outcomes in both pediatric and adult recipients allow for the consideration of the need for joint action by those hospitals where LDLT is performed in

order to increase activity. The identification of those patients in need of LDLT is of paramount importance as are systematic information and referral of patients to those centers with the experience, when the case arises.

In the last 15 years, 188 LDLT have been performed in Spain[13]. As yet no deaths have been recorded, although there has been an 8.3% rate of reoperations to solve complications. Graft survival is similar in patients who are living donor recipients (80% at one year and 65% at five years) as in those who are cadaveric donor recipients (82 and 66%, respectively). The big problem in this type of donation is the high number of complications involved.

Living donor liver transplantation in the pediatric population

Outcomes in the pediatric age group cause many fewer problems. The family relationship with the child is more reasonable and outcomes are better than those obtained with grafts that come from cadaveric donors. Only the systematic division of all liver grafts would reduce the need for this type of transplantation. Even so, at present living donation allows ensuring absence of mortality on the waiting list, something unthinkable in the 1990s when mortality on the waiting list was around 30%. Between 1993 and 2009, survival of pediatric recipients of living donor transplants in Spain was 84.8% at one year and 79.8% at five years.

Final considerations

The most important aspects to be resolved in LDLT are the establishment of standardized registries, the resolution of technical difficulties, shortening the learning curve, and improving quality of life for the donor and the efficiency of the procedure. It is also necessary to assess the possibility of expanding indications for LDLT, allowing expected survival in recipients of up to 30%.

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