

# Medical Writers' Circle

a series of articles

written by medical  
professionals about  
the management  
and treatment of  
Hepatitis C

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## Adult-to-Adult Living Donor Liver Transplantation

**L**iver transplantation is the accepted treatment for most acute and chronic liver diseases resulting in liver failure; however, the scarcity of cadaveric donors has become an insurmountable problem limiting the application of liver transplantation (1). To increase the donor supply, the concept of adult-to-child, or pediatric, living donor liver transplantation (LDLT) was introduced to clinical practice in 1989 with the first two cases being performed in Brazil, followed by other cases in Australia, Japan and in the United States (2-4). The inception of the pediatric LDLT program at the University of Chicago in the United States followed a careful stepwise process of providing adequate information to the potential living donors, local Institutional Review Board approval and proper preparation of the surgical teams. The entire process attracted much attention, both in the public arena and in clinical medicine, and became the subject of a publication discussing the ethics of this procedure in the *New England Journal of Medicine* (5). The donor operation required the removal of segments II and III of the liver (left lateral segment of the left lobe), which accounts for about 20% of the entire liver volume. The liver is divided anatomically into 8 segments, with segments II to IV composing the left lobe, segments V to VIII composing the right lobe, and segment I

being the caudate lobe. Based on the encouraging results reported by the group from Chicago, other centers in the U.S. began to offer LDLT, albeit cautiously. Our surgeons at Stanford initiated pediatric LDLT in 1992 while we were at California Pacific Medical Center, and the cumulative one-year survival rate remains greater than 90%. (6). After numerous publications by several transplant groups worldwide, pediatric LDLT has become an accepted therapy, and is often the predominant type of liver transplantation procedure for children because of the rarity of pediatric donors. The complication rate among the donors has been relatively small, and the overwhelming satisfaction of a parent or relative to save a child's life has outweighed the potential risks associated with the donor operation.

Before adult-to-adult, or adult, LDLT was ever attempted, an effort to increase the donor pool was made by performing split liver transplantation whereby a cadaveric donor liver was divided into two parts, usually a right lobe (segments V through VIII) for an adult recipient and segments II and III for a child (7,8). Occasionally, split liver transplantation has been used for two adult recipients. Unfortunately, this technique had little impact on decreasing mortality among adult patients on the waiting list, since ill patients, who have the greatest need for transplantation, did poorly when split transplantation was attempted.

Nevertheless, the experience gathered from split liver transplantation led surgeons to attempt adult LDLT, a procedure that began with some trepidation in 1994 and has been more widely applied over the past two years (8). The main reason was the valid concern that the removal of 50 to 60% of the liver from a living donor would result in unacceptable complications and possibly even death in healthy individuals who were not in need of surgery. In adult LDLT the right lobe (rarely the left lobe) is expected to provide enough liver mass to sustain the life of the recipient, and the donor is left with enough liver mass to recover from the donor operation. Over a few weeks, the liver in both the donor and the recipient regenerates into two fully functional units.

Robert Brown and coworkers recently conducted a survey of LDLT in the U.S. They sent questionnaires to the directors of all 122 liver transplant programs approved by the United Network for Organ Sharing in the U.S., and 83 programs returned questionnaires (9). Adult LDLT was being performed in 42 programs, and another 32 programs were planning to begin LDLT within 12 months. Centers that performed LDLT procedures were likely to also perform pediatric cadaveric or living donor transplants. Thirteen centers accounted for 80% of all the LDLT performed by the 42 programs and these centers were the only programs that had performed more than 10

procedures. The number of procedures performed by each of the 42 programs ranged from 1 to 71. Donor complications included biliary problems that resulted in medical intervention (6%), re-operation (5%), and a single death (0.2%). These data indicate that LDLT are performed in approximately half of the liver transplant centers in the U.S. but that most programs have done only a few procedures. Biliary complications are common and donor mortality is low. A process is needed to determine which surgeons and

donor organ to sustain life in the recipient has derived from experience with pediatric LDLT. The normal liver volume is 2.2% to 2.5% of a man's body weight. It has been postulated that the minimum liver volume procured from the donor should be 0.8% of the recipient's body weight. This formula as well as others comes from the Asian experience, in which predominantly the left lateral segment of the liver from the donor to a pediatric recipient is used. This formula may not be reliable in the United States since the habitus of

both donors and recipients. While the recipient stands to benefit with improved survival, the donor faces potentially serious short-term and relatively unknown long-term consequences. As we consider the limited treatments for end-stage organ failure, the ethical considerations become pressing issues for society as a whole. The increase in incidence of liver and other end-stage organ failure creates an urgency to find reasonable, cost-effective solutions that must be balanced against the best interests of all patients,

In addition, the recipient receives a smaller hepatic mass, but this has only rarely been a problem if the graft-to-recipient body weight ratio > 0.8% is applied. Finally, there are significant donor complication and death rates, estimated to be 10-20% and 0.2-0.5%, respectively, which necessitate fully informed consent by the donor. It is expected that LDLT will be performed with increasing frequency over the next several years as a result of the persistent discrepancy between the number of available donor cadaveric organs and need for liver transplantation.

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surgical teams are qualified to perform LDLT, which is considerably more complicated than the usual cadaveric liver transplant procedure.

A key question in adult LDLT that needs to be addressed is the extent of liver dysfunction following hepatic resection. It is known that regeneration of the liver occurs fairly quickly and within 6 to 8 weeks following resection, the remaining liver will have grown to 90-100% of the original volume. Liver resections for excision of malignant tumors have been performed for many years. During the first few days after the operation, the living donor is left with some degree of hepatic dysfunction manifested clinically by the onset of mild encephalopathy and abnormal liver chemistries, such as mild to moderate elevation of the serum bilirubin and a prolonged prothrombin time. Thus, the extent of liver impairment in the donor cannot always be predicted accurately and continues to be a critical issue in adult LDLT.

Much of the information on the minimal size required from the

Americans is certainly different from the Asian population. Furthermore, morbid obesity is a prevalent problem in this country and is almost non-existent in Asia. Thus, these formulas need to be revalidated in the United States.

Clearly a key impetus for instituting adult LDLT is the urgent need to increase the donor pool. Thus, it is critical to address whether LDLT has an impact on decreasing waiting time for an organ or on pretransplant mortality. As mentioned previously, our experience as well as the experience of other transplant centers, indicates that very sick patients undergoing split liver transplantation do fair poorly. These patients will not be the best candidates for LDLT. Most likely, the best candidates are those patients who are at home or in the hospital with mild complications of the liver disease, i.e. relatively sick status 2B patients but not critically ill status 2A patients.

Perhaps the most complex aspects of adult LDLT are the ethical implications. There may be significant psychosocial ramifications for

including voluntary, healthy donors. It is therefore critical to identify best practices when explaining risks and possible outcomes to potential donors and recipients. More information about the nature of short and long-term risks to the donor is needed to accurately inform the potential donor. It is critically important that no coercion be placed on family members to consider LDLT.

In summary, there are several potential benefits of LDLT, most importantly a reduction in waiting time and risk of death prior to a cadaveric liver transplantation. Other advantages of LDLT are the scheduling of an elective liver transplantation, allowing time to optimize the medical condition of the recipient, and use a better quality organ coming from a healthy donor with a smaller chance of potential injury based on the shorter time in preservation solution. The risks of LDLT to the recipient are generally identical to those following cadaveric liver transplantation, except for a higher likelihood of surgical complications, especially biliary problems.

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