ADULT-TO-ADULT TRANSPLANTATION OF THE RIGHT HEPATIC LOBE FROM A LIVING DONOR

JAMES F. TROTTER, M.D., MICHAEL WACHS, M.D., GREGORY T. EVERSON, M.D., AND IGAL KAM, M.D.

TRANSPLANTATION of the right hepatic lobe from an adult living donor to an adult recipient is rapidly emerging as an effective treatment for selected patients with end-stage liver disease. The development of living-donor liver transplantation in the United States over the past five years has been driven by the shortage of donor organs for transplantation. In the past decade, the number of patients awaiting liver transplantation has increased by a factor of almost eight, from 1676 in 1991 to 14,710 in 1999 (Fig. 1). During the same period, the number of liver transplantsations increased by only about 50 percent, from 2931 in 1991 to 4480 in 1999. With the growing discrepancy between the numbers of donors and recipients, the median waiting time for liver transplantation has increased dramatically, from 65 days in 1991 to 514 days in 1998. As a result, the number of patients who die while waiting is increasing. Each year, approximately 10 percent of patients on the waiting list die while waiting for liver transplantation. Many others die after removal from the list because their clinical deterioration precludes successful transplantation. To attempt to meet the growing needs of recipients, transplantation physicians are developing innovative techniques to increase the number of donated livers. These include transplantation of organs that only marginally meet the criteria for use, split-liver transplantation, and transplantation of part of the liver from living donors. This article will focus on the history of living-donor liver transplantation, the selection of donors and recipients, current outcomes, and ongoing controversies.

HISTORY OF LIVING-DONOR LIVER TRANSPLANTATION

The first successful living-donor liver transplantation was performed in 1989, with transplantation of a left hepatic lobe. In the early 1990s, living-donor liver transplantation was developed extensively in Asia, where cultural beliefs discourage cadaveric organ donation. Almost all liver transplantsations performed in Asia involve living donors. In the United States, however, relatively few living-donor liver transplantsations were performed until recently. Between 1990 and 1996, the United Network for Organ Sharing (UNOS) recorded 60 or fewer such transplantsations per year, accounting for approximately 1 percent of all liver transplantsations (Fig. 2). The procedure was reserved largely for children and used a left hepatic lobe (or one or more of its segments) from a parental donor. Left-hepatic-lobe transplantation was attempted in adults in the United States during the 1990s, but without much success. The smaller left hepatic lobe provides insufficient hepatic mass for most adult Americans, who are physically larger than most Asians. Consequently, the outcome of adult-to-adult left-
hepatic-lobe transplantation in the United States was poor, and the procedure was seldom performed.

Until 1994, all living-donor liver transplantations were performed with the left hepatic lobe (or with one or more of its segments). The first adult-to-adult transplantation of a right hepatic lobe was reported in 1994 in Japan,9 and the first series was reported shortly thereafter.10 The first successful right-hepatic-lobe transplantation in the United States was performed in 1997.11 Whereas left-hepatic-lobe transplantation was unsuccessful in U.S. adults, the efficacy of transplantation of the larger right hepatic lobe in adults became apparent. Over the next few years, the initial success of right-hepatic-lobe transplantation, coupled with the severe shortage of donor organs, led to widespread interest in this procedure in the United States. The number of living-donor liver transplantations increased dramatically in five years, from 56 procedures in 1996 to 509 in 2001 (Fig. 2).5 Currently, almost all patients undergoing adult-to-adult living-donor liver transplantation in the United States receive a right hepatic lobe.

**SELECTION OF DONORS AND RECIPIENTS**

The current process for the selection of donors and recipients for living-donor liver transplantation (Fig. 3) is evolving.12-14 In choosing appropriate recipients, the physician must recognize the potential advantages of the procedure over cadaveric transplantation. The most important advantage is a reduction in waiting time. Once a potential donor is evaluated and found suitable, living-donor liver transplantation may be scheduled within hours to weeks. In patients with decompensated liver disease, a shorter waiting time may reduce the risk of dying or of further deterioration that could render the patient too sick to undergo a successful transplantation. At our center, the median waiting time for cadaveric livers is 354 days, as compared with 178 days for living-donor livers.

Another advantage is that living-donor liver transplantation is a scheduled procedure, unlike cadaveric transplantation, which requires urgent surgery. The more flexible scheduling associated with living-donor liver transplantation allows for treatment and medical stabilization of recipients with decompensated disease so that they are in the best medical condition to undergo transplantation. A further advantage is that the graft is obtained from a healthy person who has undergone extensive testing to rule out any hepatic abnormalities. Cadaveric organs, on the other hand, are obtained from patients who have recently died after a critical illness. The function of the cadaveric organ may be compromised by prolonged mechanical ventilation, hypotension, and the use of vasoressors, which often precede the declaration of brain death in the donor.

Finally, the cold-ischemia time (the time between removal of the donor liver and its implantation in the recipient) is greatly reduced with living-donor liver transplantation. In cadaveric transplantation, the cold-ischemia time is usually 8 to 12 hours. With living-
donor liver transplantation, because the donor and recipient undergo operation in adjacent operating rooms, the cold-ischemia time is quite short, usually one hour or less. The reduction in cold-ischemia time may be beneficial, because prolonged cold-ischemia time has been associated with increased complications and graft dysfunction.

There are also some potential disadvantages to living-donor liver transplantation, the most important of which is the risk of complications in the donor. In addition, the long-term track record for recipients of living-donor grafts, as compared with that for recipients of cadaveric livers, is limited. As a result, the incidence and extent of long-term complications and outcomes are less certain than with conventional transplantation. Initial results suggest that recipients of living-donor transplants may have more biliary complications than recipients of cadaveric organs. With more patients undergoing living-donor liver transplantation and with the follow-up interval increasing, the full spectrum of complications will probably expand. Finally, the size of the hepatic mass is smaller with living-donor liver transplantation than with cadaveric transplantation, although this seldom causes major clinical problems.

The recipient of a transplant from a living donor should meet UNOS criteria for placement on the list for a cadaveric liver transplant, because a cadaveric

**Figure 3.** Evaluation Protocol for Recipients and Donors in Living-Donor Liver Transplantation.

According to the criteria of the United Network for Organ Sharing, status 1 denotes acute liver failure, status 2B decompensated chronic liver disease, and status 3 stable chronic liver disease.
Transplant may be required if the graft from the living donor fails. The initial evaluation is identical for living-donor liver transplantation and cadaveric transplantation. However, not all patients listed for cadaveric transplantation are suitable for living-donor liver transplantation. The most appropriate candidates for living-donor liver transplantation are patients in urgent need of transplantation — that is, patients with a substantial risk of dying before a cadaveric transplant is likely to become available. In patients with acute liver failure (UNOS status 1), progression to death occurs over the course of a few days or weeks. For these patients, the evaluation of potential donors must be undertaken within a few hours or days, depending on the condition of the recipient. Living-donor liver transplantation has been performed successfully in such patients. However, the effect of living-donor liver transplantation for this condition is limited, because fewer than 5 percent of all liver transplantations are performed in patients with acute liver failure.

The vast majority of recipients of transplants from living donors are patients with decompensated chronic liver disease. Among these patients, those with the most urgent need for transplantation have 10 or more points on the Child–Turcotte–Pugh scale, small hepatoma (UNOS status 2B), or both. These patients have a considerable risk of dying before conventional transplantation or of having their condition deteriorate to the point that successful transplantation is precluded. Although patients with decompensated disease are best suited for living-donor liver transplantation, some patients may become too ill to benefit. The early experience with living-donor liver transplantation in patients with chronic liver disease who require continuous care in the intensive care unit suggests that morbidity and mortality may be higher than in patients undergoing cadaveric transplantation. In addition, the recent changes in UNOS criteria that allow patients with chronic liver disease treated in the intensive care unit to be further upgraded on the transplant list (to UNOS status 2A) substantially shortens the waiting time. As a result, critically ill patients may be better candidates for expedited cadaveric transplantation than for living-donor liver transplantation.

There is controversy regarding whether patients with stable chronic liver disease (UNOS status 3) should be routinely evaluated for living-donor liver transplantation. At some centers, including ours, these patients are not routinely evaluated for such transplantation, because the risk to the donor is considered to outweigh the potential benefit to the recipient. In addition, many of these patients will eventually be able to undergo successful cadaveric transplantation. Furthermore, patients in status 3 may be considered for living-donor liver transplantation if their clinical condition deteriorates and they meet the criteria for upgrading to UNOS status 2B. At other centers, patients in status 3 are routinely considered for living-donor liver transplantation. These centers argue that stable patients in status 3 have the best chance for a favorable outcome. In addition, performing living-donor liver transplantation before clinical decompensation may reduce the risk of dying before transplantation.

The decision to consider a specific patient for living-donor liver transplantation is based on the experience and judgment of the transplantation team. Currently, patients with an urgent need and a reasonable chance of a favorable outcome are considered ideal candidates for living-donor liver transplantation. Patients with medical problems that could jeopardize the success of the transplantation, such as multiple coexisting conditions, previous major abdominal surgery, or extensive mesenteric-vein thrombosis, are marginal candidates for living-donor liver transplantation. Consequently, patients are usually left to wait for conventional transplantation. At our center, approximately half of the patients who are eligible for living-donor liver transplantation on the basis of the severity of liver disease are not evaluated because they have underlying major medical or surgical conditions (Fig. 4). The specific reasons patients are excluded from evaluation for living-donor liver transplantation include advanced age, morbid obesity, and previous transplantation. With greater experience, selected patients with complex medical problems may be considered for living-donor liver transplantation.

Once a patient has been accepted on medical grounds as a candidate for living-donor liver transplantation by the transplantation team, he or she may accept volunteer donors for evaluation. The manner in which donors are selected is important; their participation must be entirely voluntary. We require that potential donors contact our center to initiate the evaluation process. To be considered for evaluation, the donor must be 18 to 60 years old, have a blood type identical to or compatible with that of the recipient, have no major medical problems, and demonstrate a long-term, significant relationship with the recipient. Approximately half of adult patients who are potential candidates for living-donor liver transplantation are unable to identify a potential donor for evaluation because they have no children or siblings between 18 and 60 years old, they are estranged from their family, or the potential donor has an obvious serious medical problem, such as morbid obesity or coronary artery disease.

Potential donors are evaluated in a stepwise fashion that is designed to disqualify unsuitable donors as early as possible in the evaluation process (Table 1).
At our center, the first phase of donor evaluation is performed by an experienced nurse. This is usually done in a telephone conversation that gathers basic information (age, sex, height, weight, relationship to the recipient, blood type, current medications, and medical, psychiatric, and surgical history) to determine whether the potential donor is suitable for further evaluation. After this information has been obtained, the potential donor is presented to the transplantation team to determine whether he or she is suitable for formal evaluation, which includes the tests shown in Table 1. If the team finds the donor suitable for formal evaluation, then the second and, if needed, the third phases of evaluation are performed (Table 1).

At our center, 60 percent of the potential donors who go through formal evaluation are ultimately accepted as donors (Fig. 4). The evaluation of a potential donor, which is paid for by the recipient’s insurance carrier, consumes considerable time and considerable resources of both the donor and the transplantation center. Consequently, persons with no real chance of successful donation should be disqualified as early as possible. As experience with donor evaluation grows, transplantation physicians will most likely improve the efficiency of the evaluation process. A recent study showed that donors could be excluded on the basis of a simple measurement, the body-mass index (the weight in kilograms divided by the square of the height in meters). Rinella et al. determined that 76 percent of potential donors with a body-mass index of more than 28 had substantial hepatic steatosis. Because fatty livers function poorly after transplantation, potential donors with a body-mass index over 28 should be excluded from evaluation in most cases.

### Figure 4. Outcomes of 100 Potential Recipients Evaluated for Living-Donor Liver Transplantation.
Modified from Trotter.\(^2\)
SURGICAL TECHNIQUE

The most important determinants of outcome for the donor and recipient are the skill and experience of the surgical team. Therefore, living-donor liver transplantation should be performed only by a surgical team with extensive experience in hepatobiliary and liver-transplantation surgery. There are variations in surgical technique from center to center, as well as substantial ongoing technical revisions in the procedures used for donors and recipients. The right lobectomy in the donor is performed through a standard right subcostal incision with an upper midline extension (Fig. 5A). A cholecystectomy is performed, and intraoperative cholangiography may be required to define the biliary anatomy. The right hepatic artery, right portal vein, and right hepatic vein are isolated, and the entire right hepatic lobe is removed from the donor. At the same time, hepatectomy in the recipient is performed in an adjacent operating room. After removal of the entire diseased liver, the right hepatic lobe from the donor is implanted into the recipient. The following vascular anastomoses are then performed: donor’s right hepatic vein to recipient’s right-hepatic-vein remnant with a caval extension, donor’s right portal vein to recipient’s portal vein, and donor’s right hepatic artery to recipient’s hepatic artery (Fig. 5B). Depending on the biliary anatomy of the donor and recipient, anastomosis of the donor’s bile duct or ducts is performed by a Roux-en-Y anastomosis or to the recipient’s common-bile-duct remnant. After successful living-donor liver transplantation, the graft undergoes remarkable regeneration. In one series of patients, the volume of the graft increased by 87 percent, from a mean of 862 cm³ at the time of operation to a mean of 1614 cm³ seven days after operation, reaching 94 percent of its final regenerated volume at that time.23 In the same series, the donor’s liver remnant had doubled in mass seven days after hepatectomy.

OUTCOMES OF RECIPIENTS AND DONORS

Short-term survival after living-donor liver transplantation is similar to that after cadaveric transplantation. The reported rate of survival after living-donor liver transplantation in the United States and Europe is between 86 percent and 88 percent, which is similar to the rate of survival of 88 percent after cadaveric transplantation. However, the current survival statistics for living-donor liver transplantation are based on recipients who were, in many cases, selected as having the best chance of a favorable outcome. As a result, direct comparisons with survival after cadaveric transplantation may not be possible.

The spectrum of complications of living-donor liver transplantation is similar to that of cadaveric transplantation. However, there are problems inherent in living-donor liver transplantation. Although regeneration occurs very quickly in the transplanted graft, a patient undergoing living-donor liver transplantation receives a smaller hepatic mass than a patient receiving a cadaveric transplant. Therefore, there is not as much hepatic function or reserve until the transplanted lobe regenerates to full size, although this rarely causes clinical problems. The most common serious problem in patients undergoing living-donor liver transplantation is biliary complications, which occur in 15 to 32 percent of patients and may be more frequent than in patients undergoing cadaveric transplantation. The most common biliary problem is parenchymal leakage from the cut surface of the graft. During surgery in the donor, thousands of biliary radicles are transected and exposed on the cut surface of the right lobe. Even with meticulous surgical technique, bile may leak from bile radicles after transplantation. Although some leaks may cause life-threatening infection or require reoperation, most are treated by prolonged drainage through a Jackson–Pratt drain placed during the surgery.

Although most donors undergo right hepatectomy without any problems, some have complications. The exact risk of complications among donors is difficult to assess, given the lack of uniformity in the evaluation of donors, surgical technique, and the skill of the surgical team. The most common complication is a bile leak from the cut surface of the liver, which occurs in approximately 5 percent of donors. Between 9 percent and 19 percent of donors have other complications related to major abdominal surgery, including wound infection, small-bowel obstruction, and incisional hernia. The effect of liver transplantation on the donor’s quality of life was measured in a recent survey, which reported that all donors were alive and well and that 96 percent had returned to their employment status before donation after a mean of 10 weeks. However, 71 percent of donors reported ongoing mild abdominal symptoms, which they related to the surgery.

The greatest concern with respect to donors is the risk of death. Among the reported cases of living-donor liver transplantation, 2 of 706 donors died (0.28 percent). However, the exact risk of death among donors has not been established, because there is no worldwide registry of donor outcomes. Because the exact number of deaths is not known, the actual mortality rates may be higher than the reported rates. Transplantation physicians have expressed concern about mortality among donors and about underreporting of deaths. Because the accurate assessment of complications, including death, among donors is critical to assessing the long-term effect of living-donor liver transplantation, the American Society of Transplant Surgeons and the National Insti-
Institutes of Health have begun to design a data base in which donor outcomes, including mortality, can be recorded.

FUTURE ISSUES AND CONTROVERSIES

Over the next few years, the demand for living-donor liver transplantation in the United States will probably increase. On the basis of current selection criteria, an estimated 5 percent of patients on the list for a liver transplant would be considered medically eligible and would be able to identify a suitable donor, resulting in the performance of approximately 750 living-donor liver transplantations each year. The increasing number of deaths of patients on the waiting list, coupled with the growing demand for the procedure, will increase the pressure on transplantation centers to offer living-donor liver transplantation to their patients. However, many transplantation centers may not have sufficient expertise to perform the procedure. A recent editorial by Cronin et al. reported that 22 centers had performed a living-donor liver transplantation but that only 7 had performed more than 10 such procedures. The authors suggested that some programs with inadequate experience may not have “the established record of success that is required to undertake this complex and dangerous operation.” This fact could compromise the outcomes for donors and recipients at the less experienced centers. As a result, national criteria for the selection of donors and recipients, as well as certification of transplantation centers by an external regulatory agency, could help ensure uniform standards of care in living-donor liver transplantation.

The transplantation community and society as a whole will need to be informed of the potential morbidity and mortality associated with this procedure. The need for informed consent for these procedures is obvious. As liver transplantation becomes a common procedure, it will be critical that all transplantation centers be able to provide consistent training and supervision for their staff members. The development of a data base for living-donor liver transplantation is an important step in the direction of improving the outcomes for these patients.

Figure 5. Surgical Procedure for Living-Donor Liver Transplantation.
Panel A shows the transected donor liver before removal of the right hepatic lobe. Panel B (facing page) is a close-up view of the implanted right lobe showing Roux-en-Y biliary anastomosis with stent in place, anastomosis of the donor’s hepatic vein to the recipient’s vena cava, and arterial anastomosis.
whole must determine how much risk is acceptable for the donor, relative to the outcome in the recipient. Some insight is provided by a recent survey regarding the risk associated with living-donor liver transplantation. The study indicated that the lay public would be willing to undergo hepatectomy for living-donor liver transplantation, even with a marginal outcome in the recipient. In addition, the respondents were willing to accept a mortality rate among donors that was nearly 100 times the current rate. These findings indicate that the lay public may be willing to accept far greater risks for the donor and recipient than the transplantation team. This is most evident, in practice, when family members readily volunteer to donate to a recipient with a marginal chance of success, such as an elderly patient with multiple coexisting conditions and extensive carcinoma. Although the views of the family are important, the transplantation team is in the best position to decide about the suitability of potential donors and recipients for living-donor liver transplantation. In some cases, living-donor liver transplantation may be inap-
appropriate, despite assertions to the contrary by the family. However, society’s views of the risk associated with living-donor liver transplantation could affect future criteria for selecting donors and recipients. If patients and their families are willing to accept marginal outcomes in recipients and measurable risk in donors, then future selection criteria for living-donor liver transplantation could broaden to accommodate these views.

Living-donor liver transplantation is a remarkably effective lifesaving procedure for selected patients with end-stage liver disease. The demand for living-donor liver transplantation in the United States will probably increase over the next few years because of the critical shortage of donor organs and the favorable initial results. With an expert surgical team and appropriate selection of recipients and donors, the benefits to the recipient outweigh the risks to the donor. Long-term success of living-donor liver transplantation will require careful, thoughtful application of this new procedure.

REFERENCES


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