Early and Late Complications in the Right-Lobe Adult Living Donor

Elizabeth A. Pomfret

Key Points

1. Reported complication rates for right-lobe liver donors vary widely, but are estimated to be approximately 35%, with a surgical mortality rate of approximately 0.3%.

2. Biliary complications, including leak, biloma, or stricture, are the most commonly reported morbidity in right-lobe living donors.

3. Other significant donor morbidity includes portal vein thrombosis, pulmonary embolus, bowel obstruction, bleeding requiring reoperation or transfusion, and incisional hernia.

4. These data underscore the reality that living donation is associated with a small, but real, possibility of death and potentially significant morbidity, emphasizing the need for a comprehensive database to precisely define true living donor morbidity and mortality. (*Liver Transpl 2003; 9:S45-S49.*)

Live donor adult liver transplantation (**LDALT**) using right-lobe grafts has gained widespread acceptance as a life-saving surgical innovation shown to be relatively safe and efficacious. Currently, more than 1,500 live donor right hepatectomy procedures have been performed worldwide.[1-3] Potential advantages of living donor liver transplantation have been tempered by the risk of injury or death of a healthy donor. Overall donor morbidity and mortality is a critical issue and the source of much controversy currently being debated in medical, surgical, ethical, and public communities.[4-6] The majority of transplant physicians agree that a comprehensive database containing surgical outcomes of all live donors and recipients of living donor adult liver transplants is needed. To date, attempts to develop a live liver donor national database have not been successful because of economic and political reasons. Published donor complication rates differ widely among institutions, reflecting differing opinions of what constitutes a complication by various centers.[7-10] This report examines factors that contribute to the morbidity and mortality associated with right-lobe liver donation.

Avoidance of Complications

Preoperative Evaluation of Live Liver Donors

The potential risk for injury or death mandates that a complete preoperative medical and anatomic evaluation of potential liver donors be accurately performed. Our donor evaluation protocol has been refined extensively since its inception and is designed to maximize donor safety. This is achieved by thorough preoperative evaluation, proper donor education, and informed consent, while providing an opportunity for a donor to reconsider his or her decision.[7,11] In our institution, an independent donor advocate team has been established to ensure that the potential donor's best interests are served during the process of determining donor suitability from a medical, surgical, and psychological standpoint. Preoperative noninvasive imaging with computed tomographic angiography (**CTA**) or magnetic resonance angiography (**MRA**) to evaluate hepatic volume, vascular anatomy, and other intra-abdominal pathological states is crucial for surgical planning and has been shown to minimize donor morbidity and mortality.[12,13]

An accurate estimate of preoperative right- and left-lobe liver volume with correction for degree of steatosis is critical to the safety of the donor. Prolonged cholestasis and infection have been more prevalent in donors left with less than 30% of their original liver volume or those known to have more than 15% fatty change in the liver.[14,15]

Accurate CTA or MRA enables clear identification of the origin of the vessel supplying the medial segment of the left lobe of the liver (segment IV) so that this vessel can be preserved during procurement. With refinement of images obtained using CTA and MRA, many centers now perform celiac arteriography only in select cases. Branches derived from the right hepatic artery, which cross Cantle's line to supply the left lobe, are identified 15% to 30% of the time.[16,17] Segment IV receives the principle supply of these branches, and

From Live Donor Liver Transplantation, Department of Liver Transplantation and Hepatobiliary Surgery, Lahey Clinic Medical Center, Burlington; and Tufts University School of Medicine, Boston, MA.

Address reprint requests to Elizabeth A. Pomfret, MD, PhD, Director, Live Donor Liver Transplantation, Department of Liver Transplantation and Hepatobiliary Surgery, Lahey Clinic Medical Center, 41 Mall Rd, Burlington, MA 01805. Telephone: 781-744-2500; FAX: 781-744-5743; E-mail: elizabeth.a.pomfret@lahey.org

1527-6465/03/0910-2009$30.00/0

doi:10.1053/jlts.2003.50231

aggressive surgical dissection with disruption of these vessels is thought to contribute to the 5% incidence of donor bile leaks observed in LDALT.[16] Hepatic and portal vein anatomy is also carefully evaluated using three-dimensional computed tomographic imaging. Virtual resection planes and accurate liver volumes can be determined preoperatively to ensure that the anticipated graft is suitable for the recipient and minimizes donor morbidity. Careful preoperative assessment of donor arterial and venous anatomy is critical in avoiding complications in both donors and recipients.

Preoperative liver biopsy is suggested in potential donors showing mildly elevated liver enzyme levels, evidence of fatty infiltration of the liver by radiological imaging, body mass index greater than 28, or positive hepatitis B serological study results (surface and/or core hepatitis B antibody positive and surface antigen negative).[18,19] Transplant centers performing LDALT also should have the ability to allow donors to bank autologous blood before surgery to avoid banked blood transfusions.

Intraoperative Considerations

Despite extensive preoperative donor evaluation, intraoperative anatomic findings not previously appreciated or concurrent complications with anesthesia or surgery can result in termination of the donor hepatectomy. Aborted donor hepatectomy is a major complication and not currently captured in any database because no organ transplantation has taken place. Despite this, it is estimated that aborted donor hepatectomy may occur in 1% to 5% of cases.[20,21]

Variations from "normal" anatomy in the biliary tree are seen in up to 40% of all liver donors.[22] Intraoperative cholangiography, preoperative magnetic resonance cholangiography, computed tomography, and endoscopic retrograde cholangiopancreatography have all been used to assess biliary anatomy preoperatively in an attempt to prevent inadvertent ligation of significant branches draining the donor remnant liver or the graft. We have performed routine intraoperative cholangiography to evaluate biliary anatomy and guide the location of transection of the right hepatic duct to optimize the likelihood of a single bile duct for anastomosis in the recipient, while avoiding injury to the donor left hepatic duct.

Routine use of intraoperative ultrasound in conjunction with preoperative imaging is essential for identifying the course of the middle hepatic vein so that it can be preserved with the donor liver remnant. In the case of extended right donor hepatectomy, identification of the course of the middle hepatic vein is critical to guide the extent of resection because the middle hepatic vein will be included with the liver graft. Intraoperative ultrasound also has the advantage of allowing accurate identification of crossing branches from segments V and VIII draining into the middle hepatic vein, thereby preserving important vascular structures and minimizing blood loss. Techniques for parenchymal transection vary according to surgeon preference. Various surgical devices have been developed to aid the surgeon, and each claim specific advantages. These include the CUSA Ultrasonic Surgical Aspirator (Valleylab, Boulder, CO), Harmonic Scalpel (Ethicon Endo-Surgery, Somerville, NJ), and ERBE HELIX Hydro-Jet (ERBE, Marietta, GA). No prospective randomized trial comparing these devices exists; therefore, a recommendation suggesting superiority of one over the other cannot be made at the current time.

Postoperative Considerations

Avoidance of donor morbidity and mortality continues throughout the postoperative period. Minimizing donor morbidity is achieved best by impeccable postoperative management and nursing care, proper nutritional support, and careful donor follow-up after discharge. In our experience, most donors are intolerant of significant enteral nutritional intake for up to 5 days and are served best with total parenteral nutritional support. Given the rapid rate of liver regeneration during the early postoperative period, provision of adequate calories and protein avoids loss of skeletal muscle and may speed recovery. Alterations in phosphorus metabolism can lead to severe hypophosphatemia in the early postoperative period that is associated with potential neurological, cardiac, and pulmonary complications.[23] Aggressive repletion of phosphorous can avoid severe hypophosphatemia and may reduce complications.[23]

Routine use of prophylactic measures to avoid deep venous thrombosis and pulmonary complications are the mainstay of postoperative management in any surgical patient. Incentive spirometry, early ambulation, and physical therapy provide the best opportunity to avoid these complications.

Donor Morbidity

Reported morbidity rates after right-lobe liver donation vary widely. Although morbidity for right-lobe liver donation generally is considered to be low, many believe the true complication rate is underestimated.[10,11,24] In December 2000, The National Institutes of Health sponsored an international workshop reviewing the sci-

entific, medical, and psychosocial issues associated with LDALT in an attempt to improve the success and applicability of this procedure. An overall morbidity rate of 21% was estimated based on results of several large series of right- and left-lobe living donors in the world literature.[20]

Biliary tract complications were the most common and occurred in 3% to 8% of donors. Bile leaks and bilomas accounted for the majority of biliary tract complications; however, stenosis resulting from injury to the left and/or common bile duct was reported in 1% of donors. Other significant complications reported included portal vein thrombosis, pulmonary embolus, bowel obstruction, and incisional hernia.

A review of the US experience with LDALT presented at the 2000 American Transplant Congress reported a 4% biliary complication rate in donors who required surgical intervention, endoscopic retrograde cholangiopancreatography, or percutaneous catheter drainage of a postoperative biloma.[25] Surgical re-exploration was required in two patients for portal vein thrombosis and small-bowel obstruction. Seven donors (3%) had the donor hepatectomy aborted for unsuspected granulomatous disease (one patient), steatosis (two patients), prohibitive anatomy (two patients), cardiac dysfunction (one patient), and intraoperative hemorrhage (one patient). Additional complications reported in the donor population include neuropraxia, phlebitis, pressure sores, pleural effusion, pneumonia, pulmonary embolus, deep venous thrombosis, prolonged ileus, and incisional hernia.[25]

Beavers et al[10] reviewed the incidence of donor morbidity associated with right lobectomy in living donors for transplantation into adult recipients between 1995 and 2001. Reported complications in the right-lobe donor ranged from 0% to 67%, with a crude complication rate calculated to be 31% (54 events in 174 donors). The wide variation in complication rates among centers reflects the inconsistency in defining what constitutes a complication, with some centers reporting all adverse events and others reporting only major or life-threatening complications. Only three of the studies reviewed in this series provided duration of follow-up in donors, and most centers did not report aborted donor hepatectomy procedures or the incidence of readmission for the donor. On average, right-lobe donors spent 9.9 days in the hospital, returned to work 2.4 months postoperatively, and felt completely recovered by 3.4 months.[10]

A survey of 42 centers performing 449 LDALTs in the United States reported that 14 centers accounted for more than 80% of the total experience between 1997 and 2000.[26] Complications were experienced in 14.5% of donors, with a single donor death (0.2%) reported during this period. Subsequent to the completion of the survey, two additional donor deaths were reported and included in this publication. The first of these occurred in January 2002 at 3 days after right-lobe donation, and the second donor death was a suicide 2 years after donation that did not appear related to the liver-donation experience. Three donors were placed on the waiting list for liver transplantation from a deceased donor; however, only one of these donors received a transplant for a diagnosis of postdonation Budd-Chiari syndrome. Of the remaining two patients, one died before receiving an organ, and the other was removed from the list because of improvement in liver function. In this report, the investigators calculated a "catastrophic complication" rate of 0.4% (three deaths and one transplantation).[26]

Biliary leak or stricture complicated the postoperative course of 6% of donors, confirming previous reports.[26,27] Although long-term follow-up was not obtained in this study, 8.5% of donors were rehospitalized and nearly 5% required reoperation or nonautologous blood transfusion. The investigators acknowledged that underreporting of complications and the possibility of selection bias, with centers having poor outcomes choosing not to participate in the survey, may have occurred.[26]

To date, our center has performed 75 right-lobe donor hepatectomy procedures with no deaths and one aborted donor operation for an episode of severe bradycardia occurring on induction of anesthesia in an otherwise healthy 42-year-old donor who subsequently recovered without incident. It has been our practice to define a donor complication as any unexpected or untoward event and prospectively collect and record this information in a comprehensive database. Because any complication in a healthy donor is significant, both minor and major complications are recorded. Donors are monitored for 1 year postoperatively for surgical, medical, and psychiatric complications. Approximately 40% of right-lobe donors in our series experienced at least one complication.[11] Fortunately, most of these adverse events were minor and self-limited; however, several patients required additional invasive procedures, including surgery. Severe hypophosphatemia was a universal event among donors and may have contributed to some of the observed complications.[23]

A recent multicenter survey conducted in five Asian liver transplantation centers reported complications and long-term outcomes in 1,058 live donors; more than half of these were right-lobe donors (561 of 1,058

donors).[2] Although the overall morbidity rate was 15.8%, right-lobe donors had a greater incidence of complications (28%) and more serious complications compared with left-lateral segment (9%) and left-lobe donors (7.5%), respectively. The most common serious problem encountered in patients undergoing right-lobe donation was biliary complications; in particular, cholestasis, defined by a total bilirubin level greater than 5 mg/dL (7%), bile leak (6%), and biliary stricture (1%). Other serious complications included portal vein thrombosis (0.5%), intra-abdominal bleeding (0.5%), and pulmonary embolus (0.5%). Reoperation was necessary in 17 donors (1.1%) for small-bowel obstruction, biliary strictures, bile leak, bleeding, portal vein thrombosis, postoperative ileus, and incisional hernia. Only 15% of patients had follow-up longer than 3 months; however, 6 donors had residual morbidity, including 5 patients with biliary complications and 1 patient with chronic renal failure secondary to intravenous radiographic contrast. An additional patient experienced a sudden death while exercising 3 years postoperatively.[2]

The precise incidence of late complications in right-lobe donors is speculative because few, if any, studies exist reporting follow-up of donors beyond the first postoperative year. Furthermore, the impact of biliary strictures on lifetime risk for a donor to develop secondary sclerosing cholangitis necessitating future surgery and possible liver transplantation may take several decades to determine. The clinical significance of the observation that liver regeneration is a relatively protracted process in right-lobe liver donors is unclear.[11] In a prospective study from our center, liver regeneration in healthy donors was observed to continue throughout the first postoperative year, with only one donor achieving complete restoration of liver volume. Fortunately, liver function normalizes rapidly after liver donation, well before regeneration is completed. Only long-term follow-up of these donors will answer the question of whether complete restoration of liver volume is necessary to avoid future liver-related problems.

Donor Mortality

The exact number of live liver donor operations performed (left lateral segmentectomy and lobectomy) in the world is difficult to ascertain because no central reporting agency exists, but is estimated to be between 3,000 and 4,000 cases. A total of nine deaths have been known to occur worldwide (two deaths, in left lateral segmentectomy donors; seven deaths in right lobectomy donors), for an estimated surgical mortality rate between 0.2% and 0.3%. Three additional donors have undergone liver transplantation because of complications related to right-lobe donation.[2,4,28] Because the true denominator is not clearly defined, the incidence of catastrophic complications (death or need for transplantation) is imprecise, but estimated to be approximately 0.4% to 0.5%. Three deaths occurred in the United States (one death, left lateral segmentectomy; two deaths, right-lobe donors); five deaths, in Europe (one death, left lateral segment; four deaths, right-lobe donors; Dr C. Broelsch, Essen, Germany; personal communication, August 2003); and one death, in Japan (lobectomy donor[28]).

The first donor death reported in the world was related to a fatal pulmonary embolus occurring in an adult-to-child living donor liver transplantation and was reported in the literature in detail.[29] The first reported death in the United States was related to anaphylaxis secondary to medication, also in a left lateral segment donor. Three of the seven deaths in right-lobe donors (two deaths, the United States; one death, Europe) have been reported in the literature or discussed publicly.[1,4,6,30] The first death reported from Asia occurred recently in Japan in a woman who donated a lobe of her liver to her teenage daughter.[28] Unlike the two deaths reported in left lateral segmentectomy donors (pulmonary embolus and anaphylaxis), deaths occurring in right-lobe living donors have resulted from multiple organ failure and sepsis.

Although donor deaths have resulted from either technical failures or problems in the early postoperative period, these cases underscore the reality that living donation is associated with a small, but real, possibility of mortality that may approach 0.5%. Finally, the morbidity associated with right-lobe donation is significant and likely occurs in a third of all donors, emphasizing the need for a comprehensive database to precisely define true living donor morbidity and mortality.

References

1. Trotter JF, Wachs M, Everson GT, Kam I. Adult-to-adult transplantation of the right hepatic lobe from a living donor. N Engl J Med 2002;346:1074-1082.
2. Lo CM. Complications and long-term outcomes of living liver donors: A survey of 1508 cases in five Asian centers. Transplantation 2003;75(suppl):S12-S15.
3. Beavers KL, Cassara J, Russo M, Shrestha R. Practice patterns for long-term follow-up of adult-to-adult right lobectomy donors at US transplantation centers [abstract 1416]. Am J Transplant 2003;3(suppl 5):515A.
4. Surman OS. The ethics of partial-liver donation. N Engl J Med 2002;346:1038.
5. Cronin DC II, Millis JM, Siegler M. Transplantation of liver

grafts from living donors into adults—Too much, too soon. N Engl J Med 2001;344:1633-1637.
6. Malago M, Testa G, Marcos A, Fung JJ, Siegler M, Cronin OC, Broelsch CE. Ethical considerations and rationale of adult-to-adult living donor liver transplantation. Liver Transpl 2001;7: 921-927.
7. Pomfret EA, Pomposelli JJ, Lewis WD, Gordon FD, Burns DL, Lally A, et al. Live donor adult liver transplantation using right lobe grafts: Donor evaluation and surgical outcome. Arch Surg 2001;136:425-433.
8. Bak T, Wachs M, Trotter J, Everson G, Trouillot T, Kugelmas M, et al. Adult-to-adult living donor liver transplantation using right-lobe grafts: Results and lessons learned from a single-center experience. Liver Transpl 2001;7:680-686.
9. Marcos A. Right-lobe living donor liver transplantation. Liver Transpl 2000;6(suppl):S59-S63.
10. Beavers KL, Sandler RS, Shrestha R. Donor morbidity associated with right lobectomy for living donor liver transplantation to adult recipients: A systematic review. Liver Transpl 2002;8:110-117.
11. Pomfret E, Pomposelli JJ, Gordon FD, Erbay N, Price LL, Lewis WD, et al. Liver regeneration and surgical outcome of donors of right lobe liver grafts. Transplantation 2003;76:5-10.
12. Kamel IR, Raptopoulos V, Pomfret EA, Kruskal JB, Kane RA, Yam CS, Jenkins R. Living adult right lobe liver transplantation: Imaging before surgery with multidetector multiphase CT. AJR Am J Roentgenol 2000;175:1141-1143.
13. Lavelle MT, Lee VS, Rofsky NM, Krinsky GA, Weinreb JC. Dynamic contrast enhanced three-dimensional MR imaging of liver parenchyma: Source images and angiographic reconstructions to define hepatic arterial anatomy. Radiology 2001;218: 389-394.
14. Fan ST, Lo CM, Liu CL, Yong BH, Chan JK, Ng IO. Safety of donors in live donor liver transplantation using right lobe grafts. Arch Surg 2000;135:336-340.
15. Marcos A, Ham JM, Fisher RA, Olzinski AT, Posner MP. Single-center analysis of the first 40 adult-to-adult living donor liver transplants using the right lobe. Liver Transpl 2000;6:296-301.
16. Renz JF, Reichert PR, Emond JC. Hepatic arterial anatomy as applied to living-donor and split-liver transplantation. Liver Transpl 2000;6:367-369.
17. Stapleton GN, Hickman R, Terblanche J. Blood supply of right and left hepatic ducts. Br J Surg 1998;85:202-207.
18. Trotter JF. Thin chance for fat people (to become living donors). Liver Transpl 2001;7:415-417.
19. Pomfret EA, Pomposelli JJ, Jenkins RL. Live donor liver transplantation. J Hepatol 2001;34:613-624.
20. Shiffman ML, Brown RS Jr, Olthoff KM, Everson G, Miller C, Siegler M, Hoofnagle JH. Living donor liver transplantation: Summary of a conference at The National Institutes of Health. Liver Transpl 2002;8:174-188.
21. Pomfret EA. Outcomes after living donation-donors (Donor outcomes, complications, and quality of life). Presented at: American Transplant Congress; June 3, 2003; Washington DC.
22. Huang TL, Cheng YF, Chen CL, Chen TY, Lee TY. Variants of the bile ducts: Clinical application in the potential donor of living related hepatic transplantation. Transplant Proc 1996;28: 1669-1670.
23. Pomposelli JJ, Pomfret EA, Burns DL, et al. Life-threatening hypophosphatemia after right hepatic lobectomy for live donor adult liver transplantation. Liver Transpl 2001;7:637-642.
24. Inomata Y, Uemoto S, Asonuma K, Egawa H. Right lobe graft in living donor liver transplantation. Transplantation 2000;69: 258-264.
25. Marcos A. Review of the US experience with live donor adult liver transplantation. Presented at: American Society of Transplant Surgeons; May 13, 2000; Chicago, IL.
26. Brown RS Jr, Russo M, Lai M, et al. A survey of liver transplantation from living adult donors in the United States. N Engl J Med 2003;348:818-825.
27. Renz JF, Roberts JP. Long-term complications of living donor liver transplantation. Liver Transpl 2000;6(suppl):S73-S76.
28. Liver donor dies from postoperative complications in Japan. Transplant Week 2003 [serial online]. May 11, 2003; vol 4.
29. Testa G, Malago M, Broelsch CE. Living-donor liver transplantation in adults. Langenbecks Arch Surg 1999;384:536-543.
30. Kam I. Technical issues with donors and outcomes. Presented at: The Second International Symposium Dedicated to Expanding the Donor Pool: Living Donor and Split Liver Transplantation; August 26, 2000; Rome, Italy.