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Donor Complications Including the Report of One Death in Right-Lobe Living-Donor Liver Transplantation

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Key Words
Peptic ulcer · Portal vein thrombosis · Biliary fistula · Bilioma

Abstract
Background/Aims: Our objective is to assess donor complications in all right hepatic lobe living-donor liver transplantation (LDLT) at our center. ***Methods:*** Of a total of 352 liver transplantations performed, 60 were right-lobe LDLT. Most donors (88.3%) were related to the recipients. ***Results:*** Mean hospital stay was 5.4 ± 0.6 days. No complications occurred due to preoperative evaluation. Most donors received one or two units of autologous blood transfusion. Only 5 (8.3%) needed nonautologous blood transfusion. Most complications were minor and treated conservatively. Bile leaks from the cut surface of the liver occurred in 5 donors (8.3%). Two patients had potentially fatal complications: perforated duodenal ulcer and portal vein thrombosis (PVT). The donor with perforated ulcer developed septicemia and multiple organ failure. He was discharged from the hospital with hemiparesis due to cerebral ischemia. The patient with PVT remained asymptomatic and the portal vein was recanalized by the 3rd postoperative month. One donor died in the immediate postoperative period of cardiac arrest due to cardiac arrhythmia. ***Conclusion:*** Right hepatectomy for LDLT may be associated with significant morbidity, including death and it should be performed only by surgeons with great experience.

The first living-donor liver transplantation (LDLT) was performed by Raia et al. [1] in Brazil in 1989 to overcome the shortage of cadaveric organs for pediatric recipients. LDLT in children has become accepted worldwide in a few years and helped to reduce the mortality of patients on the waiting list [2]. Right lobectomy for adult-to-adult LDLT, a more complex and challenging procedure, was successfully performed by Yamaoka et al. [3] in Japan in 1994. This was followed by an extensive debate by the medical community regarding the safety and ethics of LDLT [4–8].

Due to the shortage of cadaveric donor and the elevated death rate on the waiting list, the number of LDLT has increased in 1990s. However, with recent reports of serious donor complications, including some deaths, the number of LDLT has reached a plateau and even a de-

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crease in some countries, such as the USA [9–11]. In Brazil, since the promulgation of the new transplantation law, the number of liver transplantation has increased from 131 in 1995 to 956 in 2005 [12]. The number of LDLT increased from 5 to 197 in this period [12]. Our objective is to present the donor complications of all adult LDLT performed at our institution, including the report of one death.

Patients and Methods

The protocol of this study was approved by the Research Committee of the University Hospital of the Federal University of Parana. Of a total of 352 liver transplantations performed at the Nossa Senhora das Graças and Clinical Hospitals of the Federal University of Parana, Brazil, from September 1991 to December 2005, 60 were adult-adult right-lobe LDLT. Our first adult LDLT was performed in January 2001.

Presurgical Evaluation

All donors presented voluntarily. After detailed explanation of all procedures and risks, including the risk of death, the donors were subjected to complete physical examination and laboratory tests. Imaging exams included magnetic resonance (MR) cholangiography and angiography. In the first 52 cases, conventional angiography was also performed routinely. In the last 8 cases, this exam was employed only in patients with more than one artery supplying the right lobe on the MR angiography. MR was also used to determine the volume of the right lobe and of the entire liver. Only donors with graft/recipient weight ratio >0.8% were accepted for transplantation. The lower limit of remnant liver volume was 30% of the whole liver. Hepatic biopsy was performed only in donors with a body mass index >28 kg/m^2 or in the presence of steatosis on imaging studies.

Donors with liver disease or significant co-morbidities were excluded. Presence of mild systemic disease was not necessarily a contraindication to donation. Five donors had hypercholesterolemia, 3 well controlled mild arterial hypertension, 2 diet-controlled diabetes mellitus, and 1 gastroesophageal reflux disease.

Complete psychological and social evaluations were performed on each donor. Ethical issues and potential psychological and social consequences of the donation were discussed in detail. After all the protocol requirements were fulfilled, written informed consent was obtained from the donors. Afterwards, the donation was approved by a district attorney when the donor was related to the receptor within the third degree of consanguinity and by a state judge when the donor was not related to the receptor, as required by Brazilian Federal Law. Two units of autologous blood were collected 1 and 2 weeks before the transplantation.

Operative Procedure

Donor hepatectomy was performed under general anesthesia, with a thoracic epidural catheter used for postoperative pain control. Central venous and arterial blood pressures and urinary output were monitored continuously during the procedure. Bilateral subcostal incision with upper midline extension similar to that performed on the recipient was employed.

The procedure began with a cholecystectomy. Intraoperative cholangiography was performed only in patients with biliary anomalies observed either on MR cholangiography or at operation. The right biliary duct was transected and its stump sewn. Bile leakage test with methylene blue injection through the cystic duct was not used. The right hepatic artery, the portal vein, and its right branch were isolated. The right lobe was mobilized, with care to leave the attachments of the left lobe intact in order to prevent future torsion. The inferior vena cava was dissected with ligation and section of accessory hepatic veins. Branches greater than 5 mm were preserved for subsequent anastomosis to the recipient inferior vena cava. The right hepatic vein was isolated.

The hepatic parenchyma was divided along Cantlie's line 1 cm to the right of the middle hepatic vein using electrocautery and ligatures, without temporary hilar inflow occlusion. Clamp fracture technique, harmonic scalpel (ultracision), and CUSA were used for parenchymal transection in 35 (58%), 16 (27%), and 9 (15%) donors, respectively. The vasculature to the right lobe was transected and the vascular stumps of the remaining liver were sewn over.

Postoperative Care

All donors were admitted to the intensive care unit for overnight monitoring. Laboratory tests were obtained at postoperative days 1, 2 and 4. The postoperative care was identical to that of a patient subjected to regular hepatectomy.

The electronic study protocols of all donors were reviewed to determine the demographics, duration of hospital stay, blood transfusion, and all complications. Morbidities were divided into four grades according to the classification of Broering et al. [14] that was designed for LDLT donors. Grade I is any complication that is not life-threatening, does not result in disability, and does not require a therapeutic invasive intervention or the use of drugs, except analgesics, antipyretics, anti-inflammatories, or antiemetic drugs. Grade II is any complication that is potentially life-threatening that requires the use of drug therapy or >1 foreign blood units, but that does not require a therapeutic invasive intervention and does not result in residual disability. Grade III is any complication that is potentially life-threatening that requires a therapeutic invasive intervention, the use of drug therapy/blood transfusions and/or leads to readmission in the ICU but does not result in residual disability. Grade IV is any complication with residual or lasting disability or that leads to death. Data are presented as mean ± SD.

Results

Donor demographics are shown in table 1. Most donors were male and their mean age was 33 ± 10 years. Seven donors were not related to the recipients. All 7 were close friends of the recipients for many years and had no expectation of monetary or any other direct or indirect benefit from the donors or their families, as required by Brazilian Federal Law. No complications occurred sec-

Table 1. Donor demographics

Number of donors	60
Sex	
Male	39
Female	21
Age, years	
Range	18 – 57
Mean ± SD	33 ± 10
Education	
Primary school	13
High school	33
College/University	14
Relation to the recipient	
Offspring	19
Sibling	10
Parent	9
Spouse	8
Nephew	4
Cousin	2
Uncle	1
Close friend	7

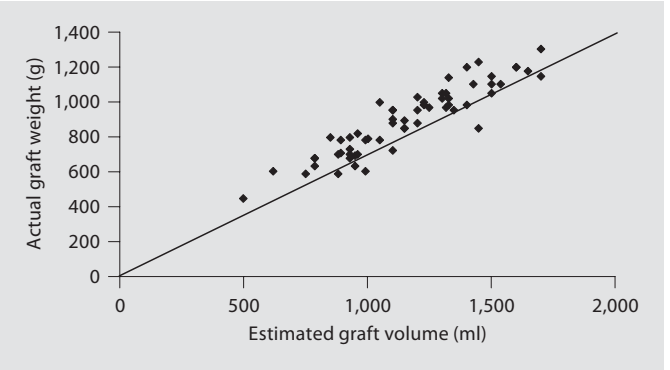

Fig. 1. Correlation between the estimated graft volume and actual graft weight.

Table 2. Intraoperative blood loss (ml) in groups of 10 donors each

Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
817 ± 444	730 ± 390	673 ± 333	588 ± 305	548 ± 219	553 ± 260

ondary to preoperative evaluation, including the imaging exams and liver biopsy.

Operative time from skin incision to closure varied from 170 to 250 min with a mean time of 195 ± 33 min. Mean hospital stay was 5.4 ± 0.6 days (range 4–68 days). The relationship between estimated graft volume and actual graft weight is showed in figure 1. The mean estimated graft volume was 1,159 ± 276 ml (range 500–1,700 ml) and the mean actual graft weight was 895 ± 198 g (range 450–1,300 g).

Table 2 shows the intraoperative blood loss in groups of 10 donors. The blood loss decreased from the first to the sixth group (p = 0.049). Thirty-eight (63.3%) donors received one or two units of autologous blood transfusion. Five (8.3%) required 1 or 2 units of nonautologous red blood cells transfusion in addition to the 2 units of autologous blood.

Donor complications are presented in table 3. Most complications were minor and treated conservatively. These complications included nausea and vomiting, superficial surgical site infection, pleural effusion, pulmonary atelectasis, and diarrhea.

The only peroperative complication was a pneumothorax secondary to subclavian catheter placement. The donor had an uneventful recovery after thoracostomy tube drainage.

Biliary fistula occurred in 5 donors (8.3%). Four of them had bile leakage exteriorized through the suction

Table 3. Donor complications[a]

Complication	n	%
Grade I[b]		
Nausea and vomiting	17	28.3
Superficial surgical site infection	8	13.3
Pleural effusion	5	8.3
Pulmonary atelectasis	5	8.3
Diarrhea	4	6.7
Grade II		
Biliary fistula treated conservatively	4	6.7
Pneumonia	3	5.0
Portal vein thrombosis	1	1.7
Duodenal ulcer	1	1.7
Grade III		
Duodenal ulcer	2	3.3
Incisional hernia	2	3.3
Pneumothorax	1	1.7
Biliary fistula treated with percutaneous drainage	1	1.7
Grade IV		
Perforated duodenal ulcer	1	1.7
Multiple organ failure	1	1.7
Death	1	1.7

[a] Some patients had more than one complication.
[b] Classification of complications for LDLT donors according to Broering et al. [14].

drain placed at hepatectomy. The amount of bile drained varied from 50 to 120 ml a day and the fistula closed spontaneously within 1–4 weeks. The other donor with biliary fistula returned after hospital discharge with nausea and vomiting, hyperthermia, and abdominal pain. Ultrasonography showed an abdominal collection of 300 ml, which was successfully treated by percutaneous drainage.

One donor developed asymptomatic portal vein thrombosis (PVT), diagnosed at the 4th postoperative day on routine color-flow duplex scanning. At operation, the portal vein trifurcated at the hilum of the liver. After transection of the anterior and posterior right branches, a moderate angulation between the portal vein and its left branch was observed. Blood flow was normal. The donor had an uneventful recovery, with no other complication. A duplex scanning performed at the 3rd postoperative month showed recanalization of the portal vein, with normal blood flow.

A donor presented with intense upper abdominal pain and sepsis on the 3rd postoperative day. At operation, a perforated duodenal ulcer was identified. Patch closure of the perforation was done. The patient persisted with septicemia for several days and had multiple organ failure and septic shock. The donor was discharged from the hospital at the 68th postoperative day with hemiparesis secondary to severe hypotension and cerebral ischemia. Another donor had a noncomplicated duodenal ulcer that was diagnosed on the 8th postoperative day and was successfully treated with proton pump inhibitor.

A 36-year-old female had an uneventful right hepatectomy. After tracheal extubation, she remained stable, with normal routine laboratory tests, including arterial blood gas analysis. Four hours later, she had hypoxia and tachycardia, followed by cardiac arrhythmia and cardiac arrest. She recovered after 10 min of cardiac resuscitation. A cerebral arteriography performed 2 days later confirmed the diagnosis of brain death. At autopsy, neither thromboembolism nor myocardial infarction was identified. All vascular and biliary duct stump sutures were intact. She had no history of previous cardiopulmonary disease.

Six donors (10%) were readmitted to the hospital after discharge because of dyspnea due to pleural effusion (n = 2), abdominal pain (n = 2), fever due to superficial surgical site infection (n = 1), and biliary leakage with bilioma (n = 1). Two patients needed reoperation for correction of an incisional hernia.

Discussion

Living donation has been employed to several organs transplants, including kidney, lung, small intestine, pancreas, and liver. Donor safety is the primary concern of living donor transplantation. Despite diligent donor selection and care, several complications, including death, have been reported following living donation of all these organs [13–17]. Donation of the right lobe is considered the riskiest for the donor of all other types of graft [14, 15].

Reported complications after right-lobe liver donation vary widely, from 0 to 100% [18, 19]. Fortunately, most complications are minor. However, major complications are not rare. Some donors may require additional invasive procedures, including surgery [13–16]. Catastrophic outcomes, such as death and need for liver transplantation, have been reported in the United States, Europe, Japan, and in other countries [11, 13, 18, 20]. In our series, we had one donor death caused by cardiac arrest due to cardiac arrhythmia. Although cardiac resuscitation was successful, she evolved to brain death. Technical complications were ruled out at autopsy.

The mortality rate after LDLT has been estimated to be between 0.2% and 1% [13, 15, 18, 21]. Donor mortality rate is lower in Japan. The first donor death occurred in that country only in 2003 after 2,300 LDLT had been performed (0.04%) [20]. Causes of donor death reported in the literature include sepsis, massive bleeding, liver insufficiency, pulmonary embolism, anesthetic complications, and multiple organ failure [9, 11, 18, 20].

Two other potentially fatal complications occurred in our series: perforated peptic ulcer and PVT. Despite immediate surgical treatment, the donor with perforated duodenal ulcer developed septicemia and multiple organ failure. After a long hospital stay he was discharged from the hospital with hemiparesis due to hypotension and cerebral ischemia. Other transplant groups have also reported the occurrence of peptic ulcer, including perforated ulcer in living liver donors. The rate of gastroduodenal ulceration in these series varied from 3 to 11% [22–24]. Our rate was 3.3%. Our 2 patients had neither history of peptic ulcer nor symptoms that suggested the diagnosis. Potential donors are not routinely subjected to upper gastrointestinal endoscopy in most institutions. Since severe peptic ulcer complications have also been reported by others in living liver donors, even after using routinely proton pump inhibitor, further prophylactic measures may be considered. Preoperative upper gastrointestinal endoscopy with search for *Helicobacter pylori*

in all donors should be considered as part of the preoperative protocol.

PVT is a potentially serious complication after liver transplantation, mainly in the immediate postoperative period. It may present with liver failure, splenomegaly, ascites, and gastrointestinal bleeding secondary to esophageal variceal rupture [25]. In our series, the donor who presented with PVT in the immediate postoperative period was asymptomatic. The diagnosis was established on a routine postoperative color-flow duplex scanning. The patient had an uneventful recovery with recanalization of the portal vein at the 3rd postoperative month. This donor had an anatomical variation of the portal vein, i.e. the portal vein trifurcated into anterior right, posterior right, and left branches. The cause of PVT in our donor was possibly due to a moderate kinking of the portal vein with its left branch that occurred after section of the two right branches at right hepatectomy. This angulation was underestimated by us because the blood flow remained normal at operation. At present, significant portal vein anatomical variation identified in the preoperative evaluation is a contraindication for donation in our institution. However, other authors do not exclude potential donors with portal vein trifurcation [28].

Anatomical variations of the portal vein are relatively common [26]. Some of these variations may exclude potential donors because of the significant increase in donor risk and recipient complications due to technical difficulty in vascular reconstruction [27]. Lee et al. [27] reported 9 cases of trifurcation of the portal vein in 214 right liver LDLT (4.2%). These authors described PVT in 2 donors with anatomical variations who were subjected to portal vein reconstruction at right hepatectomy for LDLT. A multicenter survey conducted in five Asian liver transplantation centers reported a 0.5% PVT rate in 1,058 live donors [17].

Intraoperative or postoperative bleeding may adversely affect the outcome of patients subjected to hepatectomy. Therefore, parenchymal transection with minimal blood loss is fundamental in right lobe grafting. Another adjunct to donor safety is to reduce transfusion of heterologous blood. Although nonautologous blood transfusion was not needed in some series [16, 18, 28], some authors have use it in up to 10% of patients [9, 10, 13, 15, 19, 23]. In the present series, most donors receive only 1 or 2 units of autologous blood transfusion. However, nonautologous red blood cells transfusion was needed in 8.3% of our donors.

Biliary tract complications remain one of the most common problems after living liver donation and they have been reported in from 0 to 38.6% of donors [13, 18]. Bile leakage and biliomas account for the majority of these complications. In our series, all cases of bile leakage were from the cut surface of the liver and were managed conservatively with drainage. However, endoscopic papillotomy and even surgical treatment may be necessary for some donors.

Other complications that occurred in our series included wound infection, pleural effusion, pneumothorax, pulmonary atelectasis, pneumonia, diarrhea, and incisional hernia. These complications are reported after any major abdominal procedure done under general anesthesia. Improvement in surgical technique, adequate donor selection, and appropriate postoperative care may significantly reduce perioperative morbidity [14].

In our series, the complications were limited to the perioperative period. Although donors were subjected to extensive evaluation, including invasive exams, such as percutaneous liver biopsy and angiography, no complications occurred as a result of the preoperative investigation. We have not observed long-term complications, but the potential for major complications clearly exists, especially stricture secondary to bile duct injury.

Our data suggest that LDLT should be performed only by surgeons with extensive experience with hepatobiliary surgery and liver transplantation. The procedure must be carried out with great caution because of the high risk of complications to the donor, including death.

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