Results of Surgery-Related Complications in Donors of Right Lobe Liver Graft: Analysis of 272 Cases

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ABSTRACT

Background. Living donor liver transplantation has been a new light of hope for patients with end-stage liver failure on the cadaveric waiting list. However, living donor liver transplantation still has ethical problems which cannot be overcome. Exposure of healthy donor candidates to major surgery which can be fatal is the largest of these ethical problems. In this study, we aimed to determine our rate of complications associated with surgery in donors who underwent right lobe donor hepatectomy.

Materials and Methods. Between September 2004 and December 2009, 548 liver donor candidates were examined. The right liver lobe donor hepatectomy was performed on 272 donor candidates who passed the elimination system. Demographic data as well as intra-operative findings, complication rates, and numbers were collected retrospectively. Donor complications were categorized according to the Clavien classification.

Results. Two hundred seventy-two donors who underwent right lobe donor hepatectomy were included in this study. One hundred sixteen (42.6%) of 272 donors were female, whereas 156 (57.4%) were male. There was no donor mortality. Grade 1 and grade 2 complications were observed in 105 (38%) of 272 donors. The most common complications were fever of unknown origin (20.9%) and prolonged hyperbilirubinemia (3.6%). Grade 3 complications and grade 4 complications were observed in 6 donors (2%) and 3 donors (1%), respectively. Three donors were underwent re-operation due to bleeding. The re-laparotomy rate in our series was detected as 1.10%. One donor, categorized as grade 4B according to the Clavien classification, had small bowel perforation and intra-abdominal sepsis secondary to mechanical bowel obstruction.

Conclusions. Donor mortality is a fact of living donor liver transplantation that cannot be ignored like donor morbidity. However, right liver lobe donor hepatectomy can be performed successfully with minimal complication rates with multidisciplinary and rigorous donor care in the preoperative and postoperative period.

IN 1989, the first successful living donor liver transplantation (LDLT) surgery gave a new hope to patients with end-stage liver failure who were on the cadaveric transplantation waiting list. In Asian countries, such as China, Japan, Korea, India, and Turkey, where the number of cadaveric donors is especially inadequate for religious reasons, liver transplantation is still conducted with living donors [1,2]. LDLT has distinct advantages compared to cadaveric liver transplantation, such as a directly available organ, the ability to perform surgery immediately after obtaining the liver transplant, and reduction of the occurrence of the primary organ dysfunction of short cold ischemia [3,4]. Despite all the advantages, LDLT has some ethical issues. The exposure of healthy donor candidates to...
major surgery which can be fatal is the greatest of these ethical problems. The chief concern of LDLT (described its’ “Achilles’ heel”) is donor safety. “Primum non nocere” (first do no harm) must be the basis of all LDLT. Today, there are multiple donor hepatectomy procedures. Among donor hepatectomy procedures, right lobe donor hepatectomy has the highest complication rate. After the operation of right lobe donor hepatectomy, a mortality rate of approximately 2% has been reported [5,6]. In this article, we aim to present surgery-related complication rates in donor candidates who underwent right lobe donor hepatectomy.

MATERIALS AND METHODS

Donors and Preoperative Evaluation

Donor candidates passed a 3-step elimination system defined by James F. Trotter [7] and used in many transplantation centers. In our center, we are using a modification of Trotter’s elimination system. Similarly, donor candidates must be between the ages of 18 and 60 years old and, according to hospital policy, the donor candidate must have a relationship with the recipient within the third degree of consanguinity. The potential donor candidates must be in excellent physical condition. In addition, donor candidates must be voluntary. In our center, donor candidates were evaluated by a team that included psychiatrists, psychologists, and psychiatric nurses after a detailed physical examination and medical examination. After the evaluation, in the case of detection of factors such as ambivalence, guilt, depression, substance abuse, fear of the future due to the economic concerns, family, and environmental pressure, the donor candidate is excluded from the elimination stages. Endoscopic retrograde cholangiopancreatography and hepatic angiography, which are performed as part of Trotter’s elimination stages, are not applied routinely in our center. While the graft removed must be of sufficient size for the recipient, the most important feature of donor hepatectomy is that enough of the liver must remain after surgery so as to not cause liver failure in the donor. Therefore, in our center, volumetric measurements of the liver were performed preoperatively using computed tomography imaging methods [8]. The computed tomography procedure for identification of liver volumetry and hepatic vascular anatomy is as defined by Orgu et al [9]. The retro-reconstructed images were transferred to a dedicated workstation (GE Advantage Windows 2.0) for 3-D and volumetric studies. For each case, segmentation was constructed by a radiologist on the set of helical images to select liver parenchyma and suppress adjacent organs. Liver biopsy is not routinely performed in our center. Liver biopsy was only performed when the potential donor’s body mass index was 28 or greater and when, in the presence of abnormal liver function test results, the recipient who was diagnosed with autoimmune hepatitis, primary sclerosing cholangitis, or primary biliary cirrhosis had a consanguine relationship with the donor [10,11]. However, the candidates who could pass all steps were accepted as living donors and underwent surgery.

Surgical Procedure

A bilateral low Kocher’s incision was used with an upper midline limb up to and through the xiphisternum (Mercedes incision), Invasive monitrization including central venous catheterization, nasogastric tube, arterial line, and urethral catheterization is applied to all donors undergoing right lobe liver hepatectomy. First-generation cephalosporin (cefazolin sodium, 1 g) is used for antibiotic prophylaxis. For right lobe donor hepatectomy, after the mobilization of the right lobe, the right inferior and short hepatic veins were ligatured, starting from the caudal face toward the right hepatic vein, and dissected from the liver vena cava. With the insertion of the penrose drain from the avascular tunnel, placed between the inferior vena cava and the liver, the liver hanging maneuver known as “liver hanging” (defined by Belghiti) was performed [12]. Hilar dissection began with the dissection of the Calot triangle. After cholecystectomy, a stent, which allows the performance of intraoperative cholangiography, was placed in the cystic duct. The right portal vein and right hepatic artery were dissected and suspended. In our center, hepatic artery and the portal vein variations are not contraindications to donation. For cases in which the segment 4 artery is derived from right hepatic artery, the right hepatic artery is cut from the distal part of the distinction of the segment 4 artery to avoid ischemia [13,14]. For the determination of the transection line, the right portal vein and right hepatic artery were temporarily clamped. To minimize blood loss during transection, central venous pressure is maintained at less than 5 mm Hg. For parenchymal transection, a crush clamp technique was applied to all the donors. Donor safety is a priority, but in some situations, such as when the right hepatic vein diameter is small, the remnant liver volume is more than 30%, or separate venous drainage of segment 4 is detected, the middle hepatic vein can be included in the graft to allow lesser hepatocyte damage and obtain better early graft function [15]. After parenchymal transection, intra-operative cholangiography was performed and the location of the bile duct transection was determined. Similar to the vascular system, biliary anatomic variations other than biliary hypoplasia (Alagille syndrome) do not prevent a candidate from becoming a donor in our center [16]. Low-dose heparin (dalteparin sodium injection; Pharmacia, Canada, 60 U/kg) was systemically applied before removal of the graft. The graft was perfused through the portal vein with histidine-tryptophan-ketoglutarate solution while removed from the abdomen.

Postoperative Care

As in all major surgery, the hepatectomy donors were monitored closely during the postoperative period. A nasogastric tube inserted during the operation was removed when bowel movements became normal. Prophylactic antibiotic administration that was started during the perioperative period was usually stopped in the 24th hour of the postoperative period. The devices applying intermittent compression on the lower extremities were maintained until the donor became mobile. During the first week, when remnant liver regeneration is the fastest, liver function tests (aspartate aminotransferase [AST], alanine transaminase [ALT], alkaline phosphatase, gamma glutamyl transferase, total and direct bilirubin, and pro-thrombin time), renal function tests (urea, creatinine), blood electrolytes (sodium, potassium, calcium, chloride), and complete blood count parameters were checked on a daily basis. On the 1st and 7th days after surgery, abdominal Doppler ultrasonography was performed to determine the blood flow of the remnant liver and intra-abdominal collections. Donors come to the controls after being discharged from the hospital at the 1st, 2nd, 3rd, 6th, and 12th months of the operation. The routine controls are often finished after the first year.

Statistical Analysis

Data analysis was performed using SPSS for Windows, version 17. Categorical variables were expressed as frequencies and percentages. Continuous data were presented as mean. The differences
between groups were compared using the Student t test. The categorical data was analyzed using Pearson’s chi-square test where appropriate. A P value of less than .05 was considered statistically significant.

RESULTS
Donor Data and Preoperative Evaluation
In our center, between September 2004 and December 2009, 548 donor candidates were evaluated to become liver donors. One hundred forty-eight (27%) of these candidates were removed from the process during the first step of the elimination procedure. The most common reason for rejection during the first step was age (5.8%), and lack of kindred bonds (8.7%). During the second step, 118 (21.5%) donors were eliminated due to a lack of donor volume, psychological factors, and the presence of newly diagnosed disease as a result of detailed investigations in 50 (9.1%), 38 (6.9%), and 30 (5.4%) prospective donors, respectively. During the last step, 10 (1.8%) donors were excluded as a result of the identification of steatosis detected by liver biopsy. As a result, 49.7% of 548 donor candidates became donors with appropriate criteria.

In this retrospective study, 272 donors were included who underwent right lobe liver donor hepatectomy between September 2004 and December 2009 at Ege University Faculty of Medicine, Department of Organ Transplantation. Of those donors, 116 (42.6%) were female, whereas 156 (57.4%) were male. The mean age and the mean body mass index of donors were 29.1 years (range, 18 to 53 years) and 23.6 years (range, 16 to 32.50 years), respectively. Donors had a relationship with the recipient within the third degree of consanguinity. Donors had first-degree, second-degree and third-degree consanguinity relationships with 162 (59.6%), 41 (15.1%), and 69 (25.4%) patients, respectively. Although there was history of abdominal surgery in 58 donors, the most frequent prior surgical treatment was appendectomy. One hundred seventeen donors (43%) underwent preoperative liver biopsy without complication. In preoperative volumetric studies, the mean total liver volume was found to be 1404 ± 235 mL (range, 894 to 2329 mL), whereas the mean right lobe volume was found to be 850.12 ± 168.59 mL (range, 450 to 850 mL). The mean left lateral segment volume was found to be 248 ± 56.26 mL (range, 130 to 430 mL) and the mean left medial segment volume was 290 ± 87.67 mL (range, 99 to 623 mL).

Intraoperative Results
Preoperatively, storage of autologous blood was not made for donor candidates. The intraoperative findings are summarized in Table 1. During the transection of the liver parenchyma, one donor developed intraoperative cardiac arrest that responded to resuscitation. Hyperpotassemia was identified as the cause of cardiac arrest. The donor candidate, whose hepatectomy procedure was stopped, was removed from the study. This donor’s tomography-guided average weight of the right liver lobe volume was 850.12 ± 168.59 mL, but after removal of the right lobe, the average weight calculated decreased to 792.35 ± 145.15 g (paired t test P < .001). In our series, the remnant liver volume was less than 30% in only 2 (0.73%) donors. Although in 53 (19.4%) donors, the remnant liver volume was between 30% and 40%, in 106 (39.7%) donors this rate was between 40% and 45%. It has been detected that in 69 (25.3%) and in 40 (14.7%) donors, the remnant liver volumes were between 45% and 50% and 50% and 65%, respectively. The remnant liver consisted of, on average, 44% of the total liver volume (range, 26% to 65%).

Postoperative Status
The most common complication in our series is considered a grade 1 complication according to the classification of Clavien: for some patients there was a fever table that was not connected to any infective focus and was observed within the first 3 days after operation. This fever table categorized as “fever of unknown origin,” whose highest value detected was 38.2, was found in 57 (20.9%) donors in our series. The mean duration of hospital stay for donors after the surgical procedure was 9.47 days (range, 5 to 50 days). The researchers noticed that liver function tests (ALT and AST) after the operation on the first postoperative week, the mean AST value determined as 130.47 U/L (range, 80 to 973 U/L), the mean ALT value was 286 U/L (range, 49 to 961 U/L). During the first postoperative week, the mean AST and ALT values decreased to 54 ± 22.1 U/L and 86 ± 33.5 U/L, respectively.

Blood bilirubin values were observed to increase from postoperative days 3 through 5, but usually decreased to normal limits within a week. In our series, mean bilirubin value was determined on postoperative day 3 as 3.74 ± 2.4 mg/dL (range, 0.37 to 14.26 mg/dL). However, some donors had slightly higher bilirubin values than the normal range during their hospital stay. In our series, the mean bilirubin level decreased to 1.8 ± 2.04 mg/dL during the first postoperative first. In 69 donors (25.3%), the total bilirubin level during the first week after surgery was found to be 2.1 ± 0.7 mg/dL. Prolonged bilirubin levels in these donors that, other laboratory data were within normal limits and

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**Table 1. Surgery and Graft Profile**

<table>
<thead>
<tr>
<th>Operation time (min)</th>
<th>295.06 ± 60.23 (160 to 480)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (mL)</td>
<td>600 ± 120 (100 to 2000)</td>
</tr>
<tr>
<td>Transfusion requirement</td>
<td>0.0147 (0 to 3)</td>
</tr>
<tr>
<td>Crystalloid replacement (mL)</td>
<td>2581 ± 779.03 (1000 to 5000)</td>
</tr>
<tr>
<td>Preoperative right lobe volume (mL)</td>
<td>850.12 ± 168.59 (450 to 850)</td>
</tr>
<tr>
<td>Graft weight (g)</td>
<td>792.35 ± 145.15 (450 to 1315)</td>
</tr>
<tr>
<td>Right-lobe grafts with a middle hepatic vein</td>
<td>10 (3.7%)</td>
</tr>
<tr>
<td>Graft-to-recipient weight ratio (%)</td>
<td>1.13 ± 0.43 (0.58 to 2.5)</td>
</tr>
</tbody>
</table>

*The values are expressed as the mean (range).
Fig 1. The graphical analysis of the results of postoperative aspartate aminotransferase (AST, top left), alanine aminotransferase (ALT, top right), serum total bilirubin (middle), INR (lower left), and platelet (lower right) are shown.
acid or encephalopathy were not observed, was connected with liver dysfunction. It has been determined that total bilirubin values in these donors decreased to normal range in the postoperative third-month controls.

Prothrombin time (international normalized ratio [INR]) reached its highest value 1 to 2 days after surgery, decreasing gradually over the following days. The mean INR was found to be $1.5 \pm 0.33$ (range, 0.96 to 4.50) during the first postoperative day, and $1.16 \pm 0.193$ during the first week. The platelet count decreased to its lowest value on the second or third day after surgery, and then gradually increased after the third day. Whereas the mean platelet value decreased to $170,263 \pm 466,636/mm^3$ at the third postoperative day, it increased to $235,066 \pm 191,354/mm^3$ at the first week. Postoperative laboratory results are summarized in Fig 1. There was no donor mortality in our study. For a variety of reasons, three donors required additional surgery during the early postoperative period (within the first 2 days after the operation). The re-laparotomy rate in our series was found to be 1.10%. The donor categorized as grade 4B according to the Clavien classification scheme, had small bowel perforation and developed intra-abdominal sepsis secondary to mechanical bowel obstruction. Segmental small bowel resection surgery was performed on this donor. In the two liver donors, a liver failure table responding to medical therapy and characterized by encephalopathy and high total bilirubinemia was observed. A modified Clavien classification scheme is described in Table 2. Postoperative complications are summarized in Table 3 and categorized according to that scheme.

**DISCUSSION**

Although the vast majority of donor hepatectomy procedures are performed trouble-free, donor deaths have been reported in hospitals in Asia and Europe. Although the exact number of deaths is unknown, the number of cases involving donor deaths is increasing as the procedure becomes widespread. In 2003, Brown et al reported three cases of donor death [17]. In the largest study published so far, the number of donor deaths and the incidence of donor mortality were found to be, on average, 19% and 0.2%, respectively [18]. Among donor hepatectomy surgical procedures, right lobe donor hepatectomy has the highest rate of morbidity and mortality. According to the literature, after right lobe donor hepatectomy, donor complication rates vary; however, in some studies, the rate of complications increases up to 60% [19,20]. The reason for the discrepancy between the reported rates of complications is that some facilities are hesitant to report donor deaths, some report only major complications, and some include of all minor and major complication rates [21,22]. Today, a modification of the Clavien classification system is used to standardize the recording of complications of donor and liver transplantation in data banks such as the European Liver Transplant Registry (ELTR) and the United Network for Organ Sharing (UNOS), which were established to store this information [23]. Using the Clavien classification scheme, donor complications after right liver lobe surgery occur in

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Postoperative Complications</th>
<th>Count</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever of unknown origin</td>
<td>57</td>
<td>20.9</td>
<td></td>
</tr>
<tr>
<td>Pneumonothorax (treated conservatively)</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Atelectasis</td>
<td>5</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Skin wound infection</td>
<td>5</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>3</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Radial nerve palsy (temporary)</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Minor bile leakage (treated conservatively)</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Hypertrophic scar</td>
<td>3</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Prolonged hyperbilirubinemia</td>
<td>10</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Duodenal ulcer bleeding (treated conservatively)</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>5</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Abdominal wall bleeding</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Incisional hernia requiring operative repair</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal bleeding (with necessity of foreign blood unit transfusions)</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Liver failure (temporary)</td>
<td>2</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Small bowel obstruction and perforation (septisemia)</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>41.1</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Classification of Complications According to the Clavien System

- **Grade 1**: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
- **Grade 2**: Complications requiring pharmacological treatment with drugs other than such allowed for grade 1 complications. Blood transfusions and total parenteral nutrition are also included.
- **Grade 3**: Complications requiring surgical, endoscopic, or radiological intervention.
- **Grade 3A**: Intervention not under general anesthesia
- **Grade 3B**: Intervention under general anesthesia
- **Grade 4**: Life-threatening complications (including central nervous system complications) requiring intensive care unit stay.
- **Grade 4A**: Single organ dysfunction (including dialysis)
- **Grade 4B**: Multorgan dysfunction
- **Grade 5**: Death of the patient
15.8% of cases, on average, including 6,000 donors from Asia [24]. The main factors responsible for loss of the donor are liver failure and sepsis [25]. In our study, we found grade 4 complications in three right lobe living donors (1.1%). Transient liver failure occurred in two donors. The small volume of the remaining remnant liver, excessive intraoperative blood loss, and intraoperative anesthetic management were responsible for liver failure after donor hepatectomy [26]. In the other donor with a grade 4 complication, a perforation of the small intestine secondary to mechanical bowel obstruction was treated with a segmental resection of the small intestine, and sepsis developed. According to the reports of centers in the United States, Japan, and Korea, the most common problem after right lobe donor hepatectomy is biliary tract complication. Bile leakage is often found along the surface of the cross-section; its incidence ranged from 0% to 38.6% and is approximately 6.2% on average [27,28]. The incidence of bile leaks and bile duct strictures requiring treatment is approximately 4% [29]. In our series, whereas bile leakage that improved with conservative treatment occurred in two donors, bile duct stenosis was found in none of the donor candidates during follow-up examination. The biliary complication rate in our study was 0.7%, which is markedly lower than that in other studies. To minimize injury to the bile duct, we determined not to leave any segment of the liver undrained, to avoid cautery as much as possible in the hilar plate, to reveal the intrahepatic bile duct with intraoperative cholangiography, and to close the residual biliary limb with 6/0 or 7/0 monofilaments.

Intraoperative and postoperative bleeding is another common cause of liver morbidity. Different techniques were used to avoid blood loss, especially during the liver transection stage, which sees the most blood loss for the transection of the liver; the crush clamp technique was used in all cases. In our study, intraoperative bleeding was measured, on average, as 600 mL, similar to data found in the literature [30]. We think that the clamp crush technique is a safe and inexpensive choice for donor surgery. During the postoperative period, we found postoperative bleeding in four (1.4%) liver donors. Although two had bleeding from the abdominal wall, the other two donors were re-explored. In one of these donors, the bleeding was found to be from the biliary tract, in the other it was found to be from the vena portal vein. In our series, three donors (1.1%) were re-operated due to bleeding and sepsis during their period of hospitalization, and two donors (0.7%) were re-operated more than 1 year after surgery due to an incisional hernia. The incidence of reoperation during hospitalization was found to be 1.1%, similar to data found in the literature [20]. Other complications after donor hepatectomy are urinary tract infections, wound infections, pneumonia, and pleural effusion. These are categorized as grade 1 and 2 complications in the Clavien classification system and their incidence is up to 28% [24,30]. In our study, grade 1 and 2 complications occurred in 87 (31.75%) and 16 (5%) donors, respectively. In our study, grade 1 and 2 complication rates were higher than the data found in the literature, with fevers of unknown origin (20.9%) and prolonged hyperbilirubinemia (3.6%) the most common complications observed. Unlike the description of Dondero et al, in our series, the frequency of pleural effusion (3.1%) was very low and there was no need for thoracocentesis in any donor [31]. Major problems, defined as grade 3 or 4 complications, occurred in a total of 9 (3.3%) donors. The average hospital stay was 9.4 days, in accordance with the literature [32]. No donor mortality was observed in our study.

To conclude, the rate of complications in our series is similar to that in other studies. Hepatic failure, bile leakage, and sepsis were the most dangerous and fatal complications in our study as previously described in detail. Donor right hepatectomy procedure requires great care and attention during the donor selection process, surgery, and the postoperative period. The margin of safety should be kept very narrow in right lobe liver donors.

REFERENCES