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| **ARTICLEDonor Postoperative Biliary Complications After Living-Donor Liver Transplant****Abuzer Dirican, Cengiz Ara, Koray Kutluturk, Mustafa Ozsoy, Mustafa Ates, Adil Baskiran, Burak Isik, Sezai Yilmaz** |
| ***Objectives:* Although the main factors responsible for donor deaths after living-donor liver transplant are liver failure and sepsis, the most common donor complications are associated with the biliary tract.*****Materials and Methods:* Between April 2006 and May 2012, five hundred ninety-three donors underwent living-donor hepatectomy procedures for living-donor liver transplants. The mean age of donors was 31.0 ± 9.9 years and the ratio of men to women was 341:252. Of all donors, 533 (89.9%) underwent a right lobe hepatectomy, 45 (7.6%) underwent a left lateral segmentectomy, and 15 (2.5%) underwent a left hepatectomy.*****Results:* Biliary complications were observed in 51 liver donors (8.6%). Based on the Clavien-Dindo classification, grade I and grade II complications were 3.2% and 0%, while grade IIIa and grade IIIb complications were observed in 3.5% and 1.85% of cases. Right lobe donor biliary complications occurred at the rate of 8.2% in 44 donors. Grade IV and grade V complications were not observed. Grade IIIa complications necessitating radiologic and endoscopic procedures were observed in 21 liver donors (3.5%). Bile leakage unresponsive to medical therapy was detected in 19 donors (3.2%). Nasobiliary catheters were placed in 3 of 19 donors and internal stents were placed in 1. Two sessions of balloon dilatation were performed in the 2 grade IIIb donors (0.33%). Biliary strictures observed in 2 right lobe donors and 1 left lobe donor was treated by hepaticojejunostomy an average of 14 months after surgery.*****Conclusions:* Avoidance of intraoperative issues and early recognition of bile leakage are fundamental in preventing complications in living-donor liver transplant donors.****Key words:** Liver failure, Sepsis, Bile leakage, Hepatectomy, Postoperative follow-up**Introduction**Transplant is the only known curative treatment option for patients with end-stage liver insufficiency.1 Organs from live donors have provided a new form of hope for those who need liver transplants. Living-donor liver transplants offer the advantages of direct organ availability compared to deceased-donor transplants, the ability to conduct the procedure under optimal conditions, and a reduced rate of primary organ dysfunction due to short-term cold ischemia.2 However, living-donor liver transplants also give rise to some ethical concerns. Donor hepatectomy is the only surgical procedure that exposes the patient to a major and possibly fatal operation with no benefit to the donor, while providing the possibility of saving the recipient’s life.3 Liver transplants were first conducted in pediatric patients with liver disease, using the parents of the patients as donors. The low rate of donor complications, high success rates in liver transplant recipients, and emotional satisfaction of the parents served to attenuate the ethical issues in pediatric liver transplants.4 This success achieved in pediatric liver transplants has paved the way for adult living-donor liver transplants which are characterized by the removal of 30% to 60% of the total volume of the donor's liver. Adult living-donor liver transplants had become widespread until the first donor death in 2002.5Despite geographic variations, today liver transplants are generally performed using live donors; thus, donor survival should be given the highest priority with consideration to ethical issues. Although the actual donor mortality rate is unknown, 19 donor deaths were reported in the largest series of patients to date and the average incidence of mortality was 0.2%.6 A common data bank of donor complications has not yet been created and complication rates are discussed based upon the experiences of individual centers. According to the literature, donor complication rates vary after right lobe donor hepatectomy, and in some studies the rate of complications are reportedly as high as 60%.7The reason for discrepancies between the reported rates of complications is that not all hospitals are consistent in their reporting methods regarding donor deaths, major complications, or the inclusion of all minor and major complication rates.8Hence, standardization of donor complications requires use of the modified Clavien-Dindo classification, and use of liver transplant databases, such as the European Liver Transplant Registry and the United Network for Organ Sharing, are required for storing the results.9 Although multiple donor hepatectomy procedures have been described, right and left lobe hepatectomy and left lateral segmentectomy are the most commonly applied. Liver insufficiency and sepsis are commonly deemed responsible for donor deaths; however, the most common complications encountered in liver donors are those associated with the bile ducts.10 For this reason, biliary complications are the main cause of morbidity after living donor hepatectomy.11 Unresolved biliary complications may lead to sepsis, multiorgan failure, and death. The aim of the present study was to present donor bile duct complications based upon the Clavien classification in a live donor liver transplant cohort.**Materials and Methods**Between April 2006 and May 2012, the outcomes of hepatectomies performed for the purpose of living-donor liver transplants were reviewed. All protocols conformed to the ethical guidelines of the 1975 Helsinki Declaration and were approved by the ethics committee of the institution and informed consent was obtained. Donor candidates were required to be > 18 and < 60 years of age, in excellent physical conditions, and have a relationship with the recipient within the third degree of consanguinity. In addition, willingness to be a donor candidate must have been fully voluntary. Donor candidates were evaluated by a team at our center which included psychiatrists and psychiatric nurses. If the evaluation revealed the existence of factors such as ambivalence, guilt, depression, substance abuse, fear of the future due to economic concerns, or family and environmental pressure, the donor candidate was excluded from further consideration. After psychiatric evaluation, donor candidates were required to pass a 3-step elimination system defined by James F. Trotter12 and used in many transplant centers. Briefly, in the first phase, a clinical assessment and laboratory and serologic tests were applied. All donors were assessed routinely for blood group, hemogram, biochemistry values, viral serology, and blood and urine culture. In the second phase, abdominal Doppler ultrasound was initially performed to obtain preliminary information related to vascular structure and hepatic steatosis for all liver donor candidates. Multislice-computed tomography was then used to determine the degree of fatty liver and accurate liver vascular anatomy in liver donor candidates based on any pathology revealed by the Doppler ultrasonography.13,14 In addition, volumetric measurements of the liver were performed preoperatively using computed tomography imaging methods according to procedures for identification of liver volume and hepatic vascular anatomy as defined by Orguc and associates.15The retro-reconstructed images were transferred to a dedicated workstation (GE Advantage Windows 2.0, General Electric Medical Systems, Milwaukee, WI, USA) for 3-dimensionaland volumetric studies. For each case, segmentation was constructed by a radiologist on a set of helical images to select liver parenchyma and suppress adjacent organs. In the third phase, a liver biopsy was performed when the potential donor candidate’s body mass index was ≥ 28 and when, in the presence of abnormal liver function test results, the recipient was diagnosed with autoimmune hepatitis, primary sclerosing cholangitis, primary biliary cirrhosis, and had a consanguine relationship with the donor.16 Endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiopancreatography, and hepatic angiography, which take place in Trotter elimination stages, are not applied routinely in our center. Potential donors with a mismatched blood group, positive viral serology, or hepatosteatosis rate > 20% were rejected. In our center, vascular and biliary anatomic variations of the liver do not constitute a contraindication for donor selection.**Operative technique**The detailed surgical technique of living donor hepatectomy has been previously described.17 Cholangiography was routinely used for anatomic assessment of bile ducts during surgery at the beginning of the operation, after parenchymal transaction to determine the location of the bile ducts, and to evaluate the remnant bile duct after removing grafts in questionable cases. Transection of the bile duct was always initiated after parenchymal transaction was completed (Figure 1). A donor hepatectomy can be avoided if a hemodynamically unstable recipient dies during the operation. Also, after parenchymal transection the field of view is sufficient to enable dissection of the hilar plate. To avoid damaging the bile duct, transection must be at least 2 mm from the remnant bile duct and performed in a single action. The remnant bile duct is then closed with a double layer of 6-0 nonabsorbable polypropylene suture. Biliary leakage from the closed stump or from the transection margin is checked twice by saline and methylene blue injection into a cystic duct catheter immediately after stump closure.**Postoperative care, follow-up, and data collection**The patients were followed-up at least 1 post-operative day in the intensive care unit to reveal any bleeding complication, especially during the early period. Prophylactic antibiotic administration initiated in the perioperative period was usually discontinued 24 hours after surgery. The postoperative first day early enteral nutrition was started for the patients. Devices applying intermittent compression in the lower extremities were used until the donor became mobile. In the first week, when remnant liver regeneration is the fastest, liver function tests (aspartate transaminase, alanine transaminase, alkaline phosphatase, gamma glutamyl transferase, total and direct bilirubin, prothrombin time), renal function tests (urea, creatinine), blood electrolytes (sodium, potassium, calcium, chloride), and complete blood count parameters were checked on a daily basis. The epidural catheter placed for analgesia was removed if bleeding parameters were within normal limits. Low-molecular weight heparin was not used routinely. If no abnormal situations occurred during postoperative follow-up and physical examinations, and if drainage was < 50 mL, abdominal drains were removed. On the first and seventh days after surgery, abdominal Doppler ultrasonography was performed to determine the blood flow of the remnant liver and any intra-abdominal collection.Donors were evaluated at follow-up visits after being discharged from the hospital on the 1st, 3rd, 6th, and 12th months after surgery. These routine visits were often discontinued after the first year. Donors were instructed to return if they had any complaints or abnormalities at any point during the follow-up. Liver donors developing any complications related to the biliary tract continued to be followed routinely every 3 months with phone calls and clinic examinations. In an effort to decrease the incidence of biliary complications, bilirubin content in drain effluent was routinely measured if any doubt existed until the content was less than the serum bilirubin level. Minor bile leaks were monitored carefully as they usually resolved spontaneously; however, if the patient became symptomatic based on clinical and/or laboratory measures, an abdominal computed tomography scan and/or magnetic resonance cholangiopancreatography was done immediately. Having all of the information of a given donor, a detailed discussion took place between the surgeon, endoscopist, and an interventional radiologist aimed at reaching a consensus on the appropriate intervention; that is, an ultrasound-guided aspiration, endoscopic retrograde cholangiography, percutaneous transhepatic dilatation, or surgery. Cases treated by ultrasound-guided aspiration and insertion of a pigtail catheter were followed by abdominal ultrasound. The decision to remove the pigtail was made when the amount draining was < 1.67 fl oz (50 mL)/day for 2 successive days with abdominal ultrasound documenting complete disappearance of any abdominal collection. Donor demographic data, graft type, postoperative outcomes, and postoperative biliary complications classified according to the modified Clavien classification system8 were recorded from our prospectively maintained database.**Results**During the study period, 593 donors underwent living donor hepatectomy for living-donor liver transplant. The mean age of donors was 31.0 ± 9.9 years. The ratio of men to women was 341:252. The procedures performed included, 533 right lobe donor hepatectomies (89.9%), 45 left lateral segmentectomies (7.6%), and 15 left hepatectomies (2.5%). The mean follow-up was 342 ± 8.1 days. Because of the differences in the number of patients in donor procedure groups, to better analyze demographic, intraoperative, and postoperative follow-up results, the left lateral segmentectomies and left lobe donor hepatectomies were evaluated as a single group.**Graft data and intraoperative results**The mean operation time in donors who underwent right lobe donor hepatectomy procedures was 370 ± 68.2 minutes. The mean graft weight was 28.29 ± 4.77 oz (792 ± 133.5 g), and the remnant liver volume comprised a mean 33% ± 4.5% of the total liver volume in right lobe liver donors. The mean length of stay in the intensive care unit for right lobe donors was 1.2 ± 0.4 days, and the mean length of stay in the hospital was 17.7 ± 14.2 days. In liver donors who underwent left lobe and left lateral segmentectomy procedures, the mean operation time was 340.5 ± 68.2 minutes, and mean graft weight was 11.71 ± 4.39 oz (328 ± 123 g). The mean length of stay in intensive care for this group was 1.2 ± 0.4 days, and the mean length of hospital stay was 8.2 ± 7.4 days. Demographic donor data for the hepatectomy procedures, as well as intra and postoperative follow-up results are summarized in Tables 1 and 2.**Postoperative donor biliary complications**The rate of donor bile duct complications at our center was 8.6% and included 51 liver donors. According to the Clavien-Dindo Classification, the rate of grade I complications was 3.2%, the rate of grade II complications was 0%, the rate of grade IIIa complications was 3.5%, and the rate of grade IIIb complications was 1.85%. The rate of isolated right lobe bile duct complications was 8.2% in 44 donors. We encountered no instances of grade IV or grade V complications related to the bile ducts. Based on conservative follow-up, grade I complications involving bile leakage occurred in 19 liver donors, including 17 that underwent right lobe hepatectomy (3.18%), and 1 each had a left lobe hepatectomy (1.6%) and a left lateral segmentectomy (1.6%). There were no donors in the Clavien grade II category, which is regarded as controlled sepsis.The rate of complications in the Clavien grade IIIa group treated by radiologic and endoscopic interventions was 3.5% involving 21 liver donors. Clavien grade IIIa complications were encountered in 18 (3.37%) right lobe hepatectomy liver donors, 2 left lobe hepatectomy donors (4.4%) and 1 left lateral segmentectomy (6.6%). Bile leakage was found in a total of 19 liver donors (3.2%) (3 liver donors in the left lobe and left lateral group and 16 liver donors in the right lobe hepatectomy group) that did not recover with medical therapy. These donors underwent endoscopic retrograde cholangiopancreatography and endoscopic sphincterectomy due to bile leakage. Among the donors that underwent endoscopic sphincterectomy, 3 underwent nasobiliary catheter insertion and 1 underwent internal stent application. In addition, ultrasound-guided aspiration and catheter insertion was performed in 6 liver donors that were found to have intra-abdominal fluid collection. Two donors (0.33%) with grade IIIb complications underwent endoscopic retrograde cholangiopancreatography and 2 sessions of balloon dilatation percutaneous transhepatic cholangiography. A total of 11 liver donors (1.85%) required conventional surgery under general anesthesia (9 right lobe [1.68%], 1 left lobe [2.2%], and 1 left lateral segmentectomy [6.6%]). The left lateral segmentectomy donor could not be regulated by interventional measures and therefore underwent conventional surgery involving primary suturing and insertion of a biliary draining tube.Among the right lobe donors, 9 underwent surgery for drainage of intra-abdominal fluid collection that persisted despite endoscopic and therapeutic measures. Bile leakage in liver donors in the left lateral and right lobe groups completely ceased on the second day after surgery. Biliary strictures were found in 2 donors in the right lobe group and 1 donor in the left lobe group at 14 ± 3 months after surgery that did not respond to endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography. In all 3 of these donors, the stricture in the bile duct was above the level of the cystic duct, and the basic clinical finding was jaundice. Reconstruction of the bile ducts was planned for donors that remained unresponsive to therapeutic procedures. Hepatico-jejunostomy was performed with conventional surgery, and simultaneous intraoperative liver biopsy did not reveal liver damage associated with the bile ducts in any of the donors. According to current data, the incidence of bile leakage in this series of patients was 7.7% involving 46 donors, and the rate of biliary stricture was 0.8% in 5 donors (Table 3).**Discussion**The number of liver transplants being performed is rapidly increasing. This curative procedure, which is the only known treatment option for end-stage liver failure, has led to the search for additional organ sources to meet increasing graft needs. The possibility of living-donor liver transplant surgery has provided a ray of hope to patients with end-stage liver failure waiting for deceased-donor transplants. Despite its advantages, living-donor liver transplants have some ethical issues; the main one being donor safety, as the exposure of healthy donor candidates to major surgery can be fatal adiposes significant ethical problems.18 Liver donor candidates are subjected to multiple screening steps before being accepted. The most important aspect in the donor elimination system involves determining whether donors have enough information describing these surgical procedures that could have deleterious intra- and postoperative outcomes. Therefore, the consent form received from liver donor candidates before surgery is important.19 Although donor hepatectomy has been performed around the world, no definite conclusions can be reached regarding the frequency of donor complications. In a review of 131 donors by Middleton and associates, the rate of donor complications was reported to range between 0% and 100%, and the mean donor complication rate was 16.1%.20The Clavien-Dindo classification of donor complications was introduced into clinical practice in recent years, and Shah and associates reported a 37% donor complication rate using this method,21 and in a study by Chan, using the Clavien-Dindo classification, the adult donor complication rate was reported to be approximately 20%.22 Donor com-plications most commonly occur in the postoperative period. As mentioned previously, complication data are based on the results of single centers; however, published studies are available in the literature which discuss donor complication reasons, prevalence, and association with graft type.Donor death is the most catastrophic donor complication, and liver insufficiency and sepsis are the most common factors implicated.17,23 However, donor complications occurring after surgical site infections (5.8%) are typically associated with the bile ducts.24 In research reported by Middleton and associates that evaluated 131 studies, the donor biliary complication rate was found to be 13.5%.20 More comprehensive reviews report a donor biliary complication rate of 6.2% with a range between 0% and 38.6%.11 Lower complication rates in the range of 2% to 5% were reportedly related to the bile ducts; however, these studies were mainly comprised of left lateral donor hepatectomy procedures involving segments 2 and 3.25 The rate of biliary complications varies considerably between donor hepatectomy procedures, (ie, from 10%-12% for right lobe procedures and 2%-4% for left lobe procedures).26,27 Anatomic variations in the bile ducts, presence of multiple bile ducts, a large transection surface, and extensive dissection of the right hepatic artery below the main bile duct are the major reasons for the high rate of biliary complications after right lobe donor hepatectomy procedures.28 In the current series, the rate of complications related to the bile ducts was 8.6% in 51 patients, which is high compared with other donor hepatectomy series.However, with the exclusion of 19 donors with grade I complications, the rate dropped to 5.3%. The high rate of grade I complications appears to be associated with the meticulous attention taken inherent in donor hepatectomy procedures and inclusion of even suspected cases. However, a high rate of grade III complications was found to be associated with transplants performed in the first 14 months after our center began conducting live donor liver transplants. Thus, the learning curve inherent to all major surgeries may be responsible for the high complication rates in the current series. There was no statistical difference between donor hepatectomy procedures in our series in terms of biliary complications. Despite the visual difference between graft types and biliary complications in our series, the lack of statistical significance was primarily attributed to the imbalance in the number of patients allocated to our study groups. Bile leakage from the cut surface is responsible for the majority of intra-abdominal collections after donor hepatectomy operations. The incidence of bile leakage from the resected surface is known to range from 0% to 38.6% (average 6.2%).29 The cut surface in right and left lobe hepatectomies is larger compared to that in left lateral segmentectomy procedures; thus, bile leakage from the cut surface is more common in these operations. Furthermore, the difficulty level of the procedure during caudate lobe transection and open bile ducts due to a large number of anatomic variations are implicated in bile leakage.30 However, some studies did not report a significant difference between hepatectomy procedures in terms of bile leakage.31 The incidence of bile leakage and biliary stenosis requiring therapy is known to be approximately 4%.32 The incidence of bile leakage requiring therapy in the current series of patients was 4.5% (27 donors) which appears consistent with the literature.The incidence of biliary stenosis was 0.8% (5 do-nors), which is considerably lower than that reported in the literature. In our center, biliary transection occurs after intraoperative cholangiography is performed after parenchymal transection. Some centers that perform biliary transection before parenchymal transection report that parenchymal transection would be faster and safer with this technique. Some other centers perform biliary transection after completion of two-thirds of the anterior parenchymal transection.33 According to the studies conducted in these centers, the timing of biliary transection was not associated with biliary complications. However, recipient death or other serious complications on the interface of biliary transection can occur as described by Nadalin and associates.34Biliary transection is performed after parenchymal transection at our center to avoid the orphan graft phenomenon and intraoperative donor biliary reconstruction. Closure of the remnant bile ducts after the removal of the graft is considered to be another important factor responsible for decreasing complication rates. At our center, open bile ducts of the remnant liver are closed with 6-0 nonabsorbable polypropylene double layer continuous sutures after completion of the transaction. Although there are no prospective studies on the closure of bile ducts with single interrupted or continuous sutures, as a general principle, sutures must be placed on the remnant bile ducts in a manner to avoid tissue ischemia. Uncontrollable bile leakage from the bile duct stump and donor mortality associated with resultant sepsis are known complications.32 Administration of 0.9% sodium chloride or Methylene blue are considerably effective in determining possible bile leakage. Routine testing with the administration of sodium chloride and Methylene blue from the cystic duct is performed at our center after graft removal. Our surgical principles to minimize bile duct injuries include not leaving a liver segment without drainage, avoiding cautery as much as possible in the hilar plate, visualization of intrahepatic bile trees using intraoperative cholangiography, and closure of the bile stump with 6-0 and 7-0 monofilament sutures.Early recognition of bile leakage and avoiding intraoperative causes are the foundations for preventing complications. Treatment of biliary complications after donor hepatectomy procedures involves conservative follow-up, endoscopic retrograde cholangiography, ultrasound-guided aspiration, and conservative surgery. In the current series of patients, 4 liver donors underwent conventional surgery due to biliary complications. In the early period, 1 liver donor underwent surgery due to bile leakage from the cut surface, and a biliary draining tube was inserted into the bile ducts after primary suturing of the leaking bile duct. In the long-term, 3 liver donors underwent surgery because of biliary stenosis that did not respond to medical or radiologic therapeutic procedures. In these 3 donors, bile ducts were reconstructed by hepaticojejunostomy. The follow-up of liver donors that developed biliary complications beyond the routine schedule is ongoing. The clinical findings and biopsy exam-inations in these donors did not suggest liver injury that would cause episodes of cholangitis or secondary biliary cirrhosis.The main bile duct may course between the anterior and posterior branches of the right hepatic artery in certain anatomic variations. The anatomic variation involving early branching of the right hepatic artery was found in 4 donors in the current series. With regard to donor safety as the cornerstone of the donor hepatectomy procedure, the anterior and posterior branches of the right hepatic artery should be cut separately and a double arterial anastomosis should be performed in the recipient interface. However, the diameter of the anterior and posterior branches was extremely narrow in 2 liver donors in our series and reconstruction was not possible. In these 2 donors, full-thickness transection of the main bile duct was initiated and reconstruction was performed over a biliary draining tube. The situation in these 2 donors was contrary to the donor safety principle; however, no complications occurred in the short-term or long-term related to the bile ducts.Transection of the donor bile ducts to optimally elucidate the vascular anatomy of the graft is disputable. We consider that donor trials with a follow-up of 2.5 years will contribute to the discussion on this common issue experienced by many donors and recipients. Follow-up of our donor patients is continuing and further complications will be documented. The main factors responsible for donor death are liver failure and sepsis especially due to uncontrollable bile leakage. All donor hepatectomy procedures require great attention and care preoperatively during the donor selection process, intraoperatively, as well as postoperatively during follow-up. |  |