Evaluation of surgical complications in 204 live liver donors according to the modified Clavien classification system

Amr M. Aziz, Sherif Saleh, Hossam E. Soliman, Hany Shoreem, Osama Hegazy, Mohamed Taha, Emad H. Salem, Hazem Zakaria, Sameh Hamdy, Hesham Abdeldayem, Tarek Ibrahim, Khaled Abuelella

Department of Hepatopancreaticobiliary and Liver Transplantation Surgery, National Liver Institute, Menoufia University, Menoufia, Egypt

Correspondence to Amr M. Aziz, MD, Department of Hepatopancreaticobiliary and Liver Transplantation Surgery, National Liver Institute, Menoufia University, 32511 Shebin El-Koom, Menoufia, Egypt, Tel: +20 114 999 9664; fax: +20 482 234 586
e-mail: amraziz055@yahoo.com

Received 29 March 2016
Accepted 1 May 2016

The Egyptian Journal of Surgery
2016, 35:357–366

Background Several large centers have reported outstanding outcomes of living donor liver transplantation in decreasing mortality on the liver transplant waiting list. Nevertheless, living donor liver transplantation is not without risk to the volunteer donors. The rate of complications differs widely among transplant centers. Yet, there is no consensus on how to define and stratify complications by severity.

Participants and methods This retrospective study to identify and analyze the surgical outcomes of 204 consecutive living donor hepatectomies was carried out between April 2003 and October 2013 by using the modified Clavien classification system, according to which grade I=minor complications, grade II=any deviation from the normal postoperative course requiring pharmacologic treatment, grade III=complications requiring invasive treatment, grade IV=complications causing organ dysfunction requiring ICU management, and grade V=complications resulting in death.

Results

The present study included 129 (63.2%) males and 75 (36.8%) females, with the donor's mean age being 27.72±6.4 years (range: 19–45 years). There were 64 (31.4%) donors who developed postoperative complications, with a total of 74 complications. Ten (4.9%) donors had more than one complication. Twenty-nine (39.2%) donors had Clavien's grade I complications, 38 (51.3%) donors had Clavien's grade IIIa, six (8.1%) donors had Clavien's grade IIIb complications, and there was one (0.5%) case of mortality (Clavien's grade V).

Conclusion

Donor hepatectomy is a relatively safe procedure when performed by a dedicated and well-trained team. A prompt diagnosis and meticulous intervention is considered the first priority whenever a donor complication is expected. Furthermore, a continuous standardized reporting and a comprehensive database are crucial to precisely define true donor morbidity.

Keywords:
Clavien's system, donor complications, living donor liver transplantation

Egyptian J Surgery 35:357–366

1110-1121

Introduction

Living donor liver transplantation (LDLT) was first initiated in children in 1989 in response to a severe organ shortage of pediatric donors [1,2]. LDLT has become an acceptable alternative for patients in need of liver transplantation, who are not likely to receive a deceased donor liver transplant in a timely fashion. This is seen especially in countries with severe shortage of cadaveric livers due to social customs and religious and cultural beliefs, such as in Japan, Egypt, Korea, and India [3].

Despite the satisfactory results of LDLT, there is some concern about the donor deaths, and uncertainty about recipient outcomes. The increased number of LDLTs have resulted in the reported cases of mortality and uncertain outcomes, particularly with right lobar LDLT compared with live kidney donation [4,5]. The complication rate after right liver donation is ~31% (range: 0–67%) [6–10]. The estimated surgical mortality is 0.2–0.3% [5].

It was, therefore, agreed that the rate and severity of recipient and donor complications in different centers should be described according to universally accepted evaluation parameters like the multitier grading system developed by Dindo *et al.* [11].

In this study, we retrospectively identified and analyzed the surgical outcomes of LDLT according to the multitier grading system developed by Clavien for the consistent description of surgical complications.

Participants and methods

The current study wasapproved by The National Liver Institute Ethical Committee including a total of 208 donors whowere prepared for donation in LDLT. Whenever there were conflicting results between the images and liver biopsy, laparoscopic assessment was carried out to reassess the liver morphology just before donation. In this context, 16 (7.8%) donors underwent laparoscopic assessment. The procedure was aborted for four (2%) donors due to unsatisfactory gross appearance of the liver. Therefore, this study included 204 hepatectomies of LDLT whose operations and follow-up were carried out at the National Liver Institute, Menoufia University, from April 2003 to October 2013.

Donor selection

Potential donors to be included in the study had to be healthy volunteers between the ages of 18 and 45 years. Donors needed to have normal liver function and no medical comorbidities. Donor safety was of a paramount concern.

We had a separate and dedicated team to evaluate each potential donor medically, surgically, emotionally, psychologically, and financially. Donors were fully informed about the complications that may occur, even death, so that there was no element of coercion. Potential donors were informed from the outset that they could back out at any time, right up to the time they underwent anesthesia. They were to be formally offered a 'medical out', and others would keep the reason the potential donor changed his or her mind confidential.

Initially, only relatives were allowed to be donors. More recently, donors have included friends, colleagues, and even people completely unknown to the recipient (good Samaritan living donors). Active smokers were not considered for donation. Truly committed potential donors agreed to stop smoking, often with medical assistance, to decrease their own increased perioperative risks. For females, oral contraception was temporarily stopped perioperatively as well. A BMI greater than 30 was considered at least a relative contraindication to donation.

Donor evaluation

The donor was evaluated by a multidisciplinary team that included a hepatologist, surgeon, radiologist, and a social worker. Additional consultations, including psychiatry, were considered on an individual basis as needed. Complete laboratory evaluation, including blood-type testing, serum electrolytes, liver function tests, complete blood count, kidney function test, serologies, virological assays for hepatotropic viruses [hepatitis C antibody, hepatitis B surface antigen, hepatitis B core antibody, HIV antibody, Epstein–Barr virus immunoglobulin G (IgG) and immunoglobulin M (IgM), cytomegalovirus IgG and IgM] and ceruloplasmin, α 1-antitrypsin, serum iron, transferring, and ferritin, was carried out. The donors had to have a compatible, but not necessarily identical, blood type with their intended recipients. Screening for subclinical coagulation disorders such as heterozygous factor V or protein S and C deficiency and antithrombin III was also performed. Calculations of BMI, abdominal ultrasound, ECG, and chest radiograph were carried out for all donors.

Eligible donors proceeded to further imaging studies, including 3-mm slice computed tomography (CT) scanning, for the exclusion of any unrecognized intra-abdominal pathology. A CT scan was also used for volumetric analysis of graft size matching (graft weight to recipient body weight ratio was not to be lower than 0.8–1% and the remaining liver volume for the donor had to be not <35%) as previously reported [12], detecting vascular variations or parenchymal changes. Magnetic resonance cholangiography was used to delineate the biliary anatomy.

Donor operation

The surgical techniques for various types of donor operations have previously been described in detail [13–17]. During the operative procedure, care was taken to adhere to the standard steps. In case of right lobe donation, the procedure was initiated by dissecting the anterior aspect of the cava from the right lobe till it encircled the right hepatic vein, followed by carrying out cholecystectomy and intraoperative cholangiography, and then dissecting the right hepatic artery and the portal vein. In case of left lateral segmentectomy, the procedure was initiated by dissecting the left lobe ligament and exposing the left and middle hepatic veins (MHVs), followed by dissecting the left hepatic artery and the portal vein. Parenchymal transection was carried out without any hepatic vascular occlusion using harmonic scalpel, cavitron ultrasonic surgical aspirator, and bipolar diathermy.

For the first 94 donors, the bile duct stump was closed using continuous (running) 0/6 Prolene sutures,

(Ethicon Inc., a subsidiary of Johnson and Johnson, produced in Cornelia, Georgia, USA), whereas for the next 46 donors, the bile duct stump was closed using interrupted 0/6 Prolene sutures. The rest of the donors' bile duct stumps were closed using a newly designed technique by our team of the National Liver Institute in the form of closure of the duct stump by interrupted 0/6 Prolene and reinforcing by the application of a surgical metallic clip (small or medium sized) just below the suture line [18]. Before closure, an intraoperative cholangiogram was repeated to check the anatomy of the remaining biliary tree.

Follow-up

Intrahospital donors' care was assured with special attention paid to any developed complication. On discharge, the follow-up protocol included visits every 2 weeks for the first 2 months, monthly visits for the subsequent 4 months, and then yearly for 5 years. Additional visits outside the routine follow-up were taken up when required. During each visit, routine abdominal ultrasound, complete blood count, and liver function tests were carried out.

The donor's preoperative, intraoperative, and postoperative data were collected and maintained on a secure database. The postoperative complications among liver donors were analyzed according to the modified Clavien's classification system (Table 1) [11].

Statistical analysis

Data were presented as mean±SD and range where appropriate. Comparisons between groups were carried out by using Fisher's exact test and the one-way ANOVA test. A *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using the SPSS software (version 21; SPSS Inc., Chicago, Illinois, USA).

Results

Donors' mean age was 27.7±6.4 years (range: 18–45 years). We included 129 (63.2%) males and 75 (36.8%) females in the present study. The mean BMI was 25.2 ±3.53 kg/m^2 (range: 17.7–35 kg/m^2). According to ABO blood group compatibility, there were 145 (71%) donors with identical ABO blood group, whereas in 59 (29%) donors blood groups were compatible to the recipient. The demographic criteria of the donors as well as the relationship between the donor and recipient are presented in Table 2.

Liver biopsy was performed as a routine investigation in all donors. One hundred and sixty-one (79%) donors had histologically normal liver, whereas 12 (6%) donors showed steatosis less than 10% and 31 (15%) donors showed minimal to mild periportal fibrosis (Table 2). In addition, nine donors with steatosis had BMI more

Table 1 Classification of surgical complications based on the modified Clavien system

Grade	Definition
I	**Any deviation** from the normal postoperative course without the need of pharmacological treatment or surgical, endoscopic and radiological interventions
	Allowed therapeutic regimens are : drugs as anti emetics , antipyretics , diuretics, electrolytes and physiotherapy
	This grade also includes wound infections opened at the bed side
II	Requiring pharmacological treatment with **drugs other than allowed for grade I**
	Blood transfusion and total parentral nutrition are also included
III	**Requiring surgical, endoscopic or radiological intervention**
	Intervention not under general anesthesia
	Intervention under general anethesia
IV	**Life threatening complications (including CNS complications*)requiring IC/ICU management**
	Single organ dysfunction (including dialysis)
	Multiorgan dysfunction
V	**Death** of the patient

Table 2 shows demographic data of the donors

Demographic data	
Age	
■ Mean+SD	27.72 ± 6.4 years
■ Range	18–45 years
Sex	
■ Male	129 (63.2%)
■ Female	75 (36.8%)
BMI	
■ Mean+SD	25.2 ± 3.53 kg/m^2
■ Range	17.7–35 kg/m^2
Blood group	
■ Identical	145 (71%)
■ Compatible	59 (29%)
Donor relation to recipient	
■ Off springs to their parents	N = 62 (31.9%)
■ Son	(n = 46)
■ Daughter	(n = 19)
• Siblings among each other	N = 37 (18.1%)
■ Brother	(n = 25)
■ Sister	(n = 12)
• Nephews & nieces to their uncle or aunt	(n = 22) 10.8%
• Wives to their husbands	(n = 13) 6.4%
• Cousins	(n = 11) 5.4%
• Uncle	(n = 2) 1%
• Unrelated donor	(n = 23) 11.3%
Liver biopsy	
• Histologically normal liver	161 (79%)
• Minimal to mild Periportal fibrosis	31 (15%)
• steatosis <10%	12 (6%)

than or equal to 25 kg/m^2, and three donors with steatosis had BMI less than 25 kg/m^2.

According to the age and weight of the recipients, the type of grafts was determined before the operation. Right lobe grafts represented the majority of the grafts procured: 150 (74%) grafts were the right lobe without the MHV, 11 (5%) grafts were the right lobe with MHV, and only one (0.5%) graft was posterior segments (VI and VII). On the other hand, left lobe grafts were procured in 42 cases: 27 (13%) grafts were the left lateral segments, three (1.5%) grafts were the left lobe without MHV, and 12 (6%) grafts were the left lobe with MHV. Table 3 shows the type of the graft, the calculated and actual graft weight, and the calculated and actual Graft weight to recipient body weight ratio (GRWR).

The remaining liver volumes of the donors were thoroughly assessed by using a preoperative CT volumetry. The mean remaining liver volume was 37.7% (range: 28–93%). After hepatectomy, there were 11 donors who had remaining liver volume of less than 33%, two of whom had remaining liver volume of less than 30%.

Table 3 shows operative and postoperative data of the donors

Type of the graft	
• Right lobe without MHV	151 (74%)
• The right lobe with MHV	10 (5%)
• Posterior segment (segments VI & VII)	1(0.5%)
• Left lateral segment	29 (14%)
• Left lobe with MHV	10 (5%)
• Left lobe without MHV	3 (1.5%)
Calculated graft weight	
• Mean+SD	864 ± 251 gm
• Range	115–1306 gm
Actual graft weight	
• Mean	767 ± 248.2 gm
• Range	110–1250 gm
calculated GRWR	
• Mean+SD	1.21 ± 0.37
• Range	0.8–3.3
Acutal GRWR	
• Mean+SD	1.23 ± 0.6
• Range	0.6–4.3
Operative time	
• Mean +SD	6:40 hours
• Range	(3:35–13:55 h.)
blood loss	
• Mean +SD	522 ± 419 ml.
ICU stay	
• Mean +SD	3.5 ± 2.3 days
Hospital stay	
• Mean +SD	11.5 ± 8 days
• Range	(6–70 days)
Follow up	
• Mean +SD	35.2 ± 25 months
Absenteeism from job	
• Mean +SD	6 ± 2 weeks

Using CT portography, 191 (93.6%) donors were found to have no portal vein anomalies, whereas in 13 (6.4%) of them, there were trifurcated portal vein types I, II, and III.

Regarding the hepatic arteries, 177 (86.8%) donors had normal anatomy, whereas 27 (13.2%) donors had anatomic variants as accessory right hepatic artery (HA) from superior mesenteric artery (SMA) in five cases, accessory left HA arising from left gastric artery in two cases, right HA arising from SMA and left arising from the celiac trunk in seven cases, aberrant left HA from left gastric artery in four cases, two right HA (middle from left HA) in three cases, left HA arising with separate origin from the celiac trunk in two cases, three left HA (one from left gastric, two from left HA) in one case, right, middle (to segment IV), and left HA in one case, two separate small left HA with separate origin in one case, and extrahepatic division of right HA in one case.

Regarding the hepatic veins, 156 (76.5%) donors had normal hepatic veins, with no anatomic variants, whereas in 48 (23.5%) donors, there were some anatomic variants such as large segment VIII vein from MHV in eight cases, right posterior vein to inferior vena cava (IVC) in 10 cases, right inferior vein to IVC in 14 cases, two right inferior vein to IVC in two cases, large segment V vein from the MHV in five cases, both large segment V and VIII veins from the MHV in one case, large segment VIII vein plus right inferior vein in three cases, large segment VIII vein from the MHV plus right posterior vein in one case, large segment V plus right inferior vein in two cases, right, middle, and left hepatic veins from one trunk in one case, and liver transplantation and MHVs (one trunk) in one case.

Regarding the number of bile duct after intraoperative cholangiography, there were 130 (63.7%) grafts that had only one bile duct, whereas 68 (33.3%) grafts had two ducts, six (3%) grafts had three ducts, and only one graft had four ducts to be anastomosed in the recipient.

The mean operative time of donor hepatectomy was 6:40 h (range: 3:35–13:55 h) and the mean blood loss was 522±419 ml. Intraoperative complications occurred in eight (4%) donors. Mild to moderate bleeding occurred in five (2.5%) donors, and was

successfully controlled without any residual complications. Two (1%) donors had an iatrogenic bile duct injury: the first one (0.5%) had partial injury to the left hepatic duct with immediate primary repair and stent placement, whereas the second one (0.5%) had an injury to a sectorial duct to segment IV from the right hepatic duct with intraoperative anastomotic repair by duct-to-stump of the right duct. Unfortunately, one (0.5%) donor suffered severe bleeding and, thereafter, developed postoperative portal vein thrombosis (PVT) and died 12 days later.

Postoperatively, the mean ICU stay was 3.5±2.3 days, and the mean hospital stay was 11.5±8 days, with a range of 6–70 days. The mean period of absence from work was 6±2 weeks (Table 3). The mean follow-up period was 35.2±25 months, with a minimum of 3 months.

Postoperatively, 64 (31.4%) donors developed 74 complications. Ten (4.9%) donors had more than one complication. Biliary complications represented the most frequent ones and were reported in 30 (14.7%) donors. Biliary leak occurred in 28 (13.7%) donors and biliary stricture in two (1%). The frequency of biliary complications significantly differed according to the graft type. They occurred in 24 (11.8%) donors of the right lobe and in six (3%) of the left lobe grafts ($P<0.0001$). Biliary complications were managed as follows: four cases with biliary leak improved on conservative treatment (operative drain), 18 cases underwent US-guided percutaneous drainage with pigtail catheter, seven cases underwent endoscopic retrograde cholangiopancreatography (ERCP) and stent insertion (two of these endoscopically treated donors had biliary stricture), and one donor had a major biliary leak, which was treated surgically, 1 month later, by using Roux-en-Y hepaticojejunostomy.

The second most common complication was the intra-abdominal collection, which was detected in 13 (6.4%) cases: two cases were treated with single US-guided aspiration, four cases with several US-guided aspirations, and seven cases with pigtail insertion.

The third most common complication was minimal to mild pleural effusion, which occurred in 11 (5.4%) donors and was treated conservatively. The fourth most common complication was wound infection, which developed in 10 (5%) cases, and necessitated treatment by additional antibiotics other than the prophylactic ones.

Reoperation was reported in six (2.9%) donors. Three donors underwent relaparotomy on the same day of surgery because of postoperative bleeding: the first one from the stapler line of the right hepatic vein, the second one from the arterial branch from the hilar plate dissection beside the bile duct, and the third one from the cut surface of the liver leading to hematoma. All bleeding sites were successfully controlled. The fourth donor had a compromised main portal vein flow after closure of right portal vein stump, relaparotomy, and portal vein reconstruction with vascular stent. The fifth donor had a major bile duct leak, which needed a Roux-en-Y hepaticojejunostomy. The sixth donor had repair for incisional hernia.

There were three (1.4%) donors with postoperative neuropraxia in the form of ulnar nerve injury due to malpositioning of the upper limbs, which later on resolved without any residual effect. This donor's neuropraxia was encountered in the early operations, and later disappeared because of proper padding of the limbs with jelly pads. The remaining complications and their management are shown in Table 4.

Unfortunately, there was one (0.5%) donor mortality. This donor suffered severe intraoperative bleeding because of the displacement of the clamp on the portal vein stump, which had been successfully controlled. On the tenth postoperative day and despite adequate anticoagulation, extensive PVT developed and resulted in liver and renal failure, and finally the donor died on the twelfth postoperative day.

An analysis of the spectrum of postoperative donors' complications according to the modified Clavien classification system of postoperative complications revealed the following: grade I was recorded in 14.2% of the donors, representing 39.2% of total complications; grade IIIa in 18.6% of the donors, representing 51.3% of total complications; and grade IIIb in 2.5%, representing 8.1% of total complications. Only one donor died postoperatively (grade V in 0.5% donors, representing 1.4% of total complications) (Table 5).

Discussion

Donor safety (first do no harm) is a major concern in LDLT, as it exposes a healthy individual to an ultramajor surgery without any potential health benefit apart from emotional satisfaction in treating a relative or a friend [19]. The Ethics Committee of the Transplantation Society recommended that transplantation of nonrenal organs from living

Table 4 shows Postoperative complications of donors and its management

Complications	No (74)	% (36.3)	grade	Management
			I	4 → conservative ttt (operative drain)
			IIIa	18 → pig tail
			IIIa	5 → ERCP & stent
Biliary leak	**28**	**13.7%**	IIIb	1 → had major leak, then after 1 month, hepatico-jejunostomy (Roux-en-Y) was performed.
Biliary stricture	**2**	**1%**	IIIa	2 → ERCP + Stent
			IIIb	3 → Re-laparotomy due to bleeding on the same day of surgery;
Reactionary postoperative bleeding	**3**	**1.4%**		• One from the stapler line of the Rt hepatic vein, • One from the arterial branch of the bile duct & • One from the cut surface leading to hematoma
			IIIa	2 → single aspiration
Intra-abdominal collection	**13**	**6.4%**	IIIa	4 → multiple aspirations
			IIIa	7 → pig tail insertion
Wound infection	**10**	**5%**	I	10 → Conservative
Minimal to mild pleural effusion	**11**	**5.4%**	I	11 → Conservative
Neuropraxia	**3**	**1.4%**	I	3 → Conservative & resolved without any residual effects
			IIIb	1 → Compromised
Portal vein complications	**2**	**1%**		main portal vein flow after closure of right portal vein stump → underwent re-laparotomy and main portal vein reconstruction with vascular stent inserted intra-operatively → fully recovered
			V	1 → Severe intraoperative bleeding, developed postoperative *PVT* & died after 12 days
Incisional hernia	**1**	**0.5%**	IIIb	Surgical repair
Mild Pneumothorax 2ry to CVP line placement	**1**	**0.5%**	I	Conservative

donors should be done only when 'the aggregate benefits to the donor–recipient pair (survival, quality of life, psychological, and social wellbeing) outweigh the risks to the donor–recipient pair (death, medical, psychological, and social morbidities)' [20].

Therefore, every effort should be made to avoid the donor complications and mortality. However, a wide range of postoperative donor's morbidity has been reported in the literature. Published reports on donor outcomes indicated a wide range of complication rates that varied between 9 and 67% [21]. On the other hand, the American Society of Transplant Surgeons reported a low overall donor complication rate of only 10% [22].

In the present study, we described the details of 204 donor hepatectomies, which were divided between right lobe donation in 162 cases and left lobe donation in 42 cases.

On the context of postoperative complications, the overall reported donor morbidity rate, in the present study, was 36.3%, which was close to the complication rate reported by other studies. Pomfret [7] estimated the complication rate to be ~35%, Fujita *et al.* [22] reported donor morbidity to be as high as 50%, whereas Brown *et al.* [23] detected an incidence of complications in the donors of adult-to-adult LDLT in the range of 10–20%. These variations in the figures of postoperative complications across studies were explained by Brown *et al.* [23] as reflecting the lack of consistent definitions of surgical complications. While some centers have included minor complications, others have only reported severe or life-threatening events.

In our study, the right lobe donors had more complications than did those donating the left lobe or its lateral segments: 51 (79.7%) versus 13 (20.3%), respectively. A similar difference has also been described by Umeshita *et al.* [24] and Ozgor *et al.* [10]. However, Fernandes *et al.* [25] reported that the left hepatectomy donors were only slightly less morbid than were the right lobe donors: 23.5 versus 32.6%, respectively ($P<0.23$).

Biliary complications, in the current study, were the most frequent complications detected [30 (14.7%) cases]. There were 28 (13.7%) donors with postoperative biliary leak and only two (1%) donors had biliary stricture. Biliary complications were detected in 24 (11.8%) donors of the right lobe and in six (3%) of those undergoing the left-sided procedures ($P<0.0001$). In the literature, biliary complications account for the most frequent morbidity in LDLT, widely ranging from 6 to 18%. Furthermore, the frequency of biliary complications differed significantly according to the graft type. It has been reported that, it was 2.4–5.3% for all graft types,

Table 5 showing postoperative complications according to Clavien gradient System

Type of complication	Grade I	Grade II	Grade IIIa	Grade IIIb	Grade IVa	Grade IVa	Grade V	Freq. (n = 74)	%
Biliary leak	4		23	1				28	13.7%
Biliary stricture			2					2	1%
Reactionary postoper. Bleeding				3				3	1.4%
Intra-abdominal collection / infection			13					13	6.4%
Wound infection	10							10	5%
Minimal to mild pleural effusion	11							11	5.4%
Neuropraxia	3							3	1.4%
Portal vein complications				1			1	2	1%
Incisional hernia				1				1	0.5%
Mild Pneumothorax	1							1	0.5%
Freq.(n = 74)	29	-	38	6		-	1	74	36.3%
%	39.2%	-	51.3%	8.1%		-	0.5%	100%	

Table 6 Incidence of biliary complications in donors after live donor liver transplantation

Ref.	No.	Leak (%)	Stricture (%)	Overall rate (%)
Ozgor et al [10]	500	-	-	10.8
Ghobrial et al [28]	393	9	0.5	9.5
Shio et al [30]	731	11.6	3.1	13.5
Iida et al [31]	1262	15.3	1.9	17.1
El-Meteini et al [32]	207	22	1.6	13.04
Taketomi et al [33]	206	-	-	13
Lo et al [34]	1500	6.1	1.1	7.1
European Liver Transplant Registry [35]	276	5	3	8

10–12% for the right liver graft, and 2–4% for the left liver graft (Table 6) [10,26–35]. Most of these complications were classified as Clavien's grade III or IV.

Bile leaks and biliary fistulas are more common than biliary strictures after liver donation. The Adult-to-Adult Living Donor Liver Transplantation (A2ALL) study in the USA reported almost 400 patients who donated the right lobe and found an incidence of 9% of bile leak or biloma, and an 0.5–1.5% incidence of postoperative biliary strictures as no biliary anastomosis is required in the donor [10,28]. Factors associated with developing bile leaks include elevated preoperative alkaline phosphatase levels greater than 86 IU/l and requiring a blood transfusion during surgery; however, center experience was not reported as a factor in donor's biliary complications [28]. Biliary complications were related to surgical techniques in retrieving the graft's bile duct, dealing with donor's bile duct stump, and detecting intraoperatively any bile duct leakage. Donor biliary complications generally present within 2 weeks of surgery. Bile leaks can be noticed from the bilious discharge in the drain output or can present with pain or suspicion for an intra-abdominal collection. Imaging can also be helpful. As in the recipient, strictures present with elevated cholestatic liver enzymes or jaundice [36]. Management of bile leaks and strictures is similar to what is done for the recipient with ERCP, and stent placement is the mainstay. Almost 80% of the leaks were successfully treated by ERCP or percutaneous drainage, though a few required surgical revision or repair [30]. Strictures can be more difficult to manage after right lobe donation as they form as the liver regenerates and wire access to the remaining right lobe biliary tree can be very difficult either endoscopically or percutaneously. Surgical revision is then required [36].

In an effort to reduce the rate of biliary complications in our center, we advocated a new technique for closure of the bile duct stump by using interrupted nonabsorbable sutures and reinforcing by placing a surgical clip below the suture line. Before abdominal closure, we confirmed the consistency of the bile duct system by performing cholangiography through the cannula, which had been left in place in the cystic duct. After adopting this technique, bile leak dropped from 18.5% (in previous 140 cases) to 4% in the next 50 cases. The reduction in the bile duct leak, in our study, before and after this new technique was statistically significant [18].

Postoperative complications involving the portal vein were detected in two (1%) donors in the present study. This vascular complication was described in several studies with similar incidence and treatment results. One donor with postoperative PVT was described in the respective studies by Pomfret [7], Jiang *et al.* [37], and Sevmis *et al.* [38]. Furthermore, PVT has been described in two donors in the study by Ghobrial *et al.* [28]. In these previous studies, treatment of postoperative PVT varied between conservative anticoagulant treatment, interventional radiology and

medical treatment, relaparotomy and intraoperative infusion of tissue plasminogen activator, or relaparotomy with thrombectomy. All these maneuvers resulted in satisfactory outcomes.

The second most frequent complication, in our study, was found to be intra-abdominal collections (6.4%), followed by wound infections, which 10 (5%) donors suffered from. In the study conducted by Ghobrial *et al.* [28], the most common postoperative complication was infection (12.5%). Similarly, Umeshita *et al.* [24] reported that 27 (1.5%) of 1841 donors had wound infections.

The frequency of donor reoperations has also varied. In our study, there were six (2.9%) donors who needed reoperation. In the study by Ozgor *et al.* [10], the incidence of reoperations among all donors was 7.2%. In a mega study by Umeshita *et al.* [24], an elaborated description of donor's reoperation was analyzed. There were 23 (1%) donors out of 1841 that needed reoperation; biliary reconstruction was performed for 10 donors and six were operated upon for intestinal obstruction, two of whom needed resection of a loop of the small bowel. Other two donors developed gastric stasis because of extensive adhesions between the stomach and the cut surface of the liver and which had been divided on relaparotomy. Other reasons for reoperation were intra-abdominal bleeding, abdominal sepsis, portal vein thrombus formation, and incisional hernia repair.

In our study, three donors developed postoperative ulnar nerve neuropraxia (1.4%). Neuropraxia has been previously described in the studies by Fujita *et al.* [22] and Ghobrial *et al.* [28]. This injury usually results from malpositioning of the donor on the operating table during a prolonged procedure. This can result in a major functional disability, as well as permanent work disability for donors whose occupations depend on the motor function of the arm.

A review of the literature reveals that donor morbidity has closely been related to the remnant liver volume, portal vein bifurcation pattern, and technical refinements (learning curve), especially on retrieving the bile duct and dealing with its stump [12,22,28,30,36].

The most unfortunate complication, in our study, was the death of one (0.5%) donor. Despite careful donor selection, mortality after LDLT has occurred in Europe [39], the USA [23], and Japan [40]. The results on mortality studies from different centers point to a higher risk for mortality after donation of the right liver lobe [41]. The most sobering information in the A2ALL US Consortium (2005) report was that four of the 393 donors had died, one of infection and multiple organ failure during primary hospitalization and the other three more than a year later from drug overdose, a suicide, and a pedestrian-train accident, respectively [28].

Analyzing the reasons for death after adult LDLT showed that donor mortality occurred mostly because of sepsis and liver failure [42]. Another important cause of death was pulmonary thromboembolism [43]. A history of smoking and the presence of obesity are important factors for the development of a pulmonary thromboembolism [44]. In their study, Umeshita *et al.* [24] reported that Asian-Americans have a very low risk for pulmonary embolism and deep venous thrombosis (DVT) compared with white people, thus the absence of genetic mutations with or without unspecified protective traits predisposing to thrombosis. However, the frequency of pulmonary embolism in Japan has been increasing, and in his series, four living liver donors had pulmonary embolism, although without any associated mortality.

In their study, Trotter *et al.* [42] reviewed all published articles for donor deaths from 1989 to February 2006. They classified each death as 'definitely', 'possibly', or 'unlikely' related to donor surgery. They identified 19 donor deaths (and one additional donor in a chronic vegetative state). Thirteen deaths and the vegetative donor were 'definitely', two were 'possibly', and four were 'unlikely' related to donor surgery. The estimated rate of donor death 'definitely' related to donor surgery was 0.15%. The rate of donor death 'definitely' or 'possibly' related to the donor surgery was 0.20%.

The differences between centers as regards donor complication rates could reflect, in part, diverse views about how these adverse events should be classified [45]. The formulaic grading system (the five-tier Clavien's model) has been used in other single center reports (seven other reports to our knowledge).

On analysis of donor complications according to the modified Clavien classification system, the results of the present study, as well as those of other studies by Ozger *et al.* [10], Fernandes *et al.* [25], Ghobrial *et al.* [28], Khalaf *et al.* [46], and Tamura *et al.* [47] (Table 7), it was observed that most complications after liver donation were minor and self-limited. However, several patients experienced grade IIIb

Table 7 showing postoperative complications of the donors in various studies According to the Modified Clavien classification for post operative complications

Study		Current study	Ozgor et al (2012) (10)	Fernandes et al (2010) (25)	Ghobrial et al (2008) (28)	Khalaf et al (2007) (46)	Tamura et al (2006) (47)
No of donors		204	500	100	392	44	243
No of complicated donors (%)		64 (31.4%)	93 (18.6%)	26 (26%)	148 (38%)	17(38.6%)	67(28%)
No of complications (%)		74 (36.3%)	149 (30%)	28 (28%)	220(56%)	28(63 %)	67(28%)
No of complicated donors according to Clavien grading system	I	29 (39.2%)	77 (51.6%)	11 (39.2%)	106(48%)	18	36 (15%)
	II	-	9 (6%)	8 (28.5%)	103(47%).	-	10 (4%)
	IIIa	38 (51.3%)	27 (18.1%)	7 (25%)	-	39(6.8%)	12 (5%)
	IIIb	6 (8.1%)	35 (23.4%)	2 (7.3%)	-	5(11.3%)	9 (4%)
	IVa	-	1 (0.6%)	-	8 (2%)	2(4.5%)	-
	IVb	-	-	-	-	-	-
	V	1 (1.4%)	-		3 (0.8%)	-	

complications, which were potentially threatening to the donors' lives. Major grade III or grade IV complications were often life-threatening and required surgical or endoscopic intervention.

In our study, the grade IIIa complications were higher than in other studies, and this may be attributed to our policy of rapid intervention for any sizable collection (especially bile collection) whenever detected on routine follow-up ultrasound. Delayed intervention was avoided even if the patient was asymptomatic to avoid further complications associated with bile leakage, such as an infected biloma.

One possible explanation for the wide variations in complication rates among transplant centers could be short reports of transplant centers and operative experience. Importantly, in their study, Ghobrial *et al.* [28] reported the lack of any association between LDLT center experience and donor complications, and stated that this was unlikely to be the only explanation for the variation in complication rate. This observation was in contrast to the corresponding A2ALL analyses of recipient outcomes and its predictors, in which a 'learning curve' was identified and recipient outcomes improved after center experience with more than 20 adult-to-adult LDLT procedures [48]. The lack of a significant association between center experience and donor complications may indicate that surgical experience with hepatic resections outside the transplantation setting provides an adequate training for the adult donor operation in LDLT but could also represent a type II error. Larger numbers of cases with more intensive follow-up of donors in the A2ALL prospective cohort study may yet identify other important predictors of complications that could be eliminated or ameliorated [28]. Furthermore, the few donor deaths that have been reported worldwide have generally occurred at experienced centers [49]. In addition, the long-term complications after donor right hepatectomy are essentially unknown because many donors may be lost to follow-up or be difficult to contact years after the LDLT [34].

In conclusion, donor hepatectomy is a relatively safe procedure when performed by a dedicated and well-trained team and after offering every effort on donor selection to minimize the marginal risks inherent in such major procedures. A prompt diagnosis and meticulous intervention is considered the first priority whenever a donor complication is expected. Furthermore, continuous standardized reporting and a comprehensive database to precisely define true donor morbidity are crucial for the safe implementation of this procedure.

Acknowledgements

Amr M. Aziz selected the theme, conducted and carried out follow-up research and drew their results, collected references, and wrote the article and followed up publishing. Sherif Saleh contributed in gathering the scientific material, participated in writing the article and reference collection. Hossam E. Soliman, Hany Shoreem, Osama Hegazy, Mohamed Taha, Emad H. Salem, Hazem Zakaria, and Sameh Hamdy contributed in gathering the scientific material and reference collection. Hesham Abdeldayem carried out auditing and review of research. Tarek Ibrahim selected the theme and carried out collection of references. Khaled Abuelella carried out auditing and review of research.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Strong RW, Lynch SV, Ong TH, Matsunami H, Koido Y, Balderson GA. Successful liver transplantation from a living donor to her son. N Engl J Med 1990; 322:1505–1507.

2 Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet 1989; 2:497.

3 Abdeldayem H. Transparency and living donor liver transplantation in Egypt. Nile Liver J 2010; 1:7–13.

4 Nadalin S, Malagò M, Radtke A, Erim Y, Saner F, Valentin-Gamazo C, *et al.* Current trends in live liver donation. Transpl Int 2007; 20:312–330.

5 Middleton PH, Duffield M, Lynch SV, Padbury RT, House T, Stanton P, *et al.* Living donor liver transplantation – adult donor outcomes: a systematic review. Liver Transpl 2006; 12:24.

6 Broering DC, Wilms C, Bok P, Fischer L, Mueller L, Hillert C, *et al.* Evolution of donor morbidity in living related liver transplantation: a single-center analysis of 165 cases. Ann Surg 2004; 240:1013–1024.

7 Pomfret EA. Early and late complications in the right-lobe adult living donor. Liver Transpl 2003; 9(Suppl 2): 45–49.

8 Broelsch CE, Frilling A, Testa G, Malago M. Living donor liver transplantation in adults. Eur J Gastroenterol Hepatol 2003; 15:3–6.

9 Liu CL, Fan ST, Lo CM, Chan SC, Yong BH, Wong J. Safety of donor right hepatectomy without abdominal drainage: a prospective evaluation in 100 consecutive liver donors. Liver Transpl 2005; 11:314–319.

10 Ozgor D, Dirican A, Ates M, Gönültas F, Ara C, Yilmaz S. Donor complications among 500 living donor liver transplantations at a single center. Transplant Proc 2012; 44:1604–1607.

11 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240:205–213.

12 Nakayama Y, Li Q, Katsuragawa S, Ikeda R, Hiai Y, Awai K, *et al.* Automated hepatic volumetry for living related liver transplantation at multisection CT. Radiology 2006; 240:743–748.

13 Kokudo N, Sugawara Y, Imamura H, Sano K, Makuuchi M. Tailoring the type of donor hepatectomy for adult living donor liver transplantation. Am J Transplant 2005; 5:1694–1703.

14 Takayama T, Makuuchi M, Kubota K, Sano K, Harihara Y, Kawarasaki H. Living-related transplantation of left liver plus caudate lobe. J Am Coll Surg 2000; 190:635–638.

15 Sugawara Y, Makuuchi M, Takayama T, Imamura H, Kaneko J. Right lateral sector graft in adult living-related liver transplantation. Transplantation 2002; 73:111–114.

16 Makuuchi M, Kawasaki S, Noguchi T, Hashikura Y, Matsunami H, Hayashi K, *et al.* Donor hepatectomy for living related partial liver transplantation. Surgery 1993; 113:395–402.

17 Kokudo N, Sugawara Y, Imamura H, Sano K, Makuuchi M. Sling suspension of the liver in donor operation: a gradual tape-repositioning technique. Transplantation 2003; 76:803–807.

18 Shoreem H, Hegazy O, Soliman HE *et al.* A new modified technique in closure of bile duct stump in living donorhepatectomies. Egypt J Surg 2013; 32:164–171.

19 Eghtesad B, Jain AB, Fung JJ. Living donor liver transplantation: ethics and safety. Transplant Proc 2003; 35:51–52.

20 Pruett TL, Tibell A, Alabdulkareem A, Bhandari M, Cronin DC, Dew MA, *et al.* The ethics statement of the Vancouver Forum on the live lung, liver, pancreas, and intestine donor. Transplantation 2006; 81:1386–1387.

21 Barr ML, Belghiti J, Villamil FG, Pomfret EA, Sutherland DS, Gruessner RW, *et al.* A report of the Vancouver Forum on the care of the live organ donor: lung, liver, pancreas, and intestine data and medical guidelines. Transplantation 2006; 81:1373–1385.

22 Fujita S, Kim I, Uryuhara K. Hepatic graft from live donors: donor morbidity for 470 cases of live donation. Transpl Int 2000; 13:333–339.

23 Brown RS Jr, Russo MW, Lai M, Shiffman ML, Richardson MC, Everhart JE, Hoofnagle JH. A survey of liver transplantation from living adult donors in the United States. N Engl J Med 2003; 348:818–825.

24 Umeshita K, Fujiwara K, Kiyosawa K, Makuuchi M, Satomi S, Sugimachi K, *et al.* Japanese Liver Transplantation Society. Operative morbidity of living liver donors in Japan. Lancet 2003; 362:687–690.

25 Fernandes R, Pacheco-Moreira LF, Enne M, Steinbrück K, Alves JA, Filho GD *et al.* Surgical complications in 100 donor hepatectomies for living donor liver transplantation in a single Brazilian center. Transplant Proc 2010; 42:421–423.

26 Azoulay D, Bhangui P, Andreani P, Salloum C, Karam V, Hoti E, *et al.* Short- and long-term donor morbidity in right lobe living donor liver transplantation: 91 consecutive cases in a European Center. Am J Transplant 2011; 11:101–110.

27 Berg CL, Gillespie BW, Merion RM, Brown RS Jr, Abecassis MM, Trotter JF, *et al.* A2ALL Study Group. Improvement in survival associated with adult-to-adult living donor liver transplantation. Gastroenterology 2007; 133: 1806–1813.

28 Ghobrial RM, Freise CE, Trotter JF, Tong L, Ojo AO, Fair JH, *et al.* A2ALL Study Group. Donor morbidity after living donation for liver transplantation. Gastroenterology 2008; 135:468–476.

29 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.

30 Shio S, Yazumi S, Ogawa K, Hasegawa K, Tsuji Y, Kida M, *et al.* Biliary complications in donors for living donor liver transplantation. Am J Gastroenterol 2008; 103:1393–1398.

31 Iida T, Ogura Y, Oike F, Hatano E, Kaido T, Egawa H, *et al.* Surgery-related morbidity in living donors for liver transplantation. Transplantation 2010; 89:1276–1282.

32 El-Meteini M, Hamza A, Abdalaal A, Fathy M, Bahaa M, Mukhtar A, *et al.* Biliary complications including single-donor mortality: experience of 207 adult-to-adult living donor liver transplantations with right liver grafts. HPB (Oxford) 2010; 12:109–114.

33 Taketomi A, Kayashima H, Soejima Y, Yoshizumi T, Uchiyama H, Ikegami T, *et al.* Donor risk in adult-to-adult living donor liver transplantation: impact of left lobe graft. Transplantation 2009; 87:445–450.

34 Lo CM. Complications and long-term outcome of living liver donors: a survey of 1,508 cases in five Asian centres. Transplantation 2003; 75:S12–S15.

35 European Liver Transplant Registry. Biliary complications in donors after live donor livertransplantation Available at: http://www.eltr.org/. [Accessed 8 January 2015].

36 Simoes P, Kesar V, Ahmad J. Spectrum of biliary complications following live donor liver transplantation. World J Hepatol 2015; 7:1856–1865.

37 Jiang XZ, Yan LN, Li B, Wen TF, Zeng Y, Wang WT *et al.* Safety of donor in adult-to-adult living donor liver transplantation using right lobe graft. Transplant Proc 2007; 39:150–152.

38 Sevmis S, Karakayali H, Karakayali F, Savas NA, Akkoc H, Haberal M. Postsurgical complications in living-related liver donors. Transplant Proc 2008; 40:245–247.

39 Adam R, McMaster P, O'Grady JG, Castaing D, Klempnauer JL, Jamieson N *et al.* Evaluation of liver transplantation in Europe: report of the European Liver Transplantation Registry. Liver Transpl 2003; 9:1231–1243.

40 Surman OS, Hertl M. Liver donation: donor safety comes first. Lancet 2003; 362:674–675.

41 Kamel E, Abdullah M, Hassanin A, Fayed N, Ahmed F, Soliman H, *et al.* Live donor hepatectomy for liver transplantation in Egypt: lessons learned. Saudi J Anaesth 2012; 6:234–241.

42 Trotter JF, Adam R, Lo CM, Kenison J. Documented deaths of hepatic lobe donors for living donor liver transplantation. Liver Transpl 2006; 12:1485–1488.

43 Renz JF, Roberts JP. Long-term complications of living donor liver transplantation. Liver Transpl 2000; 6(Suppl 2):73–76.

44 Malagó M, Rogiers X, Burdelski M, Broelsch CE. Living related liver transplantation: 36 cases at the University of Hamburg, Transplant Proc 1994; 26:3620–3621.

45 Sugawara Y, Tamura S, Makuuchi M. Systematic grading of surgical complications in live liver donors. Liver Transpl 2007; 13:781–782.

46 Khalaf H, Al-Sofayan M, El-Sheikh Y, Al-Bahili H, Al-Sagheir M, Al-Sebayel M. Donor outcome after living liver donation: a single-center experience. Transplant Proc 2007; 39:829–834.

47 Tamura S, Sugawara Y, Kaneko J, Yamashiki N, Kishi Y, Matsui Y, *et al.* Systematic grading of surgical complications in live liver donors according to Clavien's system. Transpl Int 2006; 19:982–987.

48 Olthoff KM, Merion RM, Ghobrial RM, Abecassis MM, Fair JH, Fisher RA, *et al.* A2ALL Study Group. Outcomes of 385 adult-to-adult living donor liver transplant recipients: a report from the A2ALL Consortium. Ann Surg 2005; 242:314-323; discussion 323-325.

49 Fan ST. Live donor liver transplantation in adults. Transplantation 2006; 82:723–732.