Donor Safety in Live-Related Liver Transplantation

V. A. Wakade · S. K. Mathur

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Abstract Living donor liver transplantation (LDLT), since its advent in late 1980's and early 1990's, has rapidly increased especially in countries like Japan, Korea and India where cadaveric programmes are not as well established as in the western world. The main advantage of LDLT is the availability of an organ in the elective setting in the course of a progressive liver disease. This is most applicable in patients with Cirrhosis and Hepatocellular carcinoma. LDLT, from the donor's perspective does carry a risk of not only morbidity but mortality. To date the surgical mortality risk is estimated at 0.1% for left lateral donation and 0.5% for right liver donation. Donor mortality has been reported from various centres in India. There are reports of complications like Hepatic artery thrombosis, portal vein thrombosis and especially biliary leaks and strictures occurring at a significantly increased frequency after living as compared to deceased donor liver transplantation. The key to reduce donor morbidity and mortality is meticulous donor selection and thorough donor work up. In the present study we will analyse the factors that contributed to donor mortality and morbidity and prepare a detailed work up plan, intraoperative and post-operative strategy to reduce donor morbidity and mortality.

Keywords Live-related liver transplant · Donor safety · Donor mortality · Donor morbidity

Introduction

The concept of living donor liver transplantation (LDLT) was first introduced by a French group (Henry Bismuth), by showing successful liver transplant by reduced-size cadaveric graft in paediatric patients.

LDLT was introduced in the paediatric population in 1989 [1], and the first successful case of adult-to-paediatric LDLT was noted in 1990 [2]. On 2 November 1993, the Shinshu group performed the first adult-to-adult transplant [3].

The number of LDLT procedures has rapidly increased since then. This is true especially for countries such as Japan, Korea and India where cadaveric programmes are not as well established as in the western world due to various reasons.

The main advantage of LDLT is the availability of an organ in the elective setting in the course of a progressive liver disease. This is most applicable in patients with cirrhosis and hepatocellular carcinoma, where about 25% patients progress to beyond the accepted criteria for transplantation while on the waiting list.

LDLT, from the donor's perspective, does carry a risk of not only morbidity but also mortality. It is generally acknowledged that the risk of left lateral segmentectomy is lesser than that of right hepatectomy. To date the surgical mortality risk is estimated at 0.1% for left lateral donation and 0.5% for right liver donation [4]. Donor mortality has been reported from various centres in India (about eight cases).

There are reports of complications such as hepatic artery thrombosis, portal vein thrombosis and especially biliary leaks and strictures occurring at a significantly increased frequency after living as compared to deceased donor liver transplantation [5–8].

The key to reduced donor mortality and morbidity is meticulous donor workup and donor selection.

In this study, we analyse the factors contributed to donor mortality and morbidity and prepare a detailed workup plan, intra-operative and post-operative strategy.

Donor Workup

By definition, a living donor is a completely healthy person physically, psychologically and mentally [9]. Although many patients with underlying medical diseases have undergone major

V. A. Wakade · S. K. Mathur (✉)
Department of Surgical Gastroenterology and Liver
Transplantation, Fortis Hospital,
Mulund Goregaon Link Road, Bhandup West,
Mumbai 400078, India
e-mail: mathur.surendrakumar@gmail.com

hepatectomy successfully, the same acceptance threshold cannot be applied to a healthy person donating a part of his liver. Because the donor must recover from the donor operation speedily and uneventfully, any error in the pre-operative evaluation is not acceptable. The workup of the potential donor is no less serious procedure than the donor operation itself. Therefore, there cannot be any compromise in the process of evaluation and acceptance of a donor.

Donor evaluation starts only when a person explicitly expresses his/her decision to donate. The donor should be fully informed about the risks involved and the benefit of the operation. The salient features of the operation must be communicated during the interview, preferably through a pamphlet. The information must include the currently available recipient mortality rates, 5-year survival rates and most importantly 0.5–1% risk of donor mortality. The rationale of opting for LDLT should be explained.

There are three important aspects of donor evaluation:

1. Detection of medical or transmissible disease, which, whether obvious or hidden, may increase the risk in both the donor and the recipient
2. Psychological status including motivation for donation
3. Study of suitability of the intended graft in terms of anatomy, volume and function

Initially, the suggested donor workup is limited; however, keeping in mind the unforeseen causes of donor mortality and morbidity, an extended workup plan is suggested (Table 1).

Donor Medical History

Importance of detailed medical history of the donor cannot be overemphasized. History of malignancy, diabetes mellitus, hypertension, ischemic heart disease, kidney disease, asthma and psychiatric disorders precludes donation. Allergy, drug and alcohol history are noted.

Smokers who are having productive cough should not be accepted for donation. Women of reproductive age who are sexually active must undergo pregnancy test. Persons with peptic ulcer disease need an upper gastrointestinal endoscopy to rule out active peptic ulcer disease.

Potential donors with active infection should be rejected [10]. Those with history of hepatitis must undergo appropriate serological workup. Those with history of tuberculosis may be accepted, provided that infection has been adequately treated and is dated many years ago [11].

Donor Age

Many institutions specify the maximum age of the living donor to be 65 years for the LDLT. The problem of LDLT in an

Table 1 Suggested extended donor workup

Stage 1			
I	Complete hemogram	IV	Lipid profile
		1	Total cholesterol
II	Liver function tests	2	HDL cholesterol
1	Total protein	3	Total/HDL ratio
2	Albumin	4	LDL cholesterol
3	Globulin	5	Triglycerides
4	A/G ratio		
5	Total bilirubin – direct and indirect	V	Viral markers
6	PT/INR	1	HIV
7	PTT	2	VDRL
8	SGOT	3	HBs Ag
9	SGPT	4	HBs Ab
10	ALP	5	HCV Ab
11	GGT		
12	LDH	VI	Blood group
13	PTT		
		VII	Tumour markers
III	Renal function tests		PSA (males)
1	Bicarbonate		CA 125 (females)
2	Sodium		CA 19-9
3	Potassium		CEA
4	Chloride		AFP
5	Urea		
6	Creatinine	VIII	Imaging
7	Glucose – FBS and PLBS	1	ECG
8	Calcium	2	Chest X-ray
9	Magnesium	3	USG abdomen
10	Phosphate		
11	Uric acid		
12	Urine routine		
Stage 2			
I	Computed tomography (CT) abdomen triphasic		
II	MRI abdomen		
Stage 3			
I	2D ECHO	V	Thrombophilia profile
			Protein C level
II	PFT		Protein S level
			Sr antithrombin III level
III	Dobutamine stress test		Anti-phospholipid antibody
			Factor V Leiden mutation
IV	Thyroid function tests		Sr homocysteine level
			Activated protein C resistance
		VI	Advanced viral markers
VII	Consultations		CMV IgM, IgG
1	Cardiologist		EBV IgM, IgG

Table 1 (continued)

2	Chest physician	HSV 1 and 2 IgM, IgG
3	Endocrinologist	Toxoplasma IgG
4	Psychiatrist	Rubella IgM, IgG
5	Liver transplant surgeon	

advanced age donor is firstly the increased risk of hepatectomy. However, because the donor's hepatectomy is an operation conducted on a healthy donor, in order to avoid post-operative complications, an evaluation of the whole body state (operability) or estimation of residual liver volume before the operation takes precedence. Secondly, it is an increased risk to the recipient due to a reduced functional reserve of the transplant graft based on the advanced age. It is thought that elderly people's liver function is greatly influenced by the ischemia and reperfusion injury compared to young livers, although it seems practically equal compared to a young liver.

For this reason, when a transplant graft is small-for-size, an aged liver graft should be avoided. Technetium-99 m-galactosyl-human serum albumin (GSA) scintigraphy, which expresses the binding ability of asialoglycoprotein of the liver, is suggested to be useful in the evaluation of potential graft quality in LDLT [12].

Donor BMI

It is generally agreed that a donor BMI of more than 30 is a relative contraindication to donation and such donors must be avoided if an alternative is available [13, 14].

If an obese donor is only available, he/she must be free of medical disease and sleep apnoea and has a normal liver biochemistry with minimal fatty liver. Such donors and their recipients must be forewarned about the higher rate of complications.

It is worth noting that Asians have a higher amount of body fat than westerners and have increased cardiovascular risk at lower BMI levels. Some studies reported that in Asian countries BMI of more than 27.5 had significantly higher rates of complications (31%) than those with BMI of less than 27.5 (13.6%) [15, 16].

There is no difference in the morbidity rates in donors with BMI less than 23 and between 23.1 and 27.5. Hence, overweight donors may be accepted, but it is preferred that they lose weight before the operation.

Donor Fatty Liver

A fatty liver is known to be unsuitable as a transplant graft, which has been pointed out from experiences of transplant from deceased donors. During a cold preservation of the fatty liver graft, the fusion and expansion of fats is made to press sinusoids and hepatocytes, leading to the circulation disturbance in the sinusoids and graft injury [17].

Because such a cold preservation period can be minimized in a LDLT, the graft with a certain degree of fatty infiltration is usable. However, there are little clear parameters to demonstrate the limits of the fatty liver. It was reported that in the LDLT the fatty liver was acceptable to the moderate grade of macrovesicular steatosis (20–50% of macrovesicular steatosis) [18]. However, recent research has showed that the breakdown of sinusoidal reconstitution occurs in the liver regeneration process of a fatty liver [19]; therefore, the fatty liver donor should be avoided in the case of the small-for-size graft. In such a case, because LDLT is a scheduled operation, diet control and/or daily exercise are recommended before an operation to improve the degree of fatty liver.

Moreover, non-alcoholic steatohepatitis (NASH) has recently attracted attention. Especially, in the case of metabolic syndrome exhibiting the symptoms and signs of high blood pressure, hyperlipidemia, diabetes, and obesity, the NASH should be ruled out using an ultrasonography and abdominal CT, furthermore and sometimes liver biopsy.

Core Antibody Positive Donors

Hepatitis B surface antigen positivity and hepatitis C positivity preclude donation. Donors with hepatitis B core antibody (HBcAb) are suitable for donation, but the potential donors need testing for HBV DNA. Recipients of grafts from such donors may require lifelong lamivudine treatment [20]. However, there are suggestions that recipients with hepatitis B surface antibody positivity and donors with hepatitis B DNA negativity may have their lamivudine terminated after transplant [21].

In general, HBcAb positivity does not adversely impact the post-operative recovery of donors. However, HBcAb positive donors have delayed normalization of serum bilirubin.

Donor Hyperlipidemia

Persons with hyperlipidemia have a higher risk of premature cardiovascular disease. It is arguable whether they should be subjected to a major hepatectomy even if cardiovascular screening is negative. It is not known how many asymptomatic hyperlipidemic donors have undergone hepatectomy uneventfully, but at least three donors who died after liver donation operation had hyperlipidemia or lipid disorder [22–24]. It is therefore safer to avoid donors with lipid abnormalities.

Donor Hypercoagulable States

Suggested workup for hypercoagulable states is as follows: protein C, protein S, antithrombin III, factor V Leiden mutation,

anti-phospholipid antibodies, anti-cardiolipin antibodies, lupus anticoagulant, serum homocysteine levels.

Beside the risks related to liver extraction surgery, both thrombotic and bleeding risks are significantly increased when the donor has a prior hemostatic anomaly, even if it is slight or unknown to the patient. Mild hemostatic defects can cause severe bleeding during major surgery; patients with thrombophilic defects may suffer venous thrombotic events during the early post-operative period [25]. In addition, the liver synthesizes all blood coagulation factors. Donor alterations are transferred to the recipient together with the liver graft. Several cases have been reported of liver recipients with an acquired prothrombotic state after receiving a liver graft from a donor carrying factor V Leiden mutation [26, 27].

Arterial and venous thrombotic events increase morbidity in liver transplant recipients, especially in children [28]. Venous thrombotic events are especially related to thrombophilia.

Although thrombosis history is one of the most important risk factors for thrombosis, most of the thrombophilia cases are asymptomatic and thrombosis is precipitated by surgery or pregnancy [29]. Thus, although interviewing for thrombotic events is important, it is not adequate to rule out thrombophilia. For accurate evaluation of thrombophilia the suggested hematological workup is essential.

In conclusion, the careful screening for coagulation and prothrombotic disorders should be performed as part of donor selection because thrombotic and bleeding risks related to LDLT are not restricted to the surgery itself, particularly involving the donor. Although cost-effectiveness has not been definitely established, this screening decreases the risks of thrombosis and bleeding in the donor, and most probably in the recipient.

Donor Anatomical Considerations

The potential donor will undergo CT with arterial, venous and delayed phases.

The anatomy of the hepatic veins is studied on axial cuts in the venous phase. Presence of inferior hepatic vein draining segment VI is noted. For the left or right liver graft operations, the middle hepatic vein (MHV) is studied thoroughly with regard to course and the veins draining into it. To increase the safety margin, the segment IVb vein should be preserved with the liver remnant for right liver donation that includes the MHV. The site of segment IVb vein joining the MHV should be studied carefully. For centres with a selective policy of including the MHV in the right liver graft, the size of the MHV may be a determining factor whether it is included in the right liver graft. However, by routinely including the MHV in the right liver graft, the number of potential donors increases.

Three-dimensional reconstruction is used to trace the course of the right and left hepatic arteries. Accessory or replaced arteries are noted. A Left Hepatic artery LHA from

the left gastric artery or the Right Hepatic Artery (RHA) from the Superior Mesenteric Artery (SMA) are preferable for donor operation. In the right graft surgery, the origin of the segment IV artery must be defined and protected. There may be two right hepatic arteries. Similar to the LHA if communication between the two exists, rendering anastomosis of either one sufficient, it is not a contraindication to donation. However, with more than two arteries, uncertain communication between them imposes a technical difficulty, and in this situation another lobe graft or alternate donor must be looked for.

Proposed classification for common variations of hepatic artery [30] is as follows:

- Type 1: Normal anatomy
- Type 2a: Accessory LHA, normal RHA
- Type 2b: Replaced LHA, normal RHA
- Type 3a: Accessory RHA, normal LHA
- Type 3b: Replaced RHA, normal LHA
- Type 4a: Accessory LHA and RHA
- Type 4b: Replaced LHA and RHA
- Type 5: Common hepatic artery from SMA

Portal venous anatomy is ascertained on the portal venous phase of CT scan. Common anomaly is the trifurcation of the portal vein and is not a contraindication to donation. Sometimes, segment V/VIII portal vein arises from the Left Portal Vein LPV. This vein is usually extrahepatic and identified during hilar dissection. A rare but dangerous anomaly is when the segment V/VIII portal vein arises from the LPV within the umbilical fissure. This vein is intrahepatic and easily injured during parenchymal transection. Absent right portal vein is a rare anomaly, but if it is encountered it precludes donation.

Proposed classification of portal venous anatomy variations [30] is as follows:

- Type 1: Normal
- Type 2: Trifurcation of portal vein
- Type 3: Right anterior portal vein from LPV

Biliary anatomy must be detailed pre-operatively. Previously pre-operative imaging with was suggested as the gold standard. The risk of Endoscopic Retrograde Cholangiopancreatography ERCP complications for a normal person is too high especially after advent of high-quality Magnetic Resonance Cholangio-pancreaticography MRCP. On MRCP the drainage of the right anterior and posterior sectoral ducts is noted. Intra-operative cholangiogram after cannulating the cystic duct further aids accurate identification of hepatic ducts and prevention of donor biliary complications.

Proposed classification of biliary anatomical variations [30] is as follows:

- Type 1: Normal
- Type 2: Trifurcation of ducts.

- Type 3a: Right anterior sectoral duct drains into the left duct.
- Type 3b: Right posterior duct drains into the left duct.
- Type 4a: Right anterior sectoral duct has a long extra-hepatic course and drains into the CHD.
- Type 4b: Right posterior sectoral duct has a long extra-hepatic course and drains into the CHD.

Donor CT Volumetry

Donor CT volumetry is performed to assess the graft and the remnant liver volumes. The importance of accurate assessment of liver volumes pre-operatively cannot be overemphasized. It is generally believed that a liver remnant of 30–35% is sufficient for the donor. For the recipient a graft that provides 40% of estimated standard liver volume (ESLV) or 0.8% of the body weight of the recipient (GRWR) is sufficient for survival. These numbers seem to be suggested by early researchers without much literature support, but have stood the test of time.

Estimation of graft weight or volume in terms of ESLV is necessary to avoid serious graft size mismatch and small-for-size syndrome. The accuracy of ESLV however depends on how the formula is derived. The formula derived from different races may not be applicable to each other. The liver size is affected by age and sex of the population with older female subjects having a smaller liver size. It would be logical from the above consideration that a formula should be established for each race or local population based on the latest local data.

It has been assumed that weight and volume of the liver are equivalent. However, in a reported study of CT volumetry and graft back-table weight, a conversion factor of 1.19 mL/g is needed.

Finally, there is a possibility that CT volumetry may under or overestimate the graft size, depending on how the line between the right and left sides of the liver is drawn along the MHV. On this issue, the surgeon must himself ascertain that the line is correctly drawn by following the course of the MHV from the inferior vena cava to the gallbladder fossa.

In our study 5% variation in donor volumes is calculated by CT volumetry when compared to back-table weight of the graft.

Donor Mortality and Morbidity

The intra-operative and post-operative complications of donors in the reported series vary from 9 to 67%. The donor complication rate is higher for right than left liver donation. The wide range in the incidence of complications is a reflection of maturation of surgical techniques, as well as how surgeons reported their complications.

The overall mortality rate is estimated to be 0.08–0.5%, with mortality being more in the right liver group than in the left liver group.

Causes of Donor Morbidity

A) Cardiopulmonary Complications

1. Pleural effusion
2. Pulmonary edema
3. Pulmonary embolism
4. Bronchopneumonia
5. Lung collapse
6. Myocardial infarction
7. Congestive Heart Failure

B) Abdominal Complications

1. Prolonged Ileus
2. Duodenal ulcer bleed/perforation
3. Small bowel obstruction
4. Acute pancreatitis
5. Intra-abdominal bleed
6. Gastric perforation

C) Hepatobiliary Complications

1. Portal vein stenosis
2. Bile duct strictures
3. Bile leak
4. Biloma
5. Liver failure
6. Ascitis
7. Encephalopathy

D) Wound complications

1. Wound infection
2. Leakage of ascetic fluid
3. Incisional hernia
4. Dog ear appearance

E) Others

1. Deep venous thrombosis
2. Urinary tract infection
3. Occipital sores
4. Ankle sores
5. Urine retention

Reported donor mortalities:

Author	Country	Graft	Causes of Mortality
Akabayashi	Japan	Right liver	NASH
	India	Not known	Suspected pulmonary embolism
Boillot	France	Right liver	Pleural effusion, multiple organ failure
Broering	Germany	Segment II/III	Massive pulmonary embolism

Brown	USA	Right liver	Pancreatitis
	USA	Not known	Not known
Malago	Germany	Right liver	Congenital lipodystrophy
Malago	Germany	Right liver	Pulmonary embolism
Miller	USA	Right liver	Gas gangrene of stomach
Widerkehr	Brazil	Right liver	Cerebral hemorrhage
Chan	Honk Kong	Right liver	Duodenocaval fistula
Polido	Singapore	Right liver	Heart attack
Coelho	Brazil	Right liver	Cardiac Arrhythmia
	Korea	Right liver	Liver failure, steatosis
	India	Right liver	Cardiac arrest – unknown cause
	France	Right liver	Multiple myeloma
Abofetouh	Egypt	Right liver	Sepsis, bile leak
Ringe	USA	Segment II/III	Drug overdose

Comments on Donor Hepatectomy Complications

Similar to any major surgery, accumulation of experience will lead to reduction in the complication rate. Comparing with partial hepatectomy in tumour-bearing cirrhotic patients, the goal of achieving 0% hospital mortality rate and a near-zero morbidity rate appears easier, provided that the liver is completely normal and the donor is free from any co-morbidity and the surgeon is fully conversant with the liver anatomy and experienced in liver transection. However, the operation by itself is ultra-major in nature and complications may be inevitable. It requires the effort and cooperation of the entire team – anaesthesiologists, nurses, support staff and the surgeon – to achieve the goal, while the surgeon himself should lead the team to ensure safety of the donor. Thus, he/she should be present right from the beginning of the operation to ensure that positioning of the donor is not potentially injurious, catheterization of the bladder is performed properly, skin preparation is carried out meticulously, prophylactic antibiotic and H₂-receptor antagonists have been given and anti-deep vein thrombosis measures are implemented. He/she should stay until the wound is closed properly and ensure that the donor is hemodynamically stable before he/she leaves. Bleeding volume is the most important indicator of performance of hepatectomy and prediction of post-operative complications [31]. It depends on the experience and skill of the surgeon. However, the bleeding volume is also dependent on the transection surface. Therefore, to be accurate scientifically, the bleeding volume is preferably expressed as mL/cm². The bleeding volume is likely higher on approaching the deeper part of the transection plane. Therefore, a large-size donor with a deep abdominal cavity may have more bleeding. In this regard, Asian surgeons are more fortunate because most of the donors have normal body mass indices and small body

sizes [32]. The bleeding volume could be reduced if the central venous pressure is low, operating table is tilted up head-end or by inflow vascular occlusion. Full muscle relaxation is also important to supplement the effect of low central venous pressure. The intravascular volume could be restored after graft retrieval. Inflow vascular occlusion is normally not employed during liver transection, but if major bleeding occurs, it should be used immediately for clear visualization of the bleeding site in the MHV or its branches. The bleeding volume is also dependent on the anatomical arrangement of the hepatic vein at the junction with the inferior vena cava. Nakamura type I (i.e., segment IVb hepatic vein, predominant drainage into the left hepatic vein) is the most favourable type [33]. For the other Nakamura types, recognition of the segment IVb hepatic vein will be helpful in preventing its damage and is made possible by keeping the transection plane close to the MHV and using the ultrasonic dissector (Cavitron Ultrasonic Surgical Aspirator, CUSA, Valley Lab, Boulder, CO, USA). Bleeding volume could be much reduced if the liver transection proceeds cautiously and slowly. Spending a long time on liver transection is not shameful, but inducing bleeding to the extent that blood transfusion is required or major complications occur is undesirable. Bleeding from the root of the MHV or inferior vena cava is potentially fatal; external compression will be helpful, and help from additional surgeons must be solicited before a disaster occurs.

Protection of the liver remnant is the most important aspect in ensuring speedy recovery of the donor. Prolonged liver rotation and compression onto the liver hilum by retractors must be avoided.

Meticulous hemostasis, preservation of hepatic vein outflow, accurate suturing of hepatic duct stump and meticulous checking for bile leakage sites are all important. Reconstitution of the falciform ligament is always necessary. Deliberate rotation of the left liver to occupy the right subphrenic cavity is absolutely wrong. Before wound closure, thorough flushing of the operation site by a large volume of normal saline can remove debris and clot and detect minor bleeding points and bile leakage. The surgeon retreats only when a pool of normal saline in the right subphrenic cavity is completely clear. Such steps appear minor or excessive but are important for smooth recovery of the donor.

Wound pain is never listed as a complication, but to the donors, wound pain is the most unbearable part of the operation. Perhaps, they do not anticipate that wound pain could be so severe. Inadequate wound pain control may lead to atelectasis and generate ill-feeling towards the donor operation. On the other hand, too much morphine may lead to respiratory depression. Accumulation of morphine dosage will lead to nausea, vomiting, ileus and delayed gastric emptying. The incidence is about 20% in the donors [34].

Such side effects may be tolerated by patients undergoing an operation for their own diseases, but may be unacceptable to the donors who undergo operations for the others. An alternative to morphine is non-steroid anti-inflammatory drugs and cyclooxygenase-2 inhibitors, but the risk of serious peptic ulcer complications is real. Epidural anaesthesia is also a possible alternative, but the risk of nerve injury, infection and bleeding complications, though low, may be too high for the donors. In case the prothrombin time is prolonged or platelet count is low after the donor hepatectomy, the epidural anaesthesia catheter cannot be removed for several days after the operation. Administration of fresh frozen plasma or platelet concentrates just for the purpose of catheter removal is undesirable for the donors who should not receive any exogenous blood or blood products. Moreover, pain relief is not complete with epidural anaesthesia.

Another strategy to reduce wound pain, which is probably the most important one, is to avoid pulling the running suture tightly. The principle of wound closure should be approximation of wound edges by strong sutures without strangulation of the tissues in between the wound. Too tight suturing is undesirable because the subsequent severe inflammatory reaction to ischemia and necrosis could be the cause of severe pain. The knots should be secure, but the tissues should not be occluded tightly and rendered ischemic or necrotic.

Postoperative care of the donor should be the same as any patient having hepatectomy. The surgeon should not overestimate the donor's ability to recover from a major hepatectomy. Chest physiotherapy, incentive spirometry and early mobilization are prerequisite to speedy recovery. However, only optimum liver function and rapid liver regeneration will allow speedy recovery. Liver regeneration will initiate early only if the liver remnant is protected during the operation [35]. If the donor shows early signs of liver failure, such as increasing international normalized ratio, rising serum bilirubin, metabolic acidosis, oliguria or fluid retention, no time should be wasted to send the donor to the intensive care unit for supportive care. Attention is paid to oxygen saturation and blood pressure. Normal liver perfusion and oxygenation are important for liver recovery and regeneration. The surgeon should not hesitate in giving low-dose inotrope to improve the blood pressure and urine output. Parenteral nutrition consisting of branched-chain amino acid-enriched solution, low-dose glucose, phosphate and medium-chain triglyceride may be useful for liver regeneration. If the donor is not suffering from delayed gastric emptying, oral preparation of branched-chain amino acid-enriched solution is also useful. Continuous veno-venous hemofiltration may have to be used for eliminating ill effects of renal function impairment.

The most important step, however, is to identify the cause of liver failure and implement remedial measures. Doppler

ultrasonography and contrast-enhanced CT scan are performed urgently for identification of abnormality of blood flow in the portal vein, hepatic artery and hepatic vein, hematoma around the liver hilum causing compression of the portal vein, infected collection, etc. Empirical antibiotic cover is given because bacterial translocation is a common event in hepatic decompensation patients. The liver biopsy taken at the end of the recipient operation should be reviewed for any unsuspected pathology of the liver. The threshold for re-laparotomy should be low for any donor who continues to deteriorate even though the cause could not be identified by imaging. All such measures may induce immense anxiety among the family members, but the surgeon must not be too optimistic and should provide all treatments to prevent the donor from further deterioration and enhance recovery. The donor must not die from the operation, whatever cause it may be.

Long-Term Outcome

There are not many data on the long-term outcome of the donors. It is undeniable that the majority of donors suffer physically, mentally and socially in the first few months after the donor operation [36].

A survey indicated that by the end of the first year, almost half of donors had minor symptoms, whether it related to the operation. However, none of them received any ongoing medical treatment [36]. Two-thirds of the donors considered their recoveries complete. Ninety per cent of them returned to the same jobs. The median time to return to work was 9 weeks. The mean Karnofsky performance scale returned to 95% after 12 months and was statistically lower than the pre-operative score (100%). The donor health transition score dropped precipitously in the first month and returned gradually in the following months, but worsening of health was still perceivable in a few donors at the end of the first year. About three-quarters of donors felt that they benefited from the donation, but about 10% of donors would not donate again if there was such a need. Using 'willingness to donate again' as a surrogate marker of their experience of the donor operation, donors >35 years of age were found to have more difficulty in adjusting to the operation. Considering that the donor operation is an ultra-major surgery and the recipient outcome is generally satisfactory, despite less satisfactory perception of the operation in a small number of donors, right liver donor hepatectomy is still an acceptable procedure. The long-term assessment of the donor could have been influenced by the recipient outcome.

While a survey in the USA indicated that donors overwhelmingly endorsed donation regardless of the recipient outcome [37], in a survey conducted in Japan, donors with recipients dying after the operation were more likely

unhappy with the donor operation and lost to follow up [4]. Similarly, in Europe, donors with recipient deaths are more likely to report various unspecific complaints and psychosocial conflicts [38]. On this issue, the surgeons must be vigilant in both donor and recipient selections. Donors who have a history of psychological illness are not suitable candidates. Liver pathology that is likely to recur after transplantation should only be accepted for LDLT after careful consideration and discussion. It is the current consensus that living donor donation should only be performed if the risk to the donor is justified by the expectation of an acceptable outcome in the recipient [4].

Liver regeneration is immense and said to be complete after partial hepatectomy in previous studies on cancer patients. However, studies on living donors indicates that regeneration to the pre-resection volume is less than complete even after 2.5 years of follow-up, though the difference between pre-resection liver volume and regeneration liver volume is statistically insignificant [39]. There is paradoxically a trend of incompleteness of regeneration in relation to the original liver volume for those with a larger remnant left liver. It may be argued that incomplete regeneration is related to absence of the MHV in the left liver remnant, but studies shows that the lack of regeneration of segment IV is compensated by that of segment II/III [40]. Perhaps the extent of regeneration is related to the metabolic demand of individual donors. Another possible explanation of incomplete regeneration is that bile ducts and blood vessels do not regenerate in proportion to the liver parenchyma. A study on hepatocellular proliferation and changes in architecture of the right liver graft indicates that there is a decrease in the number of portal tracts despite volume restoration [41].

Conclusion

The outcome of donor operation continues to improve in experienced centres, but it is disheartening to read more and more reports of donor deaths. Donor death has occurred in both experienced and inexperienced centres. Lack of vigilance and loosening of acceptance criteria are the major reasons for the donor mortalities. To avoid further donor death, the transplant surgeon should maintain his/her role as the gatekeeper in preventing unjustified and risky donor operations. Finally, he/she should have full commitment of lifelong and holistic care of the donors.

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