



Research Article

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Early (<6 months) Mortality after Adult to Adult Living Donor Liver Transplantation, Single Centre Experience: A Retrospective Cohort Study

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Abstract

Objectives: Both complications and mortality of recipients are annoying problems after living donor liver transplantation (LDLT). The aim to analyze early (<6 months) mortality of patients after adult to adult LDLT (A-ALDLT) in a single center.

Methods: Between April 2003 and February 2013, we performed 167 A-ALDLT in National Liver Institute, Egypt. We retrospectively analyzed early mortality in recipients.

Results: The overall incidence of early mortality was 34.1% (n=57), it was classified into in hospital (28.7%) and post-hospital discharge (5.4%) mortalities. The most frequent causes of in hospital and post hospital discharge mortalities were SFSS (10/48) and sepsis (5/9) respectively. On univariate analysis, the following factors were significant predictors of early mortality (Female gender, Lt Lobe graft, GRWR<0.8, mean blood transfusion 10.8 ± 9.8 units, (vascular, renal, chest, neurological, bacterial infection and small for size syndrome (SFSS)) complications. While on multivariate analysis by Cox regression, mean blood transfusion 10.8 ± 9.8 units, vascular and neurological complications were independent predictors.

Conclusion: Reduction of blood transfusion units, prevention and management of vascular and neurological complications is required for better early outcome after A-A LDLT.

Keywords

Living Donor Liver Transplantation; Mortality after LDLT

Introduction

After nearly five decades of persistent exertion, liver transplantation (LT) has become a recognized and definite therapy with a highly successful outcome for various liver diseases, such as end-stage cirrhosis of the liver, various metabolic diseases, and hepatic malignancy. The progress that has been made, resulted from improvements in disease management, better surgical techniques, advances in critical care, and better immunosuppressive medication [1].

To further extend the donor pool, successful adult LDLT were performed using left lobe graft in 1993[2] and using right lobe graft in 1996 [3]. These new surgical developments significantly reduced the mortality rate of adult patients waiting for LT and provided the alternative source of organs for LT in regions where deceased organ donation is extremely low or is not available [4].

There are several advantages in using a right lobe graft in adult LDLT. These consist of the adequate volume of functional liver mass, the reduction of incidence of SFSS, less complexity in reconstruction of liver artery and biliary tract, and the anatomical positioning of liver graft [5]. However, early mortality after LT still occurs even in the modern era. Identifying the predictors of early mortality after LT is an important issue that will allow the aggressive management of such potential events and help to minimize or even prevent these tragedies [1,6-8].

The risk factors of early mortality after LT are varied and can be classified into three categories: donor factors(poor-quality grafts, grafts that are small in size, ABO incompatible grafts), operative factors (massive intra-operative blood loss [9] and technical failures) [1,10,11] and recipient factors (the severity of the recipient's illness prior to LT, Child Pugh classification, pre-LT renal insufficiency, malnutrition, the MELD [12,13] and recipient post-operative complications I.e. neurological [14] vascular problems [10] and others [15]. The study aimed to analyze incidence and risk factors of early (<6 months) mortality of patients after adult to adult LDLT in a single center.

Methods

We performed 200 LDLT between April 2003 and February 2013, our study included 167 (A-A LDLT) patients after exclusion of the thirty three pediatric cases. After approval of institutional review board (IRB), we did this retrospective cohort study that analyzed early (<6 months) mortality in recipients in the department of hepato-pancreato-biliary (HPB) surgery, national liver institute (NLI), university of Menoufiya, Menoufiya, Egypt, in the period from the beginning of 2013 to October 2015, where patients were observed from POD 1 until the end of the 6th month post LT or until death of patients with mean follow up period of 4.23 ± 2.48 m, range: (0-6 m). The data were collected from our records in the LT unit of our institute and written informed consents were obtained from both donors and recipients regarding operations and researches. All donors were >19 years old and the donor work-up included liver function tests(LFTs), liver biopsy, ultrasound examination, psychological assessment and CT angiography, along with hepatic volumetric study and vascular reconstructions. The following data were studied (N.B, the MELD era in our institute started at 2007, so, the following data will be studied in the pre MELD (number=14 patients) and MELD eras (number=153 patients).

Preoperative variables

Donor's age, gender, body mass index (BMI), blood group matching, recipients' age, gender, the primary disease, Child Pugh and MELD scores and co-morbidity (DM, HTN,...)

Intraoperative variables

Type of graft (Right or Left), duration of the operation per hours, actual graft weight, actual graft recipient weight ratio, cold and warm ischemia times per minute, blood transfusion per units.

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The donor operation was performed through a right subcostal incision extended to the upper midline under general anesthesia. Intraoperative cholangiography was used to define the biliary anatomy of donors, the right or left lobes of the liver were mobilized and the vena cava was dissected. The CUSA device was used to divide the liver parenchyma without inflow occlusion. The falciform ligament was reconstructed, the stumps of the divided hepatic and portal veins were closed by continuous non-absorbable sutures, after graft harvesting, it was perfused in the back table with Hydroxytryptophan ketoglutarate (HTK) solution and weighted to determine the actual GRWR [16].

In the recipient surgery, the native liver was explanted while carefully preserving the inferior vena cava. After reconstructing the hepatic and portal veins, the hepatic artery was anastomosed by the use of a surgical loupe or microscopy. The biliary tract was reconstructed by a duct-to-duct hepatico-choledochostomy or a Roux-en-Y hepatico-jejunostomy [17].

Postoperative management

Based on our institutional policy: Immunosuppression and postoperative anti-HBV protocols: the standard was combination of 3 drugs calcineurin inhibitors (CNIs), steroids and mycophenolate mofetil (MMF). The initial methylprednisolone dose was 500 mg intraoperatively with a brief taper of prednisone from 240 to 40 mg/d over 6 days followed by 5-20 mg/d maintenance treatment, with complete withdrawal at the end of 3rd month post LDLT. Cyclosporine (CsA) was used when neurotoxicity or nephrotoxicity developed with Tacrolimus. When CNIs were contraindicated or their side effects (i.e. neurotoxicity) halted their use, sirolimus (SRL) was given at an initial dose of 3 mg/m² and adjusted over time to achieve blood trough levels of approximately 5–8 ng/mL. The postoperative anti-HBV protocols consisted of lamivudine combined with therapy with a low-dose of intramuscular hepatitis B immune globulin. Hepatitis B immune globulin was administered to all recipients with HBV infection during and after the transplantation [18–21].

Patients were given prophylactic therapy (Based on our institutional policy) in the form of:

Antibiotics: This began 2 days before operation by using 3rd generation cephalosporine (cefotaxime 1gm/12h, then intraoperative we began with either Tazobactam (piperacillin + sulbactam) 4.5 g/8h plus metronidazole 500 mg/8h. Or Imepanem (Tinam) 1 gm/6h plus metronidazole 500 mg/8h. Then we changed antibiotics according to culture and sensitivity [19–22].

Anticoagulants: Heparin infusion up to 180-200 units/kg/day but when thrombocytopenia occurred, heparin was shifted to clexan 20 mg/12h, then at POD8 dipyridamole was given 150 mg/12h [23–25].

Antifungal: Fluconazole (Diflucan) 100 mg/24h till pod 7 [26–28].

Antiviral: Acycloviral 200mg/8hs began from POD 8 for 6 months for prophylaxis against CMV infection [29].

Postoperative follow-up (The follow-up of post-transplant patients was conducted by a team with transplant surgeon and transplant hepatologist and recipients were followed up at our outpatient transplant clinic weekly within the first month after transplantation, and every month afterwards). through the recorded data we detected:

Early postoperative complication: was defined as complication occurring within six months of transplantation (Biliary, vascular, chest, renal, neurological, infection, small for size syndrome and etc.....). Furthermore, we classified complications according to Clavien-Dindo scoring system [30] (Table 1).

Early mortality (<6 months) that was classified into: i- In hospital mortality (during 1st hospital stay). ii- Mortality after hospital discharge until 6 months post LT (N.B. we performed strict hospital infection control policies after observing high in-hospital sepsis rate in our early cases, so we studied early mortality causes in the 1st 49 cases(early cases)(before doing strict policies), and in the last 118 cases(late cases)(after doing strict policies).

Statistical analysis: All data were tabulated and processed with SPSS software (Statistical Product and Service Solutions, version 21, SSPS Inc, Chicago, IL, USA) and Windows XP (Microsoft Corporation, Redmond, Washington, USA). Qualitative data were expressed in frequency and percentage and analyzed with the chi-square or Fisher Exact tests. Quantitative data were expressed as the mean and standard deviation and were compared with the t-test or Mann Whittney test. We compared between patients in the pre MELD and MELD eras, and between early mortality causes in early and late cases. Univariate analysis and then multivariate analysis were done to detect the predictors of early mortality. The Kaplan–Meier method was applied for survival analysis and compared using log-rank tests. In all tests, a P value of <0.05 was considered significant.

Results

Characteristics of patients and their donors (including operative parameters) according to MELD era

In the pre MELD era (n=14), patients were classified as 13 (92.9%) males, and 1 (7.1%) females. Their mean age was 44.9 ± 3.9. Their donors were classified as 8 (57.1%) males and 6(42.9%) females, their mean age was 26.6 ± 7.3. The patients were classified according to Child-Pugh score into 6(42.9%) class B, and 8(57.1%) class C, and mean model for end stage liver disease (MELD) score, MELD > 18, MELD 18-24, and MELD < 24 were 17.1 ± 3.9, 8(57.1%), 5(35.7%), and 1(7.1%) respectively. Seven (50%) of them had co morbidities, in the form of Hypertension and DM. The donor to recipient BL Group matching was classified into identical in 11 (78.6%) and Compatible in 3(21.4%) of them. The right lobe graft was given to all of them. The mean actual graft weight and actual graft recipient weight ratio (GRWR) were 889.3 ± 154.6 gm and 1.1 ± 0.20 gm respectively. While the mean cold and warm ischemia times were 160.6 ± 96.6 min and 63.5 ± 22.2 min respectively. The mean intra-operative blood transfusion was 9 ± 6.4 units, However the mean operative time and post-operative hospital stay were 16.2 ± 4.2 hours and 31.9 ± 21.6 days respectively, lastly, their early complications and mortalities were 6(42.9%) and 6(42.9%) respectively (Table 2).

On the other hand, In the MELD era (n=153), patients were classified as 134(87.6%) males, and 19(12.4%) females. Their mean age was 46.6 ± 8.5. Their donors were classified as 106(69.3%) males and 47(30.7%) females, their mean age was 26.9 ± 6.6. The patients were classified according to Child-Pugh score into 9(5.9%) class A, 44(28.8%) class B, and 100(65.4%) class C, and mean model for end stage liver disease (MELD) score, MELD > 18, MELD 18-24, and MELD < 24 were 16.03 ± 4.3, 102(66.7%), 45(29.4%), and 6(3.9%) respectively. Fifty four (35.3%) of them had co morbidities, in the form of Hypertension, DM, cardiac diseases and morbid obesity. The

Table 1: Clavien classification of surgical complications.

Grades	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications; blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic or radiological intervention a. Intervention not under general anesthesia b. Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications) requiring IC/ICU management a. Single organ dysfunction (including dialysis) b. Multiorgan dysfunction
V	Death of a patient

CNS: Central Nervous System; **IC:** Intermediate Care; **ICU:** Intensive Care Unit.

Table 2: Characteristics of patients and their donors including intra-operative parameters according to MELD era:

Category	Pre MELD era NO=14	MELD era NO=153	P value
Donor age(years) (MeanSD)	26.6 ± 7.3	26.9 ± 6.6	<0.05
Recipient age(years) (Mean ± SD)	44.9 ± 3.9	46.6 ± 8.5	<0.05
Donor gender males females	8(57.1%) 6 (42.9%)	106(69.3%) 47(30.7%)	<0.05
Recipient gender males females	13 (92.9%) 1(7.1%)	134(87.6%) 19(12.4%)	<0.05
BMI of donor (Mean ± SD)	25.2 ± 3.4		<0.05
Child class A B C	0(0%) 6(42.9%) 8(57.1%)	9(5.9%) 44(28.8%) 100(65.4%)	<0.05
MELD score (Mean ± SD)	17.1 ± 3.9	16.03 ± 4.3	<0.05
MELD >18 18-24 <24	8(57.1%) 5(35.7%) 1(7.1%)	102(66.7%) 45(29.4%) 6(3.9%)	<0.05
Co morbidity	7(50%)	54(35.3%)	<0.05
Bl. Group Compatible Identical	3(21.4%) 11 (78.6%)	45(29.4%) 108(70.6%)	<0.05
Graft type Right lobe Left lobe	14(100%) 0(0%)	145(94.8%) 8(5.2%)	<0.05
Actual graft weight (Mean ± SD)	889.3 ± 154.6	813.05 ± 172.7	<0.05
Actual GRWR (Mean ± SD)	1.1 ± 0.20	1.03 ± 0.20	<0.05
Cold ischemia time (min) (Mean ± SD)	160.6 ± 96.6	67.1 ± 37.8	0.000
Warm ischemia time (min) (Mean ± SD)	63.5 ± 22.2	51.08 ± 15.04	0.05
Intraoperative blood transfusion	9 ± 6.4	6.9 ± 7.5	<0.05
Duration of operation (hours) (Mean ± SD)	16.2 ± 4.2	12.8 ± 2.9	0.009
Hospital stay (postoperative)(days) (Mean ± SD)	31.9 ± 21.6	21.9 ± 15.3	0.1
Immunosuppression regimen Regimen including FK Regimen including Cyclosporine Regimen including sirolimus	13(92.9%) 2(14.3%) 0(0)	131(85.6%) 49(32%) 19(12.4%)	<0.05 <0.05 <0.05
Early complications	6(42.9%)	93(60.8%)	0.1
Early mortality	6(42.9%)	51(33.3%)	<0.05

BMI: Body Mass Index, **MELD:** Model for End stage Liver Disease, **GRWR:** Graft Recipient Weight Ratio

donor to recipient Bl. Group matching was classified into identical in 108(70.6%) and Compatible in 45(29.4%) of them. The right lobe graft was given to 145(94.8%) of them, and the left lobe graft was given to 8(5.2%) of them. The mean actual graft weight and actual graft recipient weight ratio (GRWR) were 813.05 ± 172.7 gm and

1.03 ± 0.20 gm respectively. While the mean cold and warm ischemia times were 67.1 ± 37.8 min and 51.08 ± 15.04 min respectively. The mean intra-operative blood transfusion was 6.9 ± 7.5 units, However the mean operative time and post-operative hospital stay were 12.8 ± 2.9 hours and 21.9 ± 15.3 days respectively, lastly, their

early complications and mortalities were 93(60.8%) and 51(33.3%) respectively (Table 2).

Comparison between patients in the pre MELD and MELD eras:

There was no statistical significant difference between both eras regarding MELD score, early complications and mortality; however, there were significant longer cold ischemia, warm ischemia and operative times in the pre MELD era, and this may be due to the location of the era in our learning curve of LT with suspected longer times (Table 2).

The primary liver diagnosis

The most frequent primary diagnoses were HCV, HCC and cryptogenic cirrhosis respectively (Table 3).

Early complications of recipients

Ninety nine (59.3%) of our patients had one or more than one early complication graded from two to five regarding Clavien's modified 5-tier scoring system where early biliary complications were the most frequent 54/167(32.4%) in the form of biliary leak, biliary stricture or leak with stricture, and according to Clavien grading, grades II, III and V involved 10, 33, and 11 of them respectively (Table 4). These biliary complications were managed as follow: 1- for biliary leak the 1st treatment option was insertion of pigtail for drainage or conservative treatment but if failed; endoscopic retrograde cholangio pancreatography (ERCP) with stent or surgical repair were done. 2- For biliary stricture, the 1st treatment option was ERCP with stent but if failed surgical repair was done (Figures 1 and 2 and Table 4).

The incidence of vascular complications was 23/167(13.8%) that was classified into HA problems (HA stenosis, HAT or HA injury), PV problems (PVT), HV problems (HV stenosis or HVT). As regard Clavien grading, grades II, III, IV and V involved 5, 7, 1 and 10 of them respectively (Table 4). The management of vascular complications included: medical (anticoagulants or thrombolytic therapy), angiography (dilatation, stenting, coling of GDA or thrombolytic therapy) or surgery (thrombectomy or reanastomosis) (Figure 3 and 4).

Neurological complications affected 13(7.8%) of patients in the form of convulsions, neurotoxicity(encephalopathy), cerebral hemorrhage, psychosis, tremors, peripheral neuropathy and drop foot, and according to Clavien grading, grades II, IV, V included 6, 6 and 1 of them respectively. They were managed as follow: 1- for convulsion we used antiepileptic drugs with control of immunosuppression therapy and metabolic control, 2- Immunosuppressive neurotoxicity: it was in the form of encephalopathy and treated by shifting the immunosuppressive drug and anti-coma measures, 3- The patient with cerebral hemorrhage was managed conservatively but unfortunately died, 4- The other complications were managed with neurological supportive treatment (Table 4).

Chest infection, pleural effusion and pneumothorax affected 9%, 0.6% and 1.2% of our patients respectively; they were mainly of grades II and V complications and were managed with antibiotics, diuretics or chest tube (Table 4).

Sixteen (9.6%) of recipients had renal impairment where 14 of them were grade II, and 2 of them were grade V, they were managed with renal supportive therapy.

Bacterial infection affected 13.8% of patients and was mainly in grades II and V, furthermore, they was treated by antibiotics according to culture and sensitivity (Table 4).

SFSS (characterized clinically by a combination of prolonged functional cholestasis, intractable ascites, and delayed functional recovery of both prothrombin time and encephalopathy) affected 21/167 (12.6%) of our patients and for prevention of this syndrome we performed splenectomy in some cases with SFSG and performed multiple HV anastomoses (MHV, RT inferior V, segment 5 or segment 8 v) to improve venous drainage. Furthermore, Clavien grades II and V involved 11 and 10 of them respectively (Table 4).

The incidence of early mortality in all our patients was 57 (34.1%) and its most frequent causes were sepsis, postoperative bleeding, SFSS, and MOF respectively. However, we found a higher early mortality rate in the early 49 cases than the late 118 ones (38.8% vs 32.2%), with a higher sepsis rate in the early than the late cases (10.2% vs 5.9%). On the other hand, the incidence of in hospital mortality in all our patients was 28.7% and its most frequent cause was SFSS (6%), furthermore, a higher in hospital mortality rate (with a trend towards significant difference) was found in the early than the late cases (38.8% vs. 24.6%)(p=0.06) with a significant higher sepsis rate in the early than the late cases (10.2% vs 1.7%)(P =0.01)(N.B. This shows the effect of strict hospital infection control policies), on the other hand, the incidence of post hospital discharge mortality was 5.4% and its most frequent cause was sepsis (7.2%) (Table 5).

On univariate analysis, the following factors were significant predictors of early mortality (Female gender, Lt Lobe graft, and GRWR < 0.8 and mean intra-operative blood transfusion 10.8 ± 9.8 units) (Tables 6 and 7).

On univariate analysis, the following complications (vascular, renal, chest, neurological, bacterial infection and SFSS) were predictors of early mortality (Tables 6-8).

On multivariate analysis by Cox regression, mean intra-operative blood transfusion 10.8 ± 9.8 units, vascular and neurological complications were independent predictors of early mortality (Table 9).

Discussion

In response to the organ donor shortage, A-ALDLT has emerged as an effective alternative to deceased donor liver transplantation (DDLTL), and its use has rapidly spread worldwide [31]. However, early mortality after LT still occurs even in the modern era [1], furthermore, they represent the majority of the deaths [32].

In this work, we studied the early (6 months) mortality after A-ALDLT where our early mortality was 34.1%, (This high rate of

Table 3: The primary liver diagnosis.

HCV	91(54.5%)
HCC on top of HCV	55(32.9%)
HCC on top of HBV	2(1.2%)
Cryptogenic cirrhosis	7(4.2%)
HBV	4(2.4%)
BCS	2(1.2%)
PSC	2(1.2%)
PBC	1(0.6%)
Wilson's disease	1(0.6%)
Autoimmune hepatitis	1(0.6%)
Alcoholic cirrhosis	1(0.6%)

HCV: Hepatitis C virus, **HCC:** Hepatocellular carcinoma, **HBV:** Hepatitis B virus, **BCS:** Budd Chiari syndrome, **PSC:** Primary sclerosing cholangitis, **PBC:** Primary biliary cirrhosis

Table 4: early complications in recipients.

Type of early complications	Clavien grade II	Clavien grade III	Clavien grade IV	Clavien grade V	Total No/167	%
Biliary					54	(32.4%)
1-Bile leak	10	12	0	8	30	(18%)
2-Biliary stricture	0	14	0	2	16	(9.6%)
3-Stricture & bile leak	0	7	0	1	8	(4.8%)
Vascular					23	(13.8%)
1-HA problems	3	4	1	5	13	(7.8%)
2-PV problems	2	1	0	5	8	(4.8%)
3-HV problems	0	2	0	0	2	(1.2%)
Neurological					13	(7.8%)
1-Psychosis	2	0	0	0	2	(1.2%)
2-Convulsions	0	0	2	0	2	(1.2%)
3-Tremors	1	0	0	0	1	(0.6%)
4-Neurotoxicity(encephalopathy)	1	0	4	0	5	(3%)
5- Cerebral hemorrhage	0	0	0	1	1	(0.6%)
6- Peripheral neuropathy	1	0	0	0	1	(0.6%)
7- Drop foot	1	0	0	0	1	(0.6%)
Chest					18	(10.8%)
1-Chest infection	9	0	1	5	15	(9%)
2-Effusion	1	0	0	0	1	(0.6%)
3-Pneumothorax	0	2	0	0	2	(1.2%)
Renal impairment	14	0	0	2	16	(9.6%)
Bacterial infection	10	0	1	12	23	(13.8%)
SFSS	11	0	0	10	21	(12.6%)
Wound						
Wound infection	6	0	0	0	6	(3.6%)
Collection					31	(18.6%)
1-Ascites	24	0	0	0	24	(14.4%)
2-Free biliary collection	0	0	0	6	6	(3.6%)
3-Blood	0	0	0	1	1	(0.6%)
Recurrent HCV	4	0	0	0	4	(2.4%)
Acute rejection	10	0	0	0	10	(6%)

Figure (1) (A)

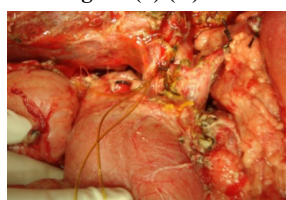


Figure (1) (B)

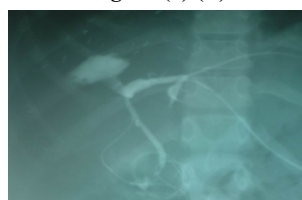


Figure (1)(C)

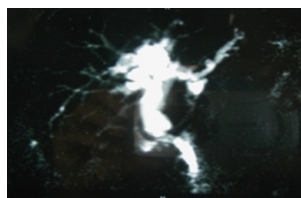


Figure (1) (D)

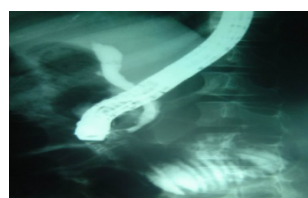


Figure 1: A- a case with 3 "duct to duct" biliary anastomoses" B- Tube cholangiogram showing a case with anastomotic biliary leak. C- Magnetic resonance cholangio pancreatography(MRCP) shows a case with anastomotic stricture. D- ERCP shows anastomotic biliary stricture.

Figure (2) (A)



Figure (2) (B)



Figure (2) (C)

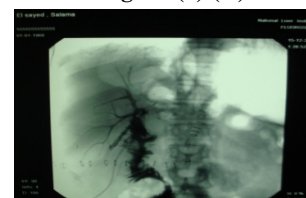


Figure (2) A- Identification of 2 graft bile ducts in case of biliary stricture after LDLTx , B- The same patient underwent biliary enteric anastomosis on the 2 graft bile ducts. C- Tube cholangiogram after HJ with good biliary drainage.

early mortality in our work was due to increased incidence in the early 49 cases than the late 118 ones (38.8% vs 32.2%), with a higher sepsis rate in the early than the late cases (10.2% vs 5.9%). Furthermore, the high rate of in-hospital mortality (28.7%) was due to higher rate(with a trend towards significant difference) in the early than the late

cases (38.8% vs 24.6%) with a significant higher sepsis rate in the early than the late cases (10.2% vs 1.7%) and this shows the effect of strict hospital infection control policies). Similarly, the early (1, 4 and 6 months) mortalities were (27%, 26.5% and 28% respectively) in Qian et al.[33], Sevmis et al.[34] and Xiao et al. [35] studies respectively.



Figure 3: A patient with HAT and multiple hepatic abscesses managed with stenting of HAT and pigtail and antibiotics for abscesses.

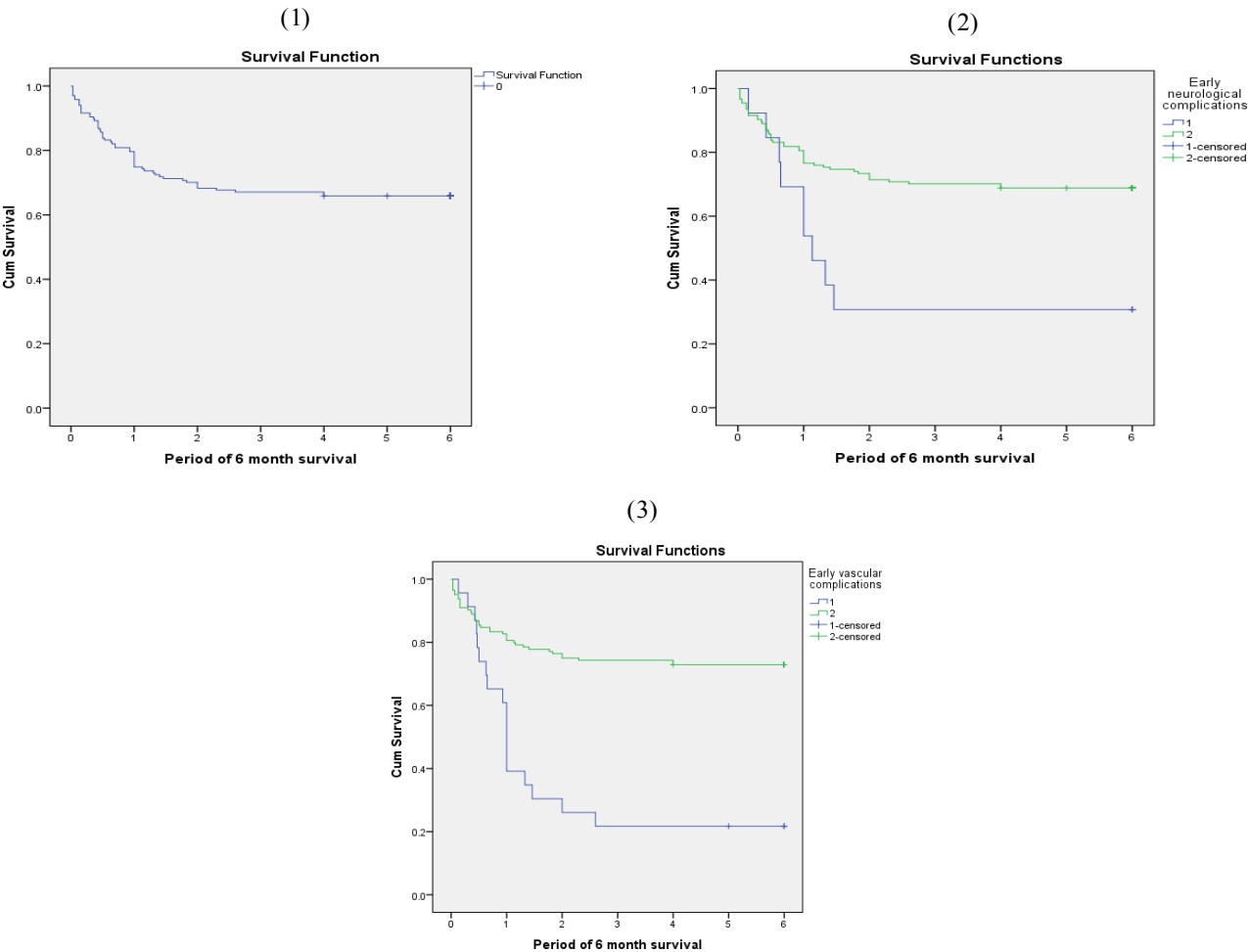


Figure 4: Kaplan-Meier survival curves (1, 2 and 3)

- 1: KM 6-month survival curve
- 2: Neurological complications and 6-month survival (Log rank=0.005)
- 3: Vascular complications and 6-month survival (Log rank=0.00)

On the other hand, the early (1month) mortality was 6%, 14% and 14.6% in Jo et al.[13], Wasilewicz et al.[36] and Bacchella et al.[37] studies respectively. Furthermore, the 3 months mortality was 18%, 5.9% and 1.4 in Chuan et al.[38], Wagener et al.[39] and Lin et al.[32] studies respectively and the 6 months mortality was 13.7% in Xu et al, 2011(40) study. However, the hospital mortality was 2.1%, 5.6%,

7% and 10.6% in Chok et al.[41], Oberkofler et al.[42], Wai et al.[43] and Lee et al.[44] studies respectively. In contrast it was higher in our study as it reached (28.7%).

Sepsis (bacterial, viral, or fungal), which is the most frequent cause of post-transplant mortality, affects about 50% of recipients

Table 5: Early Mortality in patients.

Category	All cases	Early cases	Late cases	P value
Number of patients	167(100%)	49(100%)	118(100%)	
Early mortality(>6months)	57(34.1%)	19(38.8%)	38(32.2%)	0.4
Causes: Sepsis	12(7.2%)	5(10.2%)	7(5.9%)	0.3
Postoperative bleeding	11(6.6%)	1(2%)	10(8.5%)	0.1
SFSS MOF	10(6%)	3(6.1%)	7(5.9%)	0.9
Intraoperative bleeding	8(4.8%)	2(4.1%)	6(5.1%)	0.7
PVT	6(3.6%)	3(6.1%)	3(2.5%)	0.2
Early graft dysfunction	5(3%)	3(6.1%)	2(1.7%)	0.1
Renal impairment	3(1.8%)	1(2%)	2(1.7%)	0.8
	2(1.2%)	1(2%)	1(0.8%)	0.5
	48(28.7%)	19(38.8%)	29(24.6%)	0.06
In hospital mortality	10(6%)	3(6.1%)	7(5.9%)	0.9
Causes: SFSS MOF Sepsis	8(4.8%)	2(4.1%)	6(5.1%)	0.7
Postoperative bleeding Intra-	7(4.2%)	5(10.2%)	2(1.7%)	0.01
operative bleeding PVT	7(4.2%)	1(2%)	6(5.1%)	0.3
Early graft dysfunction	6(3.6%)	3(6.1%)	3(2.5%)	0.2
Renal impairment	5(3%)	3(6.1%)	2(1.7%)	0.1
	3(1.8%)	1(2%)	2(1.7%)	0.8
	2(1.2%)	1(2%)	1(0.8%)	0.5
Post hospital discharge mortality	9(5.4%)	0(0)	9(7.6%)	0.05
Causes: Sepsis	5(3%)	0(0)	5(4.2%)	0.1
Postoperative bleeding(cerebral, iatrogenic, GIT)	4(2.4%)	0(0)	4(3.4%)	0.2

SFSS: Small for size syndrome, **MOF:** Multi-organ failure, **PVT:** Portal vein thrombosis,

GIT: Gastrointestinal tract.

Table 6: Recipient and donor factors as predictors of early mortality:

Category	Early mortality Number (%)	p-value
Number of patients	57/ 167 (34.1%)	
Recipient gender		
males	45/147(30.6%)	.009
females	12/20(60%)	
Donor gender		
males	40/114(35.1%)	> 0.05
females	17/53(32.1%)	
Co-morbidity		
Yes	16/61 (26.2%)	> 0.05
No	41/106 (38.7%)	
Child class		
A	1/9(11.1%)	> 0.05
B	17/50(34%)	
C	39/108(36.1%)	
MELD		
>18	34/110(30.9%)	> 0.05
18-24	20/50(40%)	
< 24	3/7(42.9%)	
Portal HTN		
Yes	55/160 (34.4%)	> 0.05
No	2/7 (28.6%)	
Bl. Group		
Compatible	19/48 (39.6%)	> 0.05
Identical	38/119(31.9%)	
Graft type		
Right lobe	50/159 (31.4%)	.001
Left lobe	7/8 (87.5%)	
Actual GRWR > 0.8		
Yes	44/148 (29.7%)	.001
No	13/19 (68.4%)	
Immunosuppression regimen		
Regimen including FK	47/144 (32.6%)	> 0.05
Regimen including Cyclosporine	14/51(27.5%)	
Regimen including sirolimus	0/19	

Table 7: Recipient and donor factors as predictors of Early Mortality.

Category	Early mortality (Mean± Std. deviation)	No early mortality (Mean ±Std. deviation)	p-value
Recipient age	47.3 ± 8.7	45.8 ± 7.9	> 0.05
Donor Age	25.9 ± 5.03	27.4 ± 7.2	> 0.05
BMI of Donor	24.8 ± 3.4	25.3 ± 3.4	> 0.05
MELD score	16.5 ± 4.9	15.8 ± 3.8	> 0.05
Actual graft w t	776.3 ± 186.3	841.7 ± 160.56	.019
Actual GRWR	1.002 ± 0.2	1.06 ± 0.1	0.057
Cold ischemia time/ minutes	78.02 ± 55.5	73.4 ± 50.4	> 0.05
Warm ischemia time/ minutes	50.6 ± 13.4	52.9 ± 17.2	> 0.05
Blood transfusion(units)	10.8 ± 9.8	5.1 ± 4.9	0.00
Operative time/ h	13.8 ± 3.6	12.6 ± 2.8	> 0.05

Table 8: Complications as predictors of early mortality.

Category	Early mortality Number (%)	p-value
Number of patients	57/ 167 (34.1%)	
Complications		
Yes	47/99(47.5%)	.000
No	10/68(14.7%)	
Biliary complications		
Yes	14/54(25.9%)	> 0.05
No	43/113(38.1%)	
Vascular complications		
Yes	18/23(78.3%)	0.000
No	39/144 (27.1%)	
Wound complications		
Yes	3/6(50%)	> 0.05
No	54/161(33.5%)	
Chest complications		
Yes	17/18(94.4%)	0.000
No	40/149(26.8%)	
Neurological complications		
Yes	9/13 (69.2%)	.005
No	48/154 (31.2%)	
Renal impairment		
Yes	16/16 (100%)	0.000
No	41/151(27.92)	
Recurrent HCV		
Yes	0/4 (0)	> 0.05
No	57/163 (35%)	
Bacterial infection		
Yes	18/23(78.3%)	0.000
No	39/144(27.1%)	
Small for size syndrome		
Yes	15/21(71.4%)	0.000
No	42/146(28.8%)	

Table 9: Multivariate analysis of predictors of early mortality (Cox regression):

	P value	Exp(B)	95% C.I. for EXP(B)	
			Lower	Upper
Female gender	0.52	1.3	0.56	3.1
Lt lobe graft	0.24	0.27	0.03	2.3
GRWR<0.8	0.54	1.6	0.3	8.1
Mean blood transfusion 10.8 ± 9.8 units	0.06	0.95	0.9	1.009
Vascular complications	0.02	5.5	1.2	24.4
Chest complications	0.18	6.1	0.4	88.8
Renal complications	0.96	0.000	0.000	7.2
Bacterial infection	0.99	0.001	0.2	4.9
Small for size syndrome	0.49	1.7	0.3	8.8
Neurological complications	0.004	5.2	1.7	15.8

who undergo LDLT [45]. It was the most frequent cause of death in Chuan et al.[18], Sevmis et al.[34], Xu et al.[40], Emiroglu et al.[45], and Sugawara et al.[46] studies. Similarly, it was the most frequent cause of early mortality in our work, however serious infection was the (1st and 3rd) cause of early death in Li et al.[47] and Du et al.[31] studies respectively. Furthermore, Sepsis was a major cause of early mortality in Ikegami et al. [20], Wagener et al.[39] and Wai et al.[43] studies.

Identifying the predictors of early mortality after LT is an important issue that will allow the aggressive management of such potential events and help to minimize or even prevent these tragedies [1-8]. Researchers have identified intra-operative blood loss as risk factors for early graft loss and mortality after LDLT [48-50]. Similarly, mean blood transfusion of 10.8 ± 9.8 units was independent predictor of early mortality in our study. Furthermore, Intraoperative blood loss and increased amount of blood transfusion was predictor of early mortality in Chung et al. [9], Steinbruck et al. [10], de Boer et al. [11], Ikegami et al. [20], Du et al. [31], Qian et al. [33], Chuan et al. [38] and Xu et al. [40] studies.

Complications are common in the early postoperative period after LDLT [32] and [40]. Ninety nine (59.3%) of our patients had one or more than one early complication graded from two to five regarding Clavien's modified 5-tier scoring system, similarly, Early complications were (39.9%) and 60% in Du et al. [31] and Chok et al. [41] studies respectively. On the other hand, they were 22.9% in Ho et al. [15] study.

The use of small for size graft (SFSG) leads to SFSS, including poor bile production, delayed synthetic function, prolonged cholestasis and intractable ascites, with subsequent septic complications and higher mortality [51-53]. Similarly, GRWR> 0.8 and SFSS were predictors of early mortality in univariate analysis in our study, In contrast, SFSS did not affect mortality in Kiuchi et al. [54] study. The incidence of this syndrome in our study was 12.6%, however it was 15.7% and 22% in Du et al. [31] and Goldstein et al.[19] studies respectively.

Vascular complications are serious causes of morbidity after LT. Bleeding, stenosis, thrombosis, and aneurysm can arise at any of the vascular anastomoses. The incidence is generally about 8-15 % [55]. However this rate can be as high as 20% with LDLT [56]. The incidence of early vascular complication was 12.1%, 10.9%, 10.2%, 8.5% and 7.8% in Lin et al. [32], Emiroglu et al. [45], Sevmis et al. [34], Sugawara et al. [46] and Bacchella et al. [37] studies respectively. Similarly, it was 13.8% in our study. On the other hand, it was lower

2.6%, 3.2% and 3.5% in Xu et al. [40], Lee et al. [44] and Ikegami et al. [20] studies respectively.

The early vascular complications are all well-documented prognostic factors with respect to early mortality [1] as hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT) interrupt the allograft's blood supply and produce early allograft loss, long-term dysfunction, or even patient's death [57]. In the studies by Steinbrück et al. [10], Sevmis et al. [58], and Orlandina et al. [59], vascular complications had significant poor effect on outcome. Similarly, in our study, there was significant correlation between vascular complications and early mortality.

Neurological problems are reported in 10-47% of patients after orthotopic LT [60-63] with a significantly lower incidence in LDLT. The reason for this phenomenon remains uncertain: it could be correlated with a better quality of the transplanted graft and also an improved detoxification power in comparison with longer cold ischemia time [61]. Furthermore, most neurological complications occur early after surgery [61,64-66]. The incidence of neurological complications after LDLT was 20.4%, 17% and 15.4% in Saner et al. [61], Saner et al. [67] and Kim et al. [65] studies respectively. However it was lower (7.8%) in our study as we studied early neurological complications without including late ones. Similarly, early neurological complications were 0.6% in Lee et al. [44] study.

The spectrum of the clinical presentations of neurological complications is extremely wide, ranging from mild to potentially life-threatening disorders [62], the most common neurologic complications include encephalopathy, seizures, immunosuppression induced neurotoxicity and cerebrovascular complications [67,68]. Similarly, the neurological complications in our work was in the form of convulsions, neurotoxicity(encephalopathy), cerebral hemorrhage, psychosis, tremors, peripheral neuropathy and drop foot, and according to Clavien grading, grades II,IV,V included 6,6 and 1 of them respectively.

The neurological complications are associated with significant morbidity and mortality after LT [14,68]. In similar, it was independent predictor of early mortality in our study. In contrast, Wijidicks et al. [69] indicated no impact of NC on mortality, and Saner et al. [63] observed that the occurrence of NC in adult living-donor LT did not influence the clinical outcome. In conclusion: Reduction of blood transfusion units, prevention and management of vascular and neurological complications is required for better early outcome after A-A LDLT.

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