

# Live donor hepatectomy for liver transplantation in Egypt: Lessons learned

Emad Kamel,  
Mohamed Abdullah,  
Ashraf Hassanin,  
Nirmeen Fayed,  
Fatma Ahmed,  
Hossam Soliman<sup>1</sup>,  
Osama Hegazi<sup>1</sup>,  
Yasmine Abd El Salam,  
Magdy Khalil, Khaled Yassen,  
Ibrahim Marwan<sup>1</sup>,  
Koichi Tanaka<sup>1</sup>,  
Khaled AboElla<sup>1</sup>,  
Tarek Ibrahim<sup>1</sup>

Departments of Anaesthesia,  
<sup>1</sup>Hepato-Biliary Surgery, National  
Liver Institute, Menoufiya  
University, Shebeen El-Kom,  
Menoufiya, Egypt

## Address for correspondence:

Prof. Khaled Yassen,  
11 A Khalil El Khaiat, Moustafa  
Kamael Alexandria, Egypt.  
E-mail: kyassen61@hotmail.com

## ABSTRACT

**Purpose:** To retrospectively review anesthesia and intensive care management of 145 consented volunteers subjected to right lobe or left hepatectomy between 2003 and 2011. **Methods:** After local ethics committee approval, anesthetic and intensive care charts, blood transfusion requirements, laboratory data, complications and outcome of donors were analyzed. **Results:** One hundred and forty-three volunteers successfully tolerated the surgery with no blood transfusion requirements, but with a morbidity rate of (50.1%). The most frequent complication was infection (21.1%) (intraabdominal collections), followed by biliary leak (18.2%). Two donors had major complications: one had portal vein thrombosis (PVT) treated with vascular stent. This patient recovered fully. The other donor had serious intraoperative bleeding and developed postoperative PVT and liver and renal failure. He died after 12 days despite intensive treatment. He was later reported among a series of fatalities from other centers worldwide. Epidural analgesia was delivered safely ( $n=90$ ) with no epidural hematoma despite significantly elevated prothrombin time (PT) and international normalization ratio (INR) postoperatively, reaching the maximum on Day 1 ( $16.9 \pm 2.5$  s and  $1.4 \pm 0.2$ ,  $P < 0.05$  when compared with baseline). Hypophosphatemia and hypomagnesemia were frequently encountered. Total Mg and phosphorus blood levels declined significantly to  $1.05 \pm 0.18$  mg/dL on Day 1 and  $2.3 \pm 0.83$  mg/dL on Day 3 postoperatively. **Conclusions:** Coagulation and electrolytes need to be monitored perioperatively and replaced adequately. PT and INR monitoring postoperatively is still necessary for best timing of epidural catheter removal. Live donor hepatectomy could be performed without blood transfusion. Bile leak and associated infection of abdominal collections requires further effort to better identify biliary leaks and modify the surgical closure of the bile ducts. Donor hepatectomy is definitely not a complication-free procedure; reported complication risks should be available to the volunteers during consenting.

**Key words:** Donor hepatectomy, Egypt, living donor liver transplantation, perioperative experience

## INTRODUCTION

Living donor liver transplantation (LDLT) helps in expanding organ availability, especially in the Middle East, where the concept of brain death is still not widely implemented, leading to a critical shortage of adult organ. Overall, donor morbidity and mortality is a controversial issue currently being debated in the medical, surgical, ethical

and public communities. Published donor complication rates differ widely among institutions.<sup>[1]</sup> Advances in anesthetic and surgical management over the past few years made it possible to perform liver resection with minimal risks to the donors.<sup>[2]</sup>

Preparations for the LDLT programme started at the National Liver Institute (NLI), Menoufiya University, Egypt, since 1992. With a joint team headed by Prof Nagi Habib from St Thomas Hospital in London, three cases were performed. Later, in December 2003, the program was again initiated. The LDLT program was developed in two phases: in the first phase, the first 28 cases were performed (including 16 pediatric patients) with the cooperation of Prof Koichi Tanaka and his team from Kyoto University, Japan. In the second phase, after July 2007 till November 2011, the remaining of the cases

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were performed totally and independently by our team, but with occasional visits by Prof Koichi Tanaka and his team. The total number of transplants performed is 145 by November 2011, and is expected to increase.

The aim of this current study is to review and analyze the perioperative anesthetic and Intensive Care Unit (ICU) records, blood transfusion, complications and laboratory data of the live related donors presenting for right and left lobe hepatectomy, in order to report the experience and lessons learned within the Liver Institute in Egypt. The created database will help in drawing conclusions and recommendations that will help to improve the anesthetic perioperative management, improve the data available to volunteers prior to the informed consent and increase the donor safety.

## METHODS

After obtaining approval from the ethical committee of the NLI, Menoufiya University (NLI), the demographic, anesthetic records, blood transfusion, complications and laboratory data perioperatively were retrospectively reviewed for the 145 donor hepatectomies between 2003 and 2011. All donors gave an informed and written consent.

Preoperative assessment included physical examination, ECG, chest X-ray and laboratory tests (arterial blood gases, glucose, electrolytes, complete blood count and coagulation).

Thoracic epidural catheter was inserted between T6 and T11 for intra- and post-operative analgesia before induction of general anesthesia in 90 donors who consented for epidural analgesia. A mixture of 0.125% Bupivacaine and 2 µg/mL fentanyl was used for intra- and post-operative analgesia. The remaining 55 patients had intravenous patient-controlled analgesia with fentanyl.

General anesthesia was induced with Fentanyl 2–4 µg/kg, Propofol 2 mg/kg (dose) and Rocuronium 0.6 mg/kg dose. Two large-bore peripheral and a right internal jugular central venous catheter were placed. Anesthesia was maintained with a balanced anesthetic technique, consisting of a volatile agent (Sevoflurane 0.7–1 MAC) and a mixture of air and oxygen (FiO<sub>2</sub> 0.4). For intraoperative analgesia, additional boluses of Fentanyl were used. Anesthetic management includes the use of two forced air warming blankets for upper and lower extremities and an infusion blood warmer.

Intraoperative monitoring included ECG, invasive arterial blood pressure (left radial artery), noninvasive blood pressure, continuous central venous pressure (CVP),

body temperature, oxygen saturation (SaO<sub>2</sub>), capnometry (EtCO<sub>2</sub>) and urine output (mL).

The patient's position was carefully checked before draping and both arms were tucked by the patients side and well padded to prevent injury of the brachial plexus.

Measures to reduce intraoperative bleeding included maintaining a low positive CVP during the process of transaction, careful parenchymal transaction, a combination of Cavitron Ultrasonic Surgical Aspirator (CUSA)/bipolar electrocautery and the harmonic scalpel. Structures crossing the transection line were securely closed using surgical clips, ties and sutures. One thousand International Units of heparin was given intravenously to the donor before removal of the graft to avoid thrombosis in its vasculature. Fluids given to the donor were restricted using mainly crystalloid to preserve the CVP low and around 5 cm H<sub>2</sub>O to decrease the blood loss before graft removal, but both crystalloids and colloid were used to restore the CVP between 6 and 12 cmH<sub>2</sub>O after the resection and before the end of the surgery.

At the end of the procedure, all patients were extubated in the operating theater and admitted to the ICU immediately postoperatively (The intensive care suite is available close to the operating room. An early oral nutrition was encouraged. Standard deep vein thrombosis (DVT) prophylaxis with low molecular weight (LMW) heparin was implemented. Other prophylactic measures like intermittent calf compression during surgery and the first 24 h after surgery was always applied to reduce the risk of DVT. Chest physiotherapy and early mobilization is part of the routine immediate postoperative care. Postoperative medications included prophylactic perioperative antibiotic coverage of a third-generation antibiotic, Ceftriaxone 1 g every 8 h intravenously as a prophylactic measure together with intravenous Metronidazole 500 mg 8-hourly and (explain) Histamine H<sub>2</sub> receptor antagonist as a prophylaxis for stress ulceration 50 mg intravenously every 8 h.

The standard coagulation tests included prothrombin time (PT), international normalized ratio (INR) of the PT, activated partial thromboplastin time (aPPT), fibrinogen and platelets.

Donor complications were recorded and managed accordingly.

## Statistical analysis

Data was statistically analyzed using SPSS (statistical package for social science) program version 15 for windows, and, for all the analysis, a  $P < 0.05$  was considered statistically significant. Repeated measures ANOVA test was performed

to differentiate changes in different follow-up results of normally distributed studied variables. The Friedman test was performed to differentiate changes in the different follow-up results of the different variables studied. Paired t test was performed to detect the mean and standard deviation of normally distributed pre and post values of the same variable of the same group of patients. Wilcoxon test was done to detect mean and standard deviation of not normally distributed pre and post values of the same variable of the same group of patients. Pearson's correlation test was done to study the correlation between two normally distributed quantitative variables. All data were tested with the Kolmogorov-Smirnov Z test, and most of them were found to be normally distributed and were, therefore, presented with mean±SD in tables. Both parametric and nonparametric testes were used for performing associations or correlations.

## RESULTS

### Donor data

One hundred and forty-five donor hepatectomy for LDLT were performed at the NLI, Menoufiya University, Egypt, between December 2003 and November 2011. One hundred and eighteen donors were subjected to right hepatectomy (81.37%). Twenty-seven donors were subjected to left hepatectomy (18.62%) for 26 pediatric and one adult patient. All donors were judged to be ASA I, but three were graded as ASA II. The donor's mean age was 25.53±6.39 years, with a range of 18–45 years. Males represented 69.9% of the population [Table 1].

The relationship between the donor and the recipient reflects a strong family relationship as a high portion of the donors were from a 1<sup>st</sup> degree relative; siblings represented a high percentage (90.9%).

### Intraoperative data

With a mean duration of surgery of 8.1±1.1 h, the intraoperative and immediate postoperative (8-h) mean fluid replacement of crystalloids and colloids were 4500 mL±3.25 and 500±5 mL, respectively. The mean total urine output during surgery and the immediate postoperative (8-h) period was 2421.4±342.6 mL. The mean intraoperative fentanyl consumption was 950±2.16 ug.

The preoperative radiological studies (n=145) showed the mean total estimated right lobe weight to be 927.29 gm±119.11. The mean actual weight of the resected right lobe liver was 861.39 gm±150.9. The difference between the estimated and the actual right lobe weight was statistically significant (P<0.01). The mean graft weight/recipient weight ratio was 1.08±0.2. Most donor right hepatectomies were performed with preservation of the

**Table 1: Descriptive statistics of the volunteers for donor hepatectomy (n=143)**

Variable (units)	Mean	SD
Age (years)	25.53	6.39
BMI (kg/m <sup>2</sup> )	25.7	3.1
RLV (g)	861.3	150.9
RLV (%)	37.0	4.6
Operative time (h)	8.1	1.1
Males (%)	69.9	4.1
Crystalloids (mL)	4500	3.25
Colloids (mL)	500	5
UOP (mL)	2421.4	342.6

Data are presented as mean and standard deviation (SD); Body mass index, remnant liver volume, urine output. UOP, crystalloids and colloid intraoperative and 8-h postoperative

middle hepatic vein (MHV), but, in seven donors, right hepatectomies were performed with MHV harvesting.

### Donor outcome

One hundred and forty-three donors successfully emerged from anesthesia and were extubated in the operating room.

Two donors had to be ventilated postoperatively in the ICU due to major complications. One of the two donors had to be reoperated for suspected PVT. A stent had to be inserted intraoperatively, which helped to restore the portal vein patency. This donor was ventilated for a period of 7 days in the ICU before full recovery. She is now being followed-up for 3 years without any complications.

The other donor (operated in 2007) was subjected to serious bleeding from a slipped vascular clamp for the hepatic veins during removal of the graft. Bleeding was rapidly controlled, but, on postoperative Day10, despite adequate anticoagulation, extensive PVT developed. The patient developed liver and renal failure. Thrombolytic therapy was used without any response. Unfortunately, he died on the 12<sup>th</sup> day postoperatively. The program was held up for 6 months, before being restarted with more strict criteria for donor selection. This case was reported several times during local and international conferences and also among a series of worldwide reports of mortality.<sup>[3]</sup>

No epidural hematoma, deep venous thrombosis or pulmonary embolism was reported in any of the donors.

### Laboratory test results

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB) and lactate increased significantly during and after liver resection, reaching the maximum increase at the first day, with a gradual decline. A statistically significant difference over time (30 days) (P<0.01) was observed [Table 2].

Magnesium (Mg) and phosphate also dropped significantly during the course of the perioperative events, requiring continuous monitoring and IV replacement. The mean intravenous phosphate repletion was 60 mmol and the mean Mg given was 2000 mg. Total Mg blood levels declined significantly to  $1.05 \pm 0.18$  mg/dL on the first postoperative day despite replacement [normal reference range (1.2–2.2 mg/dL)], and this required continuous monitoring and IV replacement. Phosphorous also showed a similar decline in blood levels to  $2.3 \pm 0.83$  mg/dL of the third postoperative day, below the normal reference ranges (2.7–5.5 mg/dL), and this decline was found to be statistically significant ( $P < 0.01$ ) [Table 3].

PT and INR readings reflected a degree of hypocoagulability, reaching the maximum on the postoperative first day,  $16.9 \pm 2.5$  s and  $1.4 \pm 0.2$  s (baseline value) ( $P < 0.05$  when compared with baseline).

The mean hemoglobin concentration decreased from a preoperative value of  $13.8 \pm 1.45$  mg/dL to  $11.5 \pm 1.3$  mg/dL ( $P < 0.05$ ) postoperatively, with no blood transfusion given in most of the cases (143 out of 145). The platelet count dropped postoperatively to the lowest mean value of  $160 \pm 38.8/\text{mm}^3$  ( $P < 0.01$ ) when compared with the preoperative mean value [Table 4].

### Postoperative analgesia

Epidural analgesia was used for intraoperative and postoperative pain control for 90 donors with a mean time for the epidural catheter stay of  $5.88 \pm 1.27$  days. No donors demanded fresh frozen plasma units to normalize the INR before epidural catheter removal. The mean intensity of pain on a numerical analogue scale (0–10) at rest on Day 1 was 5/10, Day 2 was 3/10 and Day 3 was 2/10. Analgesia gaps during movement and coughing were frequently reported, and required alteration of the patient-controlled epidural

**Table 2: Liver function tests, serum cholesterol and lactate at different measuring points**

Variable	Preop	Intraop	D-1	D-3	D-5	D-10	D-30
TB (mg/dL)	$0.61 \pm 0.28$	$2.1 \pm 0.8^{**}$	$1.3 \pm 1.5^{**}$	$3.12 \pm 1.9^{**}$	$2.1 \pm 1.9^{**}$	$1.3 \pm 1.5^*$	$0.69 \pm 0.24$
AST (U/L)	$19.2 \pm 6.4$	$284.9 \pm 127.8^{**}$	$327.8 \pm 106^{**}$	$134.9 \pm 50.1^{**}$	$65.0 \pm 23.6^{**}$	$44 \pm 17.7^{**}$	$23.4 \pm 7.7$
ALT (U/L)	$21.9 \pm 7.2$	$268.3 \pm 31.4^{**}$	$361.2 \pm 20^{**}$	$231.7 \pm 83^{**}$	$134 \pm 46.6^{**}$	$80 \pm 38.6^*$	$29.0 \pm 10.5$
Lactate (mg/dL)	$14.9 \pm 3.6$	$26.8 \pm 8.6^{**}$	$18.2 \pm 4.5^{**}$	$16.7 \pm 5.3^*$	$16.6 \pm 5.04$	$16.7 \pm 5.04$	$15 \pm 2.82$
Cholesterol (mg/dL)	$147 \pm 43.7$	$118.6 \pm 32.03^*$	$107.0 \pm 26^{**}$	$82.2 \pm 16^{**}$	$77.12 \pm 14^{**}$	$90 \pm 25.2^{**}$	$135.0 \pm 48.7^{**}$

Data are presented as mean  $\pm$  standard deviation (SD). Lactate and cholesterol were tested by paired t-test while TB, AST, ALT were tested with Wilcoxon test.  $*P < 0.05$  was considered as significant and  $**P < 0.01$  was considered as highly significant in comparison with the preoperative variable; Total bilirubin, aspartate aminotransferase, alanine aminotransferase; D, postoperative day

**Table 3: Renal function tests and electrolyte changes at different measuring points**

Variable	Preop	Intraop	D-1	D-3	D-5	D-10	D-30
Urea (mg/dL)	$25.4 \pm 5$	$27.3 \pm 7.5$	$21.7 \pm 7.02$	$17 \pm 6.2^{**}$	$15 \pm 5.8^{**}$	$18.8 \pm 8.0^{**}$	$22.6 \pm 6.2$
Creat (mg/dL)	$0.6 \pm 0.1$	$0.7 \pm 0.2^{**}$	$0.61 \pm 0.15$	$0.5 \pm 0.1^{**}$	$0.5 \pm 0.1^{**}$	$0.55 \pm 0.15$	$0.58 \pm 0.1$
Na (mmol/L)	$137.4 \pm 4$	$134.0 \pm 3.4^*$	$134 \pm 3^{**}$	$132 \pm 1.5^{**}$	$131.5 \pm 1.9^{**}$	$132.6 \pm 3^{**}$	$135 \pm 4.2$
K (mmol/L)	$4.2 \pm 0.2$	$4.02 \pm 0.35$	$4.01 \pm 0.27$	$3.8 \pm 0.3^{**}$	$3.9 \pm 0.43^*$	$4.1 \pm 0.4$	$4.06 \pm 0.1$
Ca (mmol/L)	$1.2 \pm 0.8$	$1.17 \pm 0.8^*$	$1.2 \pm 0.06$	$1.2 \pm 0.06$	$1.19 \pm 0.05$	$1.2 \pm 0.13$	$1.18 \pm 1^*$
Mg (mg/dL)	$1.8 \pm 0.2$	$1.6 \pm 0.3^*$	$1.05 \pm 2^{**}$	$1.7 \pm 0.2$	$1.8 \pm 0.25$	$1.8 \pm 0.32$	$1.85 \pm 0.2$
PO <sub>4</sub> (mg/dL)	$3.8 \pm 0.6$	$3.7 \pm 0.65$	$3.05 \pm 1^{**}$	$2.3 \pm 0.8^{**}$	$2.9 \pm 0.6^{**}$	$3.3 \pm 0.66^*$	$3.71 \pm 0.5$

Urea, creatinine, Na, K, Ca and Mg were tested by paired t-test, while PO<sub>4</sub> was tested with Wilcoxon test.  $*P < 0.05$  was considered as significant and  $**P < 0.01$  was considered as highly significant; Data are presented as mean  $\pm$  standard deviation (SD). Creat, creatinine; Na, sodium; K, potassium; Ca, calcium; Mg, magnesium; PO<sub>4</sub>, phosphorus; D, postoperative day

**Table 4: Blood picture and coagulation parameters at different measuring points**

Parameters	Preop	Intraop	D-1	D-3	D-5	D-10	D-30
HB (g/dL)	$13.8 \pm 1.8$	$12.8 \pm 1^{**}$	$13.4 \pm 1.03$	$11.5 \pm 0.8^{**}$	$11 \pm 0.7^{**}$	$12.05 \pm 2^{**}$	$12.5 \pm 1.2$
Hct (%)	$40.7 \pm 4.9$	$37.9 \pm 4^{**}$	$35.04 \pm 2^{**}$	$35.0 \pm 2.7^{**}$	$33.4 \pm 2^{**}$	$34.9 \pm 2^{**}$	$37.3 \pm 4.05$
INR	$1.0 \pm 0.01$	$1.1 \pm 0.09^{**}$	$1.4 \pm 0.2^{**}$	$1.3 \pm 0.16^{**}$	$1.1 \pm 0.1^{**}$	$1.03 \pm 0.1^*$	$1.01 \pm 0.01$
PT (s)	$12.3 \pm 0.07$	$13.6 \pm 1^{**}$	$16.9 \pm 2^{**}$	$15.5 \pm 2.2^{**}$	$13.1 \pm 33.6$	$12.7 \pm 1^{**}$	$12.3 \pm 0.04$
Platelets/mm <sup>3</sup>	$238.8 \pm 46$	$209.1 \pm 47.1^{**}$	$207.4 \pm 40^{**}$	$160 \pm 38^{**}$	$187.6 \pm 50^{**}$	$232.8 \pm 71$	$261.2 \pm 45.8^{**}$
aPTT (s)	$28.6 \pm 5.3$	$32.7 \pm 7.6^*$	$34.1 \pm 4^{**}$	$32.02 \pm 6^*$	$29.9 \pm 4.7$	$27.3 \pm 5.5$	$27.9 \pm 4.9$
Fib (mg/dL)	$331.9 \pm 61$	$256.7 \pm 54.1^{**}$	$298.05 \pm 96$	$371 \pm 72^{**}$	$384.3 \pm 67.5^{**}$	$383.0 \pm 90.3^*$	$325.9 \pm 44$

Data are presented as mean  $\pm$  standard deviation (SD). D, postoperative day. Hb, Hct%, platelets count, INR, aPTT and fibrinogen were tested with paired t-test. PT was tested with the Wilcoxon test.  $*P < 0.05$  was considered as being significant and  $**P < 0.01$  was considered as being highly significant. HB = hemoglobin, Hct = Hematocrite concentration, INR = International Normalization Ratio, PT = prothrombin time, aPTT = activated partial thromboplastin time, Fib = fibrinogen, FDPs = fibrinogen degradation products

analgesia (PCEA) settings or addition of intravenous systemic opioids to maximize analgesia postoperatively and help early ambulation. Seventeen of 90 donors with PCEA complained of bilateral lower limb numbness during the first day due to established epidural block, but only one patient developed moderate motor block, and epidural infusion was stopped with close follow-up of the motor status.

### Morbidity

Several postoperative complications were observed during the first week, with a morbidity rate of (50.1%). Several donors had more than one complication, the most frequent complication being infection of the intraabdominal collections (21.1%), followed by biliary leak (18.2%) and pleural effusion (8.1%). Gram negative bacteria, predominantly *Escherichia coli*, were present in most abdominal fluid cultures, probably from the bile leaks of the cutting raw surface of the remaining liver after resection. Blood and abdominal fluid cultures were performed routinely. The antibiotic cover would change according to the culture and sensitivity results. Bile leaks was reported to be around 18.2%, while the percentage of the infection of abdominal collections were close to the bile leak percentage, around 21.1%. One donor had an injury to the left hepatic duct, which required intraoperative reconstruction and stent placement. Twelve donors with bile leak were treated with endoscopic retrograde cholangio-pancreatography (ERCP) and stent insertion.

Another volunteer suffered a vasovagal syncope during epidural catheter placement, and recovered when allowed to lie down. Respiratory difficulty requiring reintubation in the immediate postoperative period due to the development of a pneumothorax secondary to central venous line placement was reported in one case, and resolved uneventfully. The ultrasound-guided central venous catheter placement was not used for this particular case. It was later introduced in the operating room and the anesthetic personnel involved in the liver transplantation programme received adequate training. You should mention whether you used ultrasound guided technique for CVC or not.

The rate of nerve injury was 2.8% in the form of ulnar nerve injury, which resolved later without any residual effect.

The 27 donors subjected to left hepatectomy demonstrated a lower incidence of morbidity related to the procedure, the most important difference being the incidence of biliary leak that was only reported in one volunteer and resolved spontaneously with no intervention. No abdominal infection or nerve injury was reported.

The surgical procedure was performed in a shorter duration ( $5.2 \pm 1.4$  h versus  $8.1 \pm 1.1$  h), with no major morbidity or mortality reported.

## DISCUSSION

One of the principal objectives of this study was to identify the risks subjected to the volunteers involved in the process of live liver donation in Egypt as reported by several and various world wide transplant centers.<sup>[4-6]</sup> This will help in drawing out conclusions and suggestions to maximize the care provided to the donors at the NLI throughout the procedure and later.

Removal of a considerable hepatic mass leads to diminished hepatic synthesis of clotting factors and the development of a hypocoagulable state.<sup>[7-10]</sup> Alternatively, a hypercoagulable profile can also result from diminished hepatic synthesis of anticoagulants, extensive tissue trauma and acute phase response.<sup>[11,12]</sup>

Living donors in this current study showed statistically significant postoperative changes in the platelet count and PT, but their means were within the acceptable range for epidural catheter removal as recommended by the American Society for Regional Anesthesia and Pain Medicine,<sup>[13]</sup> (but platelet count was still within the range acceptable for epidural catheter removal) which did not present a risk for epidural hematoma formation during the maintenance and/or removal of the epidural catheter. The peak changes on the first postoperative day were similar to the two studies by Siniscalchi *et al.* and Schumann *et al.*<sup>[9,10]</sup> In this current study, no donor with epidural catheters developed any epidural hematoma, even when severe coagulopathy and PVT developed. The removal of an epidural catheter imposes the same degree of hazard as insertion. The American Society for Regional Anesthesia and Pain Medicine recommend that epidural catheters should be removed when the INR is <1.5 and, following these recommendations, all our patients had INR below 1.5 at all measured time points, which allowed for a safe removal.

Donors of this current study also received 1000 IU of heparin at the end of liver parenchymal dissection in order to prevent blood clotting in the graft following interruptions of the hepatic artery, hepatic vein and portal vein. Cammu *et al.*<sup>[14]</sup> administered a higher dose of 50 IU/kg of heparin intravenously at the end of the hepatic dissection with no complications.

Despite the administration of heparine to prevent intravascular thrombosis of the graft, the aPTT values did not change in the current study, similar to the findings by Siniscalchi *et al.*,<sup>[9]</sup> which also reported that the aPTT in contrast to PT did not change significantly postoperatively after donor hepatectomy, probably due to the reduced dose

of the heparin used (1000 IU of heparin is not significant for postoperative clotting. Removal of right lobe leads to postoperative increased INR, prolonged Pt and low platelets. They peak on the 3<sup>rd</sup> post-operative day. They were deranged on p.o. Day 3 in your study, too, but it was not mentioned in results. The results in Table 4 demonstrated a peak on the first day and abnormal derangement on the 3<sup>rd</sup> day).

In this current study, hypophosphatemia developed in all donors, despite most donors starting oral intake within 24 h postoperatively. This requested additional intravenous replacement of phosphorous as stated in the results. The study by Salem and Tray<sup>[15]</sup> hypothesized that posthepatectomy hypophosphatemia reflects a derangement of normal hepatorenal messaging, which could reflect a transient isolated hyperphosphaturia after hepatic resection. The studies by Pomposelli *et al.*<sup>[16]</sup> and Yassen *et al.*<sup>[17]</sup> also suggested that hypophosphatemia is a “universal event” after donor hepatectomy, which was in contrast to the study by Tan *et al.*<sup>[18]</sup> that reported that no patient suffered life-threatening hypophosphatemia.

Hypomagnesemia also developed in this current study, with a maximum reduction on Day 1 postoperatively this required continuous monitoring and IV replacement.

Donor safety is the most important clinical issue related to LDLT, especially when using right lobe grafts. Sevmis *et al.*<sup>[4]</sup> believe that all potential living donors should be informed about the risks of surgery. Only highly dedicated donors should be chosen. LDLT should be performed only at well-established centers, with surgical teams having appropriate medical expertise, and grafts, donor evaluation, intense preoperative planning and meticulous surgical techniques are imperative to minimize the associated morbidity or mortality.

The frequency of complications differed significantly with graft type. More of the right lobe donors had complications than those with the lateral segment or left lobe, as reported by the Sevmisa *et al.* study. Similar findings were reported in the current study of the NLT, in which only one volunteer from the 27 left hepatotomy donors suffered from biliary leak that resolved spontaneously, and all left hepatotomy donors were practically free from morbidity and, more important, no mortality was reported. What about your study-did you notice the same trend? It would be interesting to see the percentage of complications in pts with right vs. left hepatectomy).<sup>[4]</sup>

In this current study, the morbidity rate was 52.17%, similar to the study by Fujita *et al.*, which also reported donor morbidity to be as high as 50%, but the incidence

was lower (10–20%) in another study by Brown *et al.*<sup>[19,20]</sup> In this current study, the most frequent complication was infection (23.18%), which was higher than that reported in the study by Rafik *et al.* (12.5%),<sup>[5]</sup> followed by biliary leak (20.28%), close to the 18.6% reported by the study by Fujita and coworkers.<sup>[19]</sup>

In the liver institute study, the rate of nerve injury incidence almost disappeared when the arms were kept to the side of the patients and when the moderate traction imposed on the ribs from the abdominal retractors were relaxed more frequently to reduce the compression imposed on the brachial plexus between the first rib and the retracted thoracic ribs. In a study by Rafik *et al.*,<sup>[4]</sup> neuropraxia due to brachial plexus injury occurred in 16 donors, two of whom had lasting disability.

The vascular complication in the current study was found to be around 1.4%, involving PVT. In a study by Pomfret *et al.*,<sup>[1]</sup> the authors reported PVT in one of 561 donors (0.18%). Also, in a study by Jiang,<sup>[21]</sup> a case (3.8%) with PVT was diagnosed on the third postoperative day with routine daily Doppler ultrasound examination. In another study by Yassen *et al.*, the authors reported one donor with PVT, which was managed by relaparotomy and intraoperative tissue plasminogen activator infusion.<sup>[22]</sup>

It is estimated that several donors have died during the procedure in different parts of the world, which generally occurred at experienced centers. The mortality rate among living liver donors had been reported in 2001 to be < 1% by the European Liver Transplant Registry, and a donor mortality rate as low as 0.3% was reported in the USA.<sup>[1]</sup> Seven cases of donor deaths were reported by the Surman study.<sup>[23]</sup> Three additional donors have undergone liver transplantation because of complications related to right lobe donation as reported by the Lo survey study.<sup>[24]</sup> In a study by Wiederkehr *et al.*, a 31-year-old woman who underwent a right lobectomy presented with a cerebral hemorrhage on the seventh postoperative day.<sup>[25]</sup>

Umeshita *et al.*<sup>[6]</sup> reported no perioperative deaths in living liver donors in Japan since the first operation in 1989; from June 2002, a total of 1999 LDLT have been performed in 48 Japanese centers with no perioperative donor deaths. These results might be due partly to the meticulous surgical techniques and extensive perioperative management experience for such a particular procedure.

An adult-to-adult living donor liver transplantation (A2ALL) cohort study was initiated in the United States with the participation of nine liver transplant centers involving 405 donors between the years 1998 and 2003, which reported three donor deaths (0.8%) and eight

life-threatening conditions (2%), with 62% of the donors experiencing complications including biliary leak of 9%, which was much lower than our current study reported biliary leak of 18.2% and a bacterial infection of 12% lower than the current study infection rate of 21.1%. This cohort study from the USA concluded that adult living liver donation was associated with significant complications and even mortality. They recommended that, possibly, the quantification of the complications could improve the process of informed consent and perioperative care.<sup>[26]</sup>

Complications associated with live liver donor surgery should be minimized. There is little information on the impact of team experience and learning on the surgical outcome, but results are expected to improve with the development of a learning curve.<sup>[27]</sup>

In this current study from Egypt, one donor unfortunately did not survive in 2007. This is the first mortality case to be reported by the liver institute in Egypt, and was previously also reported also by Chakravarty *et al.* in 2010.<sup>[3]</sup> This mortality again raises the issue of cadaveric liver transplantation availability and legibility as an alternative and back-up support for such procedures in countries where the legality of brain stem death is still not approved or is in the process to be approved in the near future, as in Egypt. LDLT is definitely not a complication-free procedure for donors. All potential living donor candidates should be well informed about the risks of surgery. Highly dedicated donors only should be chosen. LDLT should be performed only at well-established centers with surgical teams that have appropriate medical expertise and adequate institutional resources. Every effort should be adopted to increase donor safety.

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