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Life-threatening or nearly life-threatening complications in living liver donors

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Abstract

Objective: To determine the relationship between a transplant center's experience and life-threatening or nearly life-threatening complications during living donor hepatectomy (LDH).

Methods: The medical records of 1140 patients who underwent LDH were analyzed. To determine the relationship between life-threatening complications and a transplant center's experience, the following comparisons between LDH cases were performed: first 100 vs subsequent 100; first 100 vs subsequent 1040; first 200 vs subsequent 940; right hepatectomy vs left hepatectomy; and first 5 years of experience vs subsequent 5 years.

Results: A total of 36 life-threatening or nearly life-threatening complications developed in 34 of 1140 (2.98%) healthy individuals undergoing LDH. Of these, 5 occurred intraoperatively, 26 within 1 month, and 5 beyond 1 month. The most common complications were biliary problems and postoperative bleeding. None of the donors died at follow-up. One donor underwent deceased donor liver transplantation (DDLT) for severe hepatic failure. Only 2 comparisons were significantly different with regard to life-threatening complications: the first 100 vs the subsequent 1040 (P = .03) and the first 200 vs the subsequent 940 (P = .01).

Conclusion: This study indicates that the incidence of life-threatening or nearly life-threatening complications are reduced by increased center experience (>200 LDHs).

KEYWORDS
intraoperative complications, life-threatening complications, living donor hepatectomy, nearly life-threatening complications, postoperative complications

1 | INTRODUCTION

Since the first successful liver transplantation (LT) performed by Starzl et al[1,2] in 1967, LT has become the gold standard therapy for many liver diseases. In contrast to North America and Europe where almost the entire graft need is met by cadaveric organ pool, living liver donors (LLDs) constitute a great proportion of donor pool in many Asian countries including Turkey.[1]

Compared to deceased donor liver transplantation (DDLT), living donor transplantation (LDLT) has both advantages and disadvantages. The major advantages of LDLT are short transplant waiting list, short cold ischemia time, being a planned elective surgery, and easy access to liver graft for patients in need of urgent LT. The main disadvantages of LDLT, on the other hand, include a technically more complex vascular and biliary reconstruction. Despite its numerous advantages, LDLT has not been widely used in Western countries, mainly because of donor safety. This is because the most serious medicolegal concern in LDLT is the complications of living donor hepatectomy (LDH), both for surgeons and transplant centers.[3]

The five grade Clavien Surgical Morbidity scale modified for LLDs is the most commonly used one for categorizing complications of LDH according to their significance and to develop effective

treatment modalities.[4] This scale contains nausea and simple wound infections (grade I) in the one end and life-threatening complications and donor mortality (grade V) in the other.[4,5] The most important problem with the Clavien scale is that it is only designed to describe postoperative surgical and medical complications. In other words, it provides no information about intraoperative life-threatening or nearly life-threatening complications. Therefore, there is an unmet need for a novel terminology to draw attention to serious complications during and after LDH.

In an attempt to draw attention to the importance of life-threatening or nearly life-threatening complications, many striking terms have been used, such as Near-Miss Events, Close Call, Nearly a Collision. Life-threatening or nearly life-threatening complications are defined as complications associated with a potentially significant mortality risk where death or permanent injury is averted by chance or early intervention.[4-6] Based on this definition, serious intraoperative complications and grade IIIb-IV complications in the Clavien scale can be collectively termed as life-threatening or nearly life-threatening complications, although a consensus is yet to be reached for this subject. The primary objective of this study was to investigate the relationship between LDH experience and life-threatening or nearly life-threatening complications. Our secondary objective was to convey the message that the Clavien Surgical Morbidity scale developed to define life-threatening complications among patients undergoing donor surgery is inadequate and needs to be modified. By this way, we aim to raise awareness about the need for developing a novel scale containing all serious intraoperative and postoperative complications related to LDH.

2 | MATERIALS AND METHODS

The LT program at Inonu University Faculty of Medicine Liver Transplantation Center was started in 2002, with the first successful DDLT having been performed in March 2002. After 10 successful DDLT procedures, the first successful LDLT was carried out in September 2005. A total of 1140 LDH procedures were performed between September 2005 and December 2014. The demographic and clinical data of the LLDs were retrospectively reviewed to determine the incidence of intraoperative and postoperative complications considered as life-threatening or nearly life-threatening complications. The following information was obtained from patients' medical and operative records: age, gender, body mass index (BMI), relationship with recipient, remnant liver volume, hepatectomy type (right lobe, left lobe), type of complications, radiological tools used to definition of complications (intraoperative cholangiography, ultrasonography [US], multidetector computed tomography [MDCT], magnetic resonance cholangiopancreatography [MRCP], percutaneous transhepatic cholangiography [PTC]), and management of complications (endoscopic retrograde cholangiopancreatography [ERCP], percutaneous intra/extrahepatic biliary drainage, hepaticojejunostomy, patch venoplasty, relaparotomy, surgical biliary drainage, T-tube choledochotomy, various medical approaches etc.)

2.1 | Definition of life-threatening or nearly life-threatening complications for LLDs

We believe that the following surgical and medical complications should be defined as life-threatening or nearly life-threatening complications: biliary complication requiring radiological, endoscopic, or surgical intervention under general anesthesia; gastrointestinal hemorrhage requiring endoscopic or radiological intervention under general anesthesia; postoperative surgical site hemorrhage requiring relaparotomy; organ abscesses requiring relaparotomy or drainage by interventional radiology; organ injury/perforation requiring relaparotomy; progressive hepatic failure requiring LT; transient hepatic failure; renal failure requiring hemodialysis; multiorgan failure; cerebrovascular events requiring intensive care; and all Clavian grade IIIb-IV complications such as pulmonary embolism, cardiac or respiratory arrest.[4,5] Intraoperative hemodynamic instability requiring medical therapy; anaphylactic reactions; difficult-to-control bleeding episodes secondary to opening of hepatic or portal vein clamps; biliary tract injury requiring hepaticojejunostomy or T-tube drainage; vessel narrowings limiting blood flow developing after suturing of hepatic vein or portal vein stump; pulmonary embolism; and myocardial infarction were also defined as life-threatening or nearly life-threatening complications.

2.2 | Classification of life-threatening or nearly life-threatening complications

These complications can be divided into 3 groups, considering the timing of complications. Complications that occurred during LDH were defined as intraoperative; those that occurred within the first postoperative month as early postoperative; and those that occurred after the first postoperative month as late postoperative life-threatening or nearly life-threatening complications.

2.3 | Definition of the donor groups

One of the objectives of this study was to investigate the relationship between life-threatening or nearly life-threatening complications and our center's LDH experience. For this purpose, the patients were grouped on the basis of the number and type of LDH procedures and compared with respect to life-threatening or nearly life-threatening complications incidence as follows: the first 100 LDH vs the subsequent 100; the first 100 LDH vs the subsequent 1040; the first 200 LDH vs the subsequent 940; right hepatectomy vs left hepatectomy; and the first 5 years of experience vs the subsequent 5 years of experience.

TABLE 1 Demographic and clinic features donors with life-threatening or nearly life-threatening complications

Demographic features	n	%
Gender		
Male	23	67.6
Female	11	32.3
Age (Y)		
Mean	34.6	
Range	19-62	
BMI (kg/m^2)		
Mean	25	
Range	17.8-36.8	
Remnant volume (%)		
Mean	33.8	
Range	28-47.8	
Donor hepatectomy type		
Right hepatectomy	29	
Left hepatectomy	5	
Relationship with recipient		
Brother/sister	11	32
Son	9	26.5
Father	3	8.8
Daughter	3	8.8
Cousin	2	5.9
Wife/husband	2	5.9
Mother	1	2.9
Nephew	1	2.9
Aunt	1	2.9
Brother in law	1	2.9

2.4 | Postoperative follow-up

All cases were followed at liver transplant intensive care unit for at least 2 days after LDH. During that time, the vascular structure of the remnant liver was routinely examined by Doppler US. Donors free of complications were transferred to regular ward on the third day and discharged approximately on the fifth day. During that time period, daily complete blood count and other biochemical analyses were performed. Following their discharge, all patients were invited to routine outpatient controls on 15 days, at 1 month, 3 months, 6 months, 12 months, 24 months, and 36 months. Donors who developed intraoperative vascular complication were monitored at the intensive care unit for a longer time than those who were free of complications. Donors who developed hepatic failure following LDH were followed at intensive care unit under the assistance of liver support systems until liver function became normal. Bile drainage catheters were left in place for at least 4 weeks in both donors undergoing hepaticojejunostomy (radiologically or intraoperatively placed transanastomotic biliary catheter) and those undergoing transcystic catheter/T-tube drainage. The catheters were removed after confirming the absence of a leak or stricture on a control cholangiogram.

2.5 | Statistical analysis

SPSS version 22.0 (Statistical Package for the Social Sciences, Inc., Chicago, IL, USA) was used for statistical analyses. Chi-square test with Yates correction was used for the comparison of categorical variables. A P value of <.05 was considered as statistically significant.

3 | RESULTS

3.1 | Demographic and clinical features

A total of 36 life-threatening or nearly life-threatening complications developed in 34 LLDs consisting of 23 male and 11 female patients aged between 19 and 62 years. Twenty-six of life-threatening or nearly life-threatening complications occurred at early postoperative period; 5 at late postoperative period; and the remaining 5 at intraoperative period. Volumetric measurements with MDCT revealed a mean remnant liver volume (RLV) of 33.8% (range: 28%-47.8%). Twenty-nine (85.3%) of 34 donors with life-threatening or nearly life-threatening complications underwent right LDH and 5 (14.7%) left LDH. The life-threatening or nearly life-threatening complications in patients who underwent left lobe LDH were as follows: benign biliary stricture (n = 1), persistent biliary leakage (n = 1), right posterior bile duct injury (n = 1), ischemic necrosis of segment IV (n = 1), and postoperative bleeding (n = 1). The remaining 31 life-threatening or nearly life-threatening complications developed in 29 patients who underwent right lobe LDH. The donors diagnosed with life-threatening or nearly life-threatening complications had an average hospital stay of 21.4 days (range 5-41 days). The mean±SD time between LDH procedure and last outpatient clinic visit/telephone contact was 2247 ± 1023 days (median: 1947 range: 1018-3798 days). The average time between the complications management and last outpatient clinic visit/telephone contact was 2166 ± 1063 days (median: 1703 range: 1017-3720 days). Other clinical and demographic characteristics were summarized on Table 1.

3.2 | Comparison of groups according to complications

To investigate the relationship between surgical expertise and life-threatening or nearly life-threatening complications, 1140 donors were compared with regard to several aspects. First, the relationship between life-threatening or nearly life-threatening complications and the duration of our center's LDH experience was tested. Life-threatening or nearly life-threatening complications occurred in 12 (4.4%) of 271 LDH performed in the first 5 years and 22 (2.53%) of 869 LDH performed in the next 5 years (P = .16). Second, the donors were compared according to the type of hepatectomy performed. Accordingly, life-threatening or nearly life-threatening complications occurred in 29 (2.97%) of 975 right LDH and 5(3.0%) of 165 left LDH

TABLE 2 Comparison of life-threatening or nearly life-threatening complications with different aspects

Groups	n	Complications n (%)	*P*
Between 2005 and 2009	271	12 (4.4)	.16
Between 2010 and 2014	869	22 (2.5)	
Right hepatectomy	975	29 (2.9)	.96
Left hepatectomy	165	5 (3.0)	
First 100 LDH	100	7 (7.0)	.76
Subsequent 100 LDH	100	5 (5.0)	
First 100 LDH	100	7 (7.0)	**.03**
Subsequent 1040 LDH	1040	27 (2.6)	
First 200 LDH	200	12 (6.0)	**.01**
Subsequent 940 LDH	940	22 (2.3)	

LDH, living donor hepatectomy.
Complications: life-threatening or nearly life-threatening complications.

(*P* = .96). Third, the correlation between the number of LDH procedures and life-threatening or nearly life-threatening complications was analyzed. Life-threatening or nearly life-threatening complications occurred in 7 (7.0%) donors after the first 100 LDH vs 5 (5.0%) donors after the next 100 LDH (*P* = .76); 7 (7.0%) donors after the first 100 LDH vs 27 (2.6%) donors after the next 1040 LDH (*P* = .03); 11 (6.0%) donors after the first 200 LDH vs 22 (2.34%) after the next 940 LDH (*P* = .01). The inter-group comparisons according to the number of Life-threatening or nearly life-threatening complications were presented on Table 2.

3.3 | Classification and management of complications

3.3.1 | Intraoperative complications

Five (13.9%) of 36 life-threatening or nearly life-threatening complications occurred at intraoperative period. The problems arose during portal vein division in two donors with anomalous portal venous branching. A significant narrowing was detected at the level of portal vein bifurcation after right portal vein stump closure in both cases. In both cases, a vascular clamp was placed to the main and left portal vein, the stump was opened, and a patch venoplasty was performed with a saphenous vein graft. Postoperative Doppler US and MDCT confirmed a normal portal venous flow (Figure 1). In two other donors, an inferior caval vein narrowing was noted after the closure of the right hepatic vein stump. In both cases, the hepatic vein stump was opened after a side-biting Satinsky clamp was placed on the inferior caval vein. Patch venoplasty was performed in both cases, with a saphenous vein graft in one of them and a peritoneal patch in the other.[7] The right posterior bile duct was injured during parenchyma transection with CUSA during left LDH. A feeding tube 7 Fr in size was inserted into the right posterior bile duct from the stump of the cystic canal, and a primary repair using a single suture was performed perpendicular to the incision in the bile tract. The patient was ultimately discharged uneventfully. The details of intraoperative complications are given in Table 3.

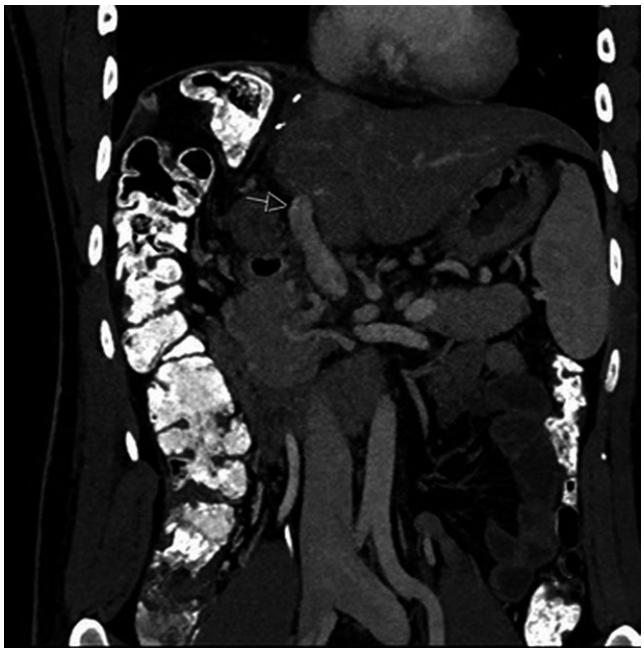

FIGURE 1 Postoperative contrast-enhanced MDCT view of the portal vein reconstructed with patch venoplasty

3.3.2 | Early postoperative complications

Twenty-six (72.2%) of 36 life-threatening or nearly life-threatening complications occurred at early postoperative period. Biliary leaks occurred in 7 donors at early postoperative period. Two of these cases had persistent leak and stricture despite endoscopic and percutaneous interventions and thus were treated with hepaticojejunostomy. In 1 patient, T-tube drainage was performed by placing a T-tube.

Six donors suffered bleeding from the drain at postoperative follow-up. The patients with clinical signs and symptoms of hemorrhagic shock were urgently taken to relaparotomy. Some bleedings originated from the periductal vascular plexus around the bile duct draining the caudate lobe divided at the time of parenchyma transection. The remainders originated from the hilar plate that was rich in intraparenchymal arterial collateral circulation. Hemostasis was achieved by suturing hemorrhagic foci single or multiple sutures. None of these cases had recurrent bleeding following relaparotomies.

Four donors developed respiratory arrest within 1 hour after the procedure. As all of these patients were closely monitored at the time of arrest, and all were intubated within 1 minute. The real problem with these donors was that they were extubated too early to resume spontaneous respiration. Hence, all of them were re-extubated soon thereafter without further complication. The fifth patient, however, suffered progressive respiratory difficulty and was re-intubated within a couple of minutes on the first postoperative

TABLE 3 Management of donor with life-threatening or nearly life-threatening complications

Life-threatening or nearly life-threatening complications	n	Management
Intraoperative complications	5	
Portal vein injury	2	Patch venoplasty with vein graft (n = 2)
Vena cava inferior injury	2	Patch venoplasty with vein graft (n = 1) Patch venoplasty with peritoneal patch (n = 1)
Right posterior bile duct injury	1	Primary repair over transcystic catheter extending into right posterior bile duct (n = 1)
Postoperative complication		
Early (≤1 mo)	26	
Bile leakage	7	Hepaticojejunostomy (n = 2) Choledochotomy with T-tube insertion (n = 1) Drainage (n = 2) Primary suture repair over internal stent insertion (n = 1) Primary suture repair (n = 1)
Postoperative bleeding	6	Hemostasis with relaparotomy (n = 6)
Respiratory arrest	4	Reintubation and respiratory support (n = 4)
Hepatic failure	4	Falciformopexy (n = 1) Repositioning of the remnant Liver (n = 1) Supportive therapy with MARS (n = 1) Liver transplantation (DDLT) (n = 1)
Infected biloma	3	Drainage with relaparotomy
Pulmonary embolism	1	Heparin followed by warfarin
Liver abscess/necrosis	1	Segment IV resection with drainage
Late (>1 mo)	5	
Benign biliary stricture	3	Hepaticojejunostomy followed by ERCP/PTC (n = 3)
Intestinal perforation	1	Resection with anastomosis (n = 1)
Postoperative bleeding	1	Hemostasis with relaparotomy (n = 1)

PTC, percutaneous transhepatic cholangiography; ERCP, endoscopic retrograde cholangiopancreatography; MARS, Molecular Adsorbent Recirculating System; DDLT, deceased donor liver transplantation.

day. That patient was diagnosed with pulmonary thromboembolism by arterial blood gas analysis and CT angiography, and immediately heparinized with heparin infusion followed by warfarin administration. The patient did not develop any further complication during follow-up.

Three patients developed fever and leukocytosis during postoperative follow-up. In all of them, a MDCT taken to evaluate abdominal cavity showed biloma like collection at the surgical site. All 3 patients underwent relaparotomy and infected biloma was detected at the surgical site. Subsequent controls revealed no bile leak at the cut surface of the remnant liver. Cholangiography did not show any leak, either. However, the infected biloma formation was still considered to occur due to a bile leak that was spontaneously closed at early postoperative period.

FIGURE 2 Demonstration of percutaneous transhepatic cholangiography. An external biliary drainage catheter was inserted into remnant bile duct for postoperative severe stricture

Four patients developed hepatic failure at early postoperative period. We encountered the first of them during the initial years of our LDLT experience. In that case, we unfortunately forgot to perform falciformopexy after having completed the LDH procedure. The patient had liver function tests increased, and we detected portal vein compression with the imaging studies. The patient was taken to relaparotomy on the first postoperative day and had a dramatically improved clinical status thereafter. One of the right LDH cases had a rise in liver function tests and thus we performed imaging studies and revealed a positional hepatic outflow obstruction by the remnant liver. That patient was taken to relaparotomy where repositioning was performed under the guidance of US. In the third case, a borderline RLV was shown, and liver function tests and ammonia level were indicative of hepatic failure at postoperative period. In that case, liver support system (Molecular Adsorbent Recirculating System-MARS) was used. The patient was discharged uneventfully.

The fourth case as follows: A 33-year-old male donor candidate (BMI: 27.1 kg/m^2, Anti HBc Total [+], Anti HBS [+]) presented to our center to donate liver to her brother, who had cryptogenic cirrhosis. A preoperative MDCT quantified a RLV of 30%. After completion of preoperative preparations, the donor underwent right lobe LDH procedure. The macroscopic structure of the liver was assessed by two surgeons experienced in LDH, who concluded that they found no disturbing finding other than a mild firmness. Furthermore, no finding in favor of marked hepatosteatosis or fibrosis was present in the frozen examination of the sample sent during surgery. Since the first postoperative day, he had persistently elevated liver function tests (AST, ALT, bilirubin, INR) and blood ammonia level, which we attempted to lower by daily liver support system MARS to allow the liver to improve. As Doppler US indicated an increase in portal blood flow, medical therapy was commenced to reduce splanchnic blood flow. Beginning from the 6th day, however, blood liver function test levels entered a new increase trend. Therefore, remnant liver was evaluated with MDCT, which revealed that the liver was volumetrically adequate but developed patchy areas of impaired perfusion. Meanwhile, indocyanine green test carried out every other day to quantify plasma disappearance rate (PDR) was 8.9% and 3.9% (normal range: 18%-25%). A control MDCT on the ninth day indicated that the parenchyma was markedly heterogenous and showed patchy areas of necrosis. The patient developed grade III encephalopathy and was listed for urgent liver transplantation. A cadaveric liver graft harvested from a 22-year-old male killed in a traffic accident was transplanted to the patient in December 2014. In the laparotomy operation performed for DDLT, the remnant liver was considerably firm, swollen, and contained patchy necrotic areas. The pathologists reported that the histopathological findings in the remnant liver were compatible with paracetamol toxicity. In other words, paracetamol was considered as a contributing factor of the remnant liver failure. He had no complications at thirty-eight months follow-up.

A patient who underwent left lobe lateral segment resection was diagnosed with an abscess in segment IV. He developed elevated liver enzymes and fever at postoperative follow-up. A contrast-enhanced MDCT showed ischemia and abscess formation secondary to ischemia in segment IV. That patient was managed with relaparotomy with necrotic segment IV resection at an early period. The patient was discharged uneventfully. Details of early postoperative complications are given in Table 3.

3.3.3 | Late postoperative complications

Five (13.9%) of 36 life-threatening or nearly life-threatening complications occurred at late postoperative period. Of these patients, 3 presented with jaundice and itching. A MRCP revealed bile duct stenosis. Two cases were treated by stent implantation via ERCP and the other via percutaneous transhepatic biliary drainage (Figures 2 and 3). All 3 patients underwent hepaticojejunostomy due to persistent symptoms at follow-up. One patient presented with signs and symptoms of acute abdomen at late postoperative period and underwent laparotomy on the basis of findings on physical examination. Laparotomy revealed an intestinal perforation probably secondary to cautery burn, which was treated by partial small bowel resection with end-to-end anastomosis. One patient presented with abdominal pain and malaise. A MDCT showed a surgical site collection consistent with a hematoma, which was removed with laparotomy.

4 | DISCUSSION

Experienced centers performing LDLT have devised algorithms taking into account several important factors such as appropriate donor age, BMI, vascular anatomy, biliary structure, graft selection, postoperative care, adequate remnant liver volume, meticulous surgical technique, and experience of the center and the surgeons to avoid complications and appropriately manage complicated cases.[5,8-12] Nevertheless, a consensus is lacking as to how these parameters

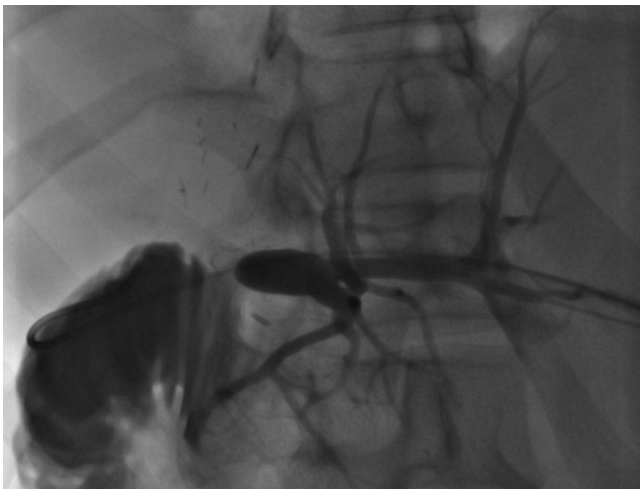

FIGURE 3 Demonstration of percutaneous transhepatic cholangiography following hepaticojejunostomy

affect the incidence of complications. For instance, many centers do not report serious intraoperative complications as long as they can effectively manage them.[4] Therefore, the information about the true incidence of intraoperative complications affecting donors is scarce, and this study aimed to create awareness about this subject.

Shin et al[13] reported that serious complications occurred in 1.2% of 827 LDH cases. The authors reported that (i) they failed to reveal any relationship between transplant center experience and complication rate (especially bile tract complications and grade IIIb complications); (ii) the rate of complications could not be reduced, even toward figures lower than those of the former periods despite all kinds of training; (iii) they were disappointed by the absence of an expected drop in grade IIIa and grade IIIb complications; and (iv) biliary complications were more common among the younger patients. Lee et al[14] observed serious complications in only 0.36% of 832 LDH cases and Kim et al[15] in 4.5% of 288 LDH cases. However, Gruttadauria et al[3] detected complications in 29% of 100 LDH cases, of which 21% were serious. In our study, the initial overall life-threatening or nearly life-threatening complications incidence was 3.1% which dropped to 2.34% as more experience had been gained by the time of 200th LDH. Differences between these results indicate that there is a close relationship between experience and serious complications. It is obvious that significant experience is essential to reach a life-threatening or nearly life-threatening complications incidence 0.36% reported by a multicenter study from Korea.[14] In summary, we believe that serious complications would become less common as more experience is gained, and our outcomes also support this hypothesis.

The debate continues as to whether there is a close association between lobectomy type and complications. A widely accepted view is that, as compared with left/left lateral lobectomy, right/extended right lobectomy is associated with more severe and numerous complications.[16-19] Lo[16] reviewed the outcomes of 1508 LDH cases from five Asian countries and noted that the descending order hepatectomy types by the complication rate were right lobectomy (28%), left lateral segmentectomy (9.3%), and left lobectomy (7.5%). Shio et al[19] reported that, as compared to left lobectomy, right lobectomy was associated with a higher rate of complications. Shin et al[13] performed a multivariate analysis and found no correlation between right or left lobectomy and complications. Yi et al[5] reported similar complication rates following right and extended right hepatectomy. Lee et al[14] demonstrated that the complication rates after right and left LDH were statistically similar. The authors also compared hepatectomy subgroups (left lateral, left lobe, extended left lobe, right lobe, extended right lobe, and right posterior section) and were not able to detect any significant difference between the subgroups with respect to overall, biliary, and serious complications. Uchiyama et al[20] reported that as experience was gained, the incidence of grade IIIa and grade IIIb complications was reduced after right hepatectomy, approaching to that seen after left/left lateral segment LDH. Although we are less experienced in left lobectomy than we are in right lobectomy, we did not observe any statistically significant difference between the two. An important point to note here is that we performed segment II-III-IV resection for left LDH because we experienced a larger volume of biliary leak from the remnant caudate lobe in left LDHs that also included segment I although the volume of segment I is negligible. To summarize, reports from experienced centers suggest that hepatectomy type and complications are not correlated. While some authors advocate that this depends on surgeon experience, some others argue the contrary.

There is an ongoing debate whether there is a relationship between RLV and complications. Shi et al[21] demonstrated that significant complications were less common among donors with a RLV greater than 35%. Facciuto et al[22] reported that donors with a RLV below 30% were not significantly different from those with a RLV above 30% with regard to complications, although they stressed that 30% should be considered a cutoff level. Cho et al[23] also reported no difference between RLV below and above 35% in this regard. Lee et al[14] categorized donors into 4 RLV groups (<30%, 30%-34%, 35%-39%, ≥40%); they failed to show statistically significant differences between the groups with respect to overall, biliary, and serious complications. In a study where 288 cases with a RLV <%30 vs ≥%30 were compared, Kim et al[15] showed similar rates of both overall and serious complications. In contrast, Yaprak et al[24] compared donors with RLV≤%30 vs RLV>%30 and demonstrated that overall complications were more prevalent among low-RLV group but serious complications had similar rates in both groups. Our personal experience is that as RLV increases, liver function tests improve more rapidly. However, we also demonstrated that absence of any relationship between RLV size and life-threatening or nearly life-threatening complications. In our opinion, donor age, the status of the middle hepatic vein, and presence of hepatosteatosis are perhaps more important than the remnant volume.

As with many other complex surgical procedures, a learning curve exists for both LDLT and LDH procedures. A clear consensus has not yet been established as to the relationship between transplant centers', surgeons' experience, and complications. According to a guideline published by Miller et al[25] for ILTS in

2017, centers reach a steady state after they perform 15-20 LDLT procedures, with the learning curve having an impact on patient outcomes (Class I, Level B). However, Cheah et al[4] advocated that the number of learning threshold should be increased from its current recommended level of 20 cases to minimize complications. Hence, a literature review by Cheah et al[4] indicated that as the number of LDLT is increased, morbidity remained essentially unchanged but the rate of complications like life-threatening or nearly life-threatening complications dramatically decreased. They even showed that the incidence of life-threatening or nearly life-threatening complications dramatically fell at centers with a LDLT volume of >200 LDLT. While the rate of the complications defined as life-threatening or nearly life-threatening following the first 200 LDHs performed at our center was 6%, it was reduced to 2.3% for the 940 subsequently performed LDHs. This difference was statistically significant ($P < .01$). Our findings perfectly match with the findings of a worldwide questionnaire published by Cheah et al.[4] Unlike what many authors have recommended, we believe that the center's learning curve threshold for LDH procedure should not be 20, as considered by many, but much more. Furthermore, there is no information in the literature as to the relationship between life-threatening or nearly life-threatening complications and expertise of the surgeons. Indeed, it is hard to comment on this subject. During the period when the present study was performed, all LDHs were performed by a total of 3 surgeons, one of whom was a pioneer in this field, and all of whom were extremely experienced in both hepatobiliary surgery (a minimum of 100 liver and biliary tract surgeries) and LDH (a 50-case experience). When we closely examine the distribution of the complications, the complication rates of the 3 surgeons were very close to each other.

One of the most important issues is bleeding, particularly during accidental opening of the portal and hepatic vascular clamps. Bleeding is the most important indicator for hepatectomy and predicts postoperative complications. It depends on the experience and skills of a surgeon. The important point to remember here is that bleeding should be carefully managed. Proper surgical or medical treatment should be applied rapidly. Early recognition of postoperative bleeding and early relaparotomy as needed is very important. The delay can result in life-threatening complications.

Prolonged rotation of liver and external compression during hepatectomy procedure must be avoided. Careful hemostasis, protection of hepatic vein flow, fully and properly suturing bile tract stump, and carefully controlling bile leakage have great importance in terms of development of life-threatening or nearly life-threatening complications. The falciform ligament should be properly sutured to the anterior abdominal wall after right hepatectomy. Inadequate control of wound pain may lead to atelectasis and generate ill-feeling toward 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.

Developing postoperative early respiratory arrest can be life-threatening for a completely healthy LLDs. Close monitoring is necessary, and reintubation as needed is a life-saving intervention. Another possible complication is pulmonary embolism. Unless treated in time, it can be fatal.[4] Therefore, it is important to eliminate predisposing factors for pulmonary embolism, to encourage early mobilization, and to apply preoperative embolism stockings, etc.

In this study, one of the limiting factors for us was to investigate whether there was any psychosocial difference between cases with and without complications following LDH. As this study entirely focused on intraoperative and postoperative life-threatening or nearly life-threatening complications, we did not specifically study psychosocial problems. Having said that, a doctorate thesis investigating post-LDH problems is ongoing at our clinic for the time being, and its findings will be published soon.

5 | TOPIC HIGHLIGHT

1. Assessing hepatic vascular and biliary anatomy carefully, both before (MDCT, MRCP) and during (cholangiography) the operation, is the most important task to reduce the rate of serious LDH-associated complications to acceptable levels.
2. Strict compliance with the guidelines for donor selection provided by centers experienced in LDLT is greatly effective at eliminating serious complications.
3. We believe that the Modified Clavien scale developed for categorization of postoperative complications falls short of defining donor complications. To our opinion, a novel classification method should be developed, which preferentially takes into consideration severe intraoperative complications. The complications we termed as life-threatening or nearly life-threatening complications clearly demonstrate the necessity of such a classification.
4. We are of the opinion that there is a linear association between transplant centers and surgeons' experience and the incidence of serious intra/postoperative complications but a general consensus in the literature is yet to be reached. To our opinion, the ideal cutoff level of a center's learning curve is 200 LDH. However, almost no information exists for a cutoff level for transplant surgeons.
5. Our 12-year experience has taught us not to use some donors (HBcTotal [+], RLV <30%, >30% macrosteatosis, BMI>30 km/m^2, age >35 years) whenever possible. However, we surely push our limits for cases who have no other donor option or those with an urgent transplant indication.
6. It is impossible to prevent all serious complications, although the majority appears preventable.

CONFLICT OF INTEREST

The authors declare no conflict of interests regarding this manuscript.

AUTHORS' CONTRIBUTIONS

Dirican A, Isik B, and Yilmaz S: Performed LDH; Onur A, Dirican A, and Akbulut S: Collected the data, designed the study, and analyzed

literature; Dirican A, Akbulut S, and Yilmaz S: Contributed to manuscript preparation; Akbulut S, Isik B, and Yilmaz S: Completed final revision of the manuscript.

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