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Implementation of a living donor liver transplantation program in the Republic of Uzbekistan: a report of the first 40 cases

Konstantin Semash[1,2,3], Timur Dzhanbekov[1,2,3], Mirshavkat Akbarov[1,2], Miraziz Mirolimov[1], Azimjon Usmonov[1], Navruz Razzokov[1], Ziyodulla Primov[1], Temurbek Gaybullaev[1,2], Sardor Yigitaliev[1]

[1]Department of HPB Surgery and Liver Transplantation #1, Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V. Vakhidov, Tashkent, Uzbekistan
[2]Department of Faculty and Hospital Surgery and Transplantation, Tashkent Medical Academy, Tashkent, Uzbekistan
[3]Department of Minimally Invasive Pediatric Surgery, National Children's Medical Center, Tashkent, Uzbekistan

Background: Living donor liver transplantation (LDLT) is an effective treatment for patients with end-stage liver disease. This study was performed to evaluate the outcomes of the initial series of LDLT procedures performed in the Republic of Uzbekistan and to demonstrate that liver transplantation is viable under the conditions in this country.
Methods: Between October 2021 and December 2023, we performed 40 LDLTs. We evaluated both immediate and long-term outcomes.
Results: Thrombosis of the hepatic artery developed in one case (2.5%). Arterial anastomotic stenoses were diagnosed in three cases (7.5%) and were successfully treated with endovascular balloon vasodilation. Splenic artery steal syndrome arose in three patients (7.5%) and was managed with endovascular embolization of the splenic artery. One patient (2.5%) developed portal vein thrombosis. Portal vein stenosis occurred in two patients (5%) at 10 months posttransplantation and was addressed with endovascular balloon angioplasty, yielding good clinical outcomes. Biliary complications were observed in 45% of the cases, with bile leakages accounting for 89% of these issues and strictures of the biliary anastomoses for 11%. The in-hospital mortality rate was 12.5%.
Conclusions: Our research findings and analysis of complications align with the international literature, and the results are deemed acceptable during this implementation phase of the liver transplantation program. Accordingly, liver transplantation is feasible in the Republic of Uzbekistan; however, improvements in surgical and therapeutic methods are necessary to minimize the development of both early and late postoperative complications.

Keywords: Liver transplantation; Living donors; End-stage liver disease

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Corresponding author: Konstantin Semash
Department of Minimally Invasive Pediatric Surgery, National Children's Medical Center, 294 Parkent St, Tashkent 100020, Uzbekistan
E-mail: doctorsemash@gmail.com

HIGHLIGHTS

- This study describes the first series of living donor liver transplants performed in the Republic of Uzbekistan.
- The immediate and long-term outcomes were evaluated in both recipients and donors.
- The challenges encountered during the implementation stage of the liver transplantation program were also emphasized.
- The program was established at the Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V. Vakhidov in 2021.

INTRODUCTION

Since Thomas Starzl performed the first liver transplantation (LT) in 1963 [1], the global transplant community has evolved from isolated clinical attempts to widespread acceptance of LT as a treatment for acute and chronic liver diseases, malignant tumors, and various other liver conditions. Over time, the list of indications for LT has expanded to include dozens of etiologically distinct entities. As the demand for LT continues to rise, living donor LT (LDLT) has become a life-saving option for many patients who would otherwise die while waiting for a cadaveric organ. In recent years, LDLT has been shown to be a clinically safe complement to deceased donor LT, meaningfully expanding the limited donor pool [2].

In the Republic of Uzbekistan, more than 50 people per 100,000 population die each year from liver cirrhosis and its complications. The predominant causes of liver cirrhosis in this region are viral hepatitis B and C [3,4]. Prior to 2018, the country had no legal framework in place for organ transplantation. However, in 2018, the Government of the Republic issued a decree authorizing LDLT. Following this, in February 2018, a team from Russia's V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs carried out the first series of LTs in the Republic of Uzbekistan. We began performing these operations independently in October 2021 [5].

The purpose of this study was to assess the outcomes of the first 40 cases of self-performed LDLT in the Republic of Uzbekistan. Additionally, we aimed to demonstrate the feasibility of LT under the conditions in this country.

METHODS

This study was approved by the Institutional Review Board of Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V. Vakhidov (IRB No. 73 - 22.02.2024). Written informed consent was obtained for publication of this study.

In October 2021, we launched an LDLT program in the Republic of Uzbekistan, which we have continued to develop. Currently, two principal surgeons carry out all phases of the LDLT procedure for both donors and recipients, while also overseeing the entire perioperative treatment process. Prospectively collected data from our database were retrospectively reviewed and analyzed, covering procedures performed between October 2021 and December 2023. The median follow-up duration was 7 months (range, 1–26 months).

Recipients

During the study period, we performed 40 LDLTs in adults. The recipients included 28 males (70.0%) and 12 females (30.0%). The median age of the recipients was 40 years (range, 18–56 years), and the average model for end-stage liver disease score was 18 (range, 10–30). The primary causes of liver failure were viral hepatitis B/D (34 cases), viral hepatitis C (three cases), autoimmune hepatitis (two cases), and toxic hepatitis (one case). All patients presented with portal hypertension and associated complications, which included esophageal varices in all cases (100%), esophageal bleeding in seven cases, splenomegaly in all cases (100%), and cytopenia in all cases (100%). To prevent esophageal bleeding, seven patients underwent ligation of esophageal varices. Prior to LDLT, three patients received splenic artery embolization due to hypersplenism. Two patients were found to exhibit stage 3 portal vein thrombosis (PVT) according to the Yerdel classification. ABO-incompatible transplantation was not performed in our cohort. The baseline demographic and clinical characteristics of the patients are summarized in Table 1. For perioperative management, we adhered to the Enhanced Recovery After Surgery (ERAS) Society recommendations for LT [6]. Before transplantation, all patients with viral hepatitis were treated with antiviral therapy until a sustained virological response was achieved.

Donors

All recipients received right-lobe liver grafts from living donors. Overall, 37 cases involved related donorship. The

Table 1. Baseline demographics and perioperative characteristics of recipients

Variable	Value (n=40)
Age (yr)	40 (18–56)
Sex	
Male	28 (70.0)
Female	12 (30.0)
Indications for transplant	
Viral hepatitis B/D	34 (85.0)
Viral hepatitis C	3 (7.5)
Autoimmune hepatitis	2 (5.0)
Toxic hepatitis	1 (2.5)
MELD score	18 (10–30)
Signs of portal hypertension	40 (100)
PVT before LDLT	2 (5.0)
Follow-up (mo)	7 (1–26)
Operative time (min)	570 (410–785)
Estimated blood loss (mL)	1,200 (600–5,000)
Graft weight (g)	720 (515–940)
GRWR (%)	1.05 (0.7–2.0)
Graft vein outflow plasty	
Single RHV, no plasty	28 (70.0)
Two RHVs, no plasty	3 (7.5)
Three RHVs, unification plasty	2 (5.0)
S8 vein and RHV unification plasty	2 (5.0)
PTFE graft, S5 vein	1 (2.5)
PTFE graft, S8 vein	1 (2.5)
PTFE graft, S5 and S8 veins connected	1 (2.5)
FL graft, S5 and S8 veins connected	2 (5.0)
Caval anastomoses	
1	26 (65.0)
2	14 (35.0)
Arterial anastomosis type	
Interrupted	17 (42.5)
Continuous	21 (52.5)
Interrupted using SA	2 (5.0)
Splenic artery ligation	
HA diameter (mm)	4.2 (2.8–6.0)
SA diameter (mm)	8.8 (5.2–10.1)
Difference between SA and HA diameters, % of HA	95 (4–239)
SA ligated	35 (87.5)
Biliary anastomosis	
Duct-to-duct (single bile duct)	11 (27.5)
Duct-to-duct + Roux-en-Y	1 (2.5)
Roux-en-Y	
Single bile duct	7 (17.5)
2 Bile ducts, single anastomosis after plasty	10 (25.0)
2 Bile ducts, 2 anastomoses	4 (10.0)
3 Bile ducts, single anastomosis after plasty	1 (2.5)
3 Bile ducts, 2 anastomoses after plasty	6 (15.0)

Values are presented as median (range) or number (%).

MELD, model for end-stage liver disease; PVT, portal vein thrombosis; LDLT, living donor liver transplantation; GRWR, graft-to-recipient weight ratio; RHV, right hepatic vein; PTFE, polytetrafluoroethylene; FL, falciform ligament; SA, splenic artery; HA, hepatic artery.

relationships of donors to recipients were as follows: 11 sons, 10 brothers, nine sisters, four cousins, one father, one nephew, and one aunt. Additionally, under the laws of the Republic of Uzbekistan, spouses are eligible to be organ donors if they have been married for over 3 years. In this study, three wives were approved as donors.

All donors were examined based on a standard protocol adapted for our center [7]. This evaluation encompassed an initial assessment, which included medical history, body mass index, and blood type determination. It also involved clinical and biochemical blood analyses, coagulation profiles, virological screenings for the hepatitis B and C viruses, electrocardiography, echocardiography, abdominal organ ultrasound, chest radiography, contrast-enhanced computed tomography (CECT) for assessing the variant anatomy of the liver vessels, magnetic resonance cholangiopancreatography to examine the bile duct anatomy, and esophagogastroduodenoscopy. Additionally, all donors underwent liver elastometry to evaluate the extent of fatty steatosis. Furthermore, each donor received a psychosocial evaluation and legal consultation to verify their relationship with the recipient. We excluded donors with cardiovascular, neurological, or psychological disorders, as well as those with liver steatosis of grade S1 or higher as determined by elastometry. Donors with a low graft-to-recipient weight ratio or variant portal vein anatomy were also excluded, except for those categorized as type 1 under the Nakamura classification [8]. In terms of liver volumetry, we selected donors with an estimated residual liver parenchymal volume of at least 35%. Donors with a right hepatic artery diameter of less than 2 mm were excluded. Additionally, we excluded donors with complex venous anatomy in segments 5 and 8, characterized by multiple S5 and S8 branches, which would necessitate highly intricate venoplasty. For the perioperative management of donors, we adhere to the ERAS Society recommendations, specifically the guidelines for perioperative care for liver surgery [9].

Surgical Techniques

The graft used in our series was the right liver. Donor liver procurement adhered to a conventional method. Prior to the dissection of the hilar vascular and biliary structures, an ultrasound examination was conducted. The data obtained from this examination informed the determination of the transection plane. Parenchymal transection was carried out using a CUSA Excel device (Integra LifeScienc-

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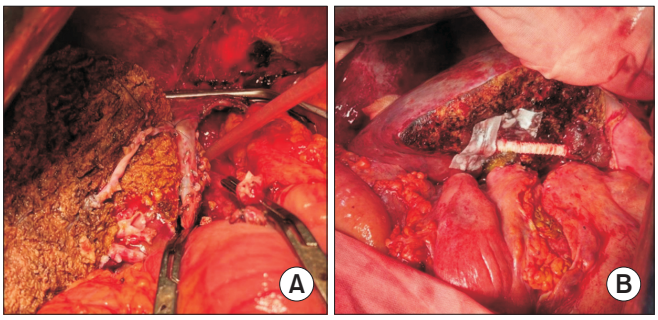

Fig. 1. Vein outflow reconstruction techniques. (A) Venoplasty using donor falciform ligament. (B) Venoplasty using a polytetrafluoroethylene graft.

es) and bipolar forceps equipped with continuous irrigation. This step followed the establishment of the transection plane, which was achieved by transiently clamping the right hepatic artery and the right portal venous branch. All vessels supplying the left lobe were preserved with minimal dissection.

Histidine-tryptophan-ketoglutarate preservation solution was utilized in all cases. Venoplasty was conducted on grafts with S5 and S8 veins 5 mm in diameter or larger, employing polytetrafluoroethylene (PTFE) grafts in seven instances and donor falciform ligament in two instances (Fig. 1). The biliary ducts were also evaluated, and when multiple bile duct openings were found in close proximity, bile duct plasty was performed by unifying the ducts with 5-0 polydioxanone suture.

For technical variant grafts, we employed a "piggyback" technique for caval reconstruction. In grafts containing multiple right hepatic veins (RHVs), additional anastomoses were created. The portal anastomosis was executed either end-to-end or by utilizing the interposition method with 5-0 polypropylene monofilament suture.

To establish arterial anastomoses, we employed a range of surgical techniques. If the donor hepatic artery had a diameter smaller than 2.5 mm or a large size discrepancy was noted between donor and recipient arteries, we utilized individual interrupted sutures with 7-0 polypropylene monofilament thread with surgical loupes with 3.5× magnification. Conversely, when the donor's hepatic artery diameter exceeded 2.5 mm, we applied continuous sutures using 7-0 polypropylene monofilament thread.

To reduce the risk of splenic artery steal syndrome (SASS), we established criteria for the ligation of the splenic artery. Specifically, if the diameter of the splenic artery was at least 50% larger than that of the hepatic artery, as determined by CECT, we proceeded with splenic artery ligation. This procedure was performed either at the hilum of the spleen or at the level of the celiac trunk. To prevent low arterial supply and to mitigate portal hyperperfusion [10,11], we aimed to use grafts with a graft-to-recipient weight ratio exceeding 0.9%. Intraoperative Doppler ultrasound (DUS) was routinely employed to monitor vascular supply following the establishment of arterial anastomosis, after biliary reconstruction, and to ensure final hemostasis.

For biliary reconstruction, we employed either duct-to-duct anastomoses or Roux-en-Y hepaticojejunostomy with external stents. When the graft presented a single bile duct opening with a diameter exceeding 3 mm, duct-to-duct anastomosis was utilized. In all other instances, we performed Roux-en-Y hepaticojejunostomy with the placement of external stents.

Immunosuppression

Basiliximab was used to induce immunosuppression. Following portal reperfusion, methylprednisolone (10 mg/kg) was administered. The standard immunosuppressive regimen consisted of tacrolimus and low-dose methylprednisolone. Mycophenolate mofetil was prescribed as an optional addition. The serum tacrolimus concentration was maintained between 6 and 9 ng/mL. The side effect profiles of the immunosuppressants were factored into considerations of drug discontinuation or conversion.

Posttransplant Blood Flow Monitoring and Prophylaxis against Vascular Complications

All patients underwent staged thromboprophylaxis to minimize the risk of vascular complications. In our standard postoperative protocol to prevent arterial complications, the first stage involved the administration of alprostadil (prostaglandin E1) following reperfusion. The second stage entailed the administration of low-molecular-weight heparin (LMWH), starting on the first postoperative day. The third stage of prophylaxis included the initiation of low-dose aspirin on the fourth postoperative day. Alprostadil administration was discontinued 7 days after surgery, while LMWH treatment was maintained for up to 2 weeks following LT. Aspirin therapy was continued for up to 3 months after the procedure. In instances of significant coagulopathy, bleeding signs, or a platelet count below 50 × 10^9/L, thromboprophylaxis was either fully or partially withheld until the adverse event resolved. Additionally, we ensured adequate intravenous fluid vol-

ume with daily monitoring of fluid balance. The volume of infusion, fluid intake, diuresis and drainage losses were monitored.

For the first 7 days following transplantation, patients underwent regular DUS monitoring. Logiq P6 (GE Healthcare) and DC-40 (Mindray) ultrasound systems, equipped with standard C6-2 convex sensor units, were utilized for these routine DUS assessments. The initial postoperative DUS to assess arterial flow was conducted upon the patient's arrival in the intensive care unit following transplant surgery. Subsequent evaluations were carried out at least every 6 hours during the first postoperative week. During the following week, DUS monitoring was performed once daily. In cases with complications, the duration of DUS monitoring could extend beyond this point [11].

We considered the following DUS signs to be indicative of deteriorating arterial blood flow: difficulty visualizing the artery, a resistance index greater than 0.85 or less or equal to than 0.5, and a decrease in arterial peak systolic velocity to less than 15 cm/sec. In such instances, we initiated a continuous infusion of heparin, starting with a bolus dose of 80 U/kg followed by a maintenance dose of 18 U/kg/hr, and monitored the partial thromboplastin time every 6 hours [12]. If hepatic arterial flow could not be visualized on DUS, we promptly performed CECT or transferred the patient to an interventional radiology suite for diagnostic angiography. Upon confirmation of impaired hepatic arterial flow, we immediately proceeded with revascularization.

For the portal vein, volume and linear blood flow velocity were assessed using DUS data. If signs of occlusive thrombosis in the portal vein were detected within the first 72 hours posttransplantation, relaparotomy and revision of the anastomosis were performed. In other cases, heparin prophylaxis was initiated.

Data Analysis

Baseline variables, including patient age (in years), sex, and date of surgery, were analyzed. Postoperative complications were evaluated using the Clavien-Dindo classification [13], and the comprehensive complication index was determined for these cases [14]. We defined short-term outcomes as events occurring during hospitalization. In contrast, long-term outcomes encompassed the period from discharge through follow-up, which in some cases exceeded 2 years.

Continuous variables are presented as medians and ranges, while categorical variables are expressed as numbers and percentages. Patient survival rates were generated using the Kaplan-Meier method. A P-value of 0.05 or less was considered to indicate statistical significance. Statistical processing was carried out using Orange3 (University of Ljubljana) and SPSS ver. 26 (IBM Corp.).

RESULTS

Recipients

The median operative time for recipients was 570 minutes (range, 410–785 minutes), and the median estimated blood loss was 1,200 mL (range, 600–5,000 mL). In 28 patients (70.0%), we observed a single RHV with no significant additional veins, eliminating the need for outflow plasty. In five cases, additional inferior RHVs (iRHVs) were present: three patients had one additional iRHV, while two patients had two. For patients with two iRHVs, we performed unification plasty of the iRHVs, and two caval anastomoses were created. When only one additional iRHV was present, two caval anastomoses were performed without venoplasty. In three cases, PTFE grafts were utilized for venous outflow plasty due to significant S5 and S8 veins in the graft. In two instances, a graft created from the falciform ligament of the donor's liver was employed for venoplasty. For 14 patients, the application of two caval anastomoses was required. Arterial anastomoses were performed using the recipient's common hepatic artery. However, in two cases involving severe atherosclerotic lesions in this vessel, the splenic artery was utilized instead.

In 35 of the 40 cases, the diameter of the splenic artery was at least 50% larger than that of the recipient's hepatic artery. The median diameter of the hepatic artery was 4.2 mm (range, 2.8–6.0 mm), while that of the splenic artery was 8.8 mm (range, 5.2–10.3 mm). The median difference in diameter between the splenic and hepatic arteries, expressed as a percentage of the hepatic diameter, was 95% (range, 4%–239%). The splenic artery was ligated in all 35 (87.5%) cases where its diameter exceeded that of the hepatic artery by 50% or more. Of these cases, ligation of the splenic artery was performed at the spleen hilum for three patients and at the level of the celiac trunk for 32 patients.

Based on the anatomical characteristics of the donor graft, we employed various techniques for biliary reconstruction (Fig. 2). Duct-to-duct anastomosis was

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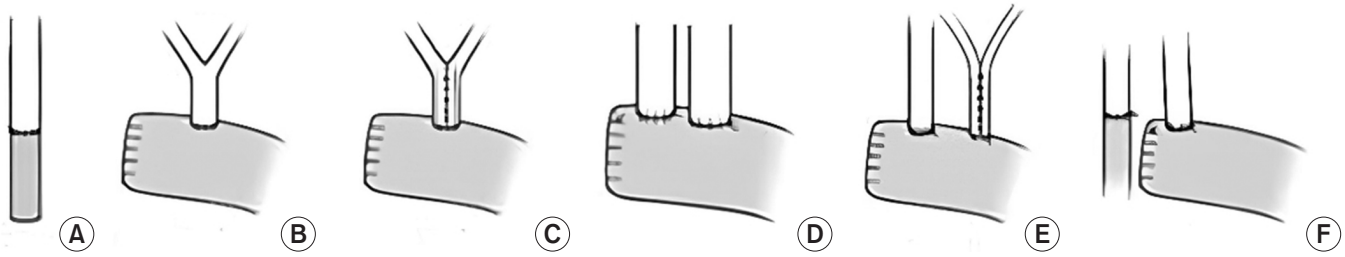

Fig. 2. Biliary reconstruction techniques. (A) Duct-to-duct anastomosis. (B) Anastomosis of a single duct with a Roux-en-Y loop. (C) Anastomosis of unified bile ducts with a Roux-en-Y loop. (D) Separate anastomoses of two bile ducts with a Roux-en-Y loop. (E) Three bile ducts opening onto the graft, with unification plasty of two ducts and two separate anastomoses of bile ducts with a Roux-en-Y loop. (F) Anastomosis of the main duct with a Roux-en-Y loop and duct-to-duct anastomosis with an aberrant bile duct in the right lobe.

performed in 11 patients. In 28 cases, biliodigestive anastomoses were created using a Roux-en-Y loop. One patient presented with an aberrant right hepatic duct, necessitating the anastomosis of the main duct with a Roux-en-Y loop, in conjunction with a duct-to-duct anastomosis involving the aberrant bile duct of the right lobe. The perioperative characteristics of the patients are summarized in Table 1.

Rejection

Among the observations analyzed, an acute rejection crisis occurred in 10% of patients, ranging from 2 to 14 days postsurgery. Pulse therapy with methylprednisolone yielded positive results in 50% of these cases. However, two patients died of acute graft dysfunction during the early postoperative period. In all patients exhibiting signs of graft rejection, a reduction in corticosteroid dosage was implemented, followed by the introduction of mycophenolic acid as a third component of the immunosuppressive regimen.

Vascular Complications

Hepatic artery complications were observed in seven patients. All instances of reduced hepatic artery flow occurred within the first week after surgery. Hepatic artery thrombosis (HAT) was observed in one patient. Hepatic artery stenosis (HAS) was identified in three patients, accounting for 42.8% of the cases with hepatic complications. Additionally, three patients developed SASS, all of whom had a nonligated splenic artery.

Among other patients, three experienced complications related to the portal vein. One patient developed acute PVT on the second postoperative day. Within 1 year following the LDLT procedure, two patients developed portal vein stenosis (PVS).

In all cases of identified arterial impairment, celiac angiography was performed. Patients diagnosed with HAS were treated with balloon angioplasty. The patient who developed HAT received balloon angioplasty followed by arterial stenting. Patients with SASS underwent coil embolization of the splenic artery. In one case of SASS, the arterial anastomosis of the graft sustained damage during angiography; this necessitated urgent open surgery to control bleeding from the anastomosis and to ligate the splenic artery. Throughout the observation period, no additional episodes of diminished arterial supply were observed.

Regarding portal vein complications, the patient who experienced PVT underwent relaparotomy, revision of the portal anastomosis, and thrombus extraction. Despite receiving normal blood supply and treatment, which included extracorporeal detoxification methods, the patient developed severe liver graft dysfunction and died on the ninth postoperative day.

Additionally, two patients with PVS, who presented with clinical features of bilirubinemia and signs of portal hypertension (including cytopenia and ascites), underwent percutaneous transhepatic correction of PVS using balloon angioplasty [15]. These patients survived with good liver graft function.

Biliary Complications

Biliary complications were observed in 16 patients. Bile leakage was the most common clinical complication, occurring in 14 cases. Additionally, two patients developed late bile duct strictures: one exhibited anastomotic stricture of a duct-to-duct anastomosis 18 months after transplantation, while the other developed anastomotic

stricture of a biliodigestive anastomosis 12 months following the transplant.

Biliary complications occurred in four patients (57.1%) with arterial complications: HAT in one individual, steal syndrome in two, and HAS in one. Bile leakage was observed in all of these cases, but no biliary strictures were noted. In one patient with a biliodigestive anastomosis, ultrasound-guided puncture drainage of the biloma was performed. Additionally, a patient with a biliary-biliary anastomosis received stent placement via endoscopic retrograde cholangiography, which stopped the bile leak. In the other patients, bile leakage occurred while drainage tubes were in place but resolved spontaneously without any intervention. By comparison, among patients without arterial complications, bile leakage occurred in 10 (30.3%, P=0.039) during the early postoperative period. This group also included the cases of late anastomotic bile duct stricture described above, which required reconstructive surgery.

Other Complications

Complications, categorized as either early or late, are detailed in Table 2. Early complications included wound seromas in two patients (Clavien-Dindo grade 1), pleural effusions necessitating drainage in seven patients, and intestinal bleeding in one patient (Clavien-Dindo grade 3a). Severe complications comprised two cases of bile peritonitis that required surgical intervention and two patients with internal bleeding (one due to disseminated intravascular coagulation and the other from arterial bleeding at the remaining coronary ligament of the liver; Clavien-Dindo grade 3b). Additionally, three cases of sepsis and one severe aspiration event were successfully managed. One patient experienced convulsions due to a high blood-serum tacrolimus concentration; this was addressed by administering valproic acid and reducing the tacrolimus dosage. Another patient exhibited demyelination of the pons, accompanied by neurological deficits, decreased consciousness, and loss of speech. This condition was associated with a rapid increase in plasma sodium levels (11 μmol/L over 24 hours) and manifested on the eighth day after surgery. The patient gradually improved and was discharged on day 30 after transplantation. This individual is being monitored by a neurologist.

Late complications included an episode of chronic rejection and a case of *de novo* hepatitis B virus, which was managed conservatively. Three patients developed liver abscesses that were treated with drainage. Another

Table 2. Early and late complications following living donor liver transplantation

Complication (Clavien-Dindo grade)	Early complications (n)	Late complications (n)
Grade 1		
Wound seroma	2	-
Grade 2		
Bile leakage	6	-
Acute rejection	2	-
Chronic rejection	-	1
De novo HBV	-	1
Grade 3a		
Bile leakage	6	-
Right-sided pleural effusion	5	-
Bilateral pleural effusion	2	-
Intestinal bleeding	1	-
Liver abscess	-	3
HAT	1	-
HAS	3	-
SASS	3	-
PVS	-	2
Grade 3b		
Bile peritonitis (leakage)	2	-
Anastomotic stricture	-	2
Internal bleeding	2	-
SASS	1	-
Grade 4		
Convulsions	1	-
Demyelination of the pons	1	-
Cholangitis	-	1
Aspiration	1	-
Sepsis	3	-
Grade 5		
PVT	1	-
Sepsis, PODS	2	-
Acute rejection	2	-
COVID-19 pneumonia	-	1
Aspiration	-	1
Chronic rejection (noncompliant)	-	1
Median CCI among patients with complications (range)	42.6 (8.7–100)	80.1 (39.7–100)

HBV, hepatitis B virus; HAT, hepatic artery thrombosis; HAS, hepatic artery stenosis; SASS, splenic artery steal syndrome; PVS, portal vein stenosis; PVT, portal vein thrombosis; PODS, polyorganic dysfunction syndrome; COVID-19, coronavirus disease 2019; CCI, comprehensive complication index.

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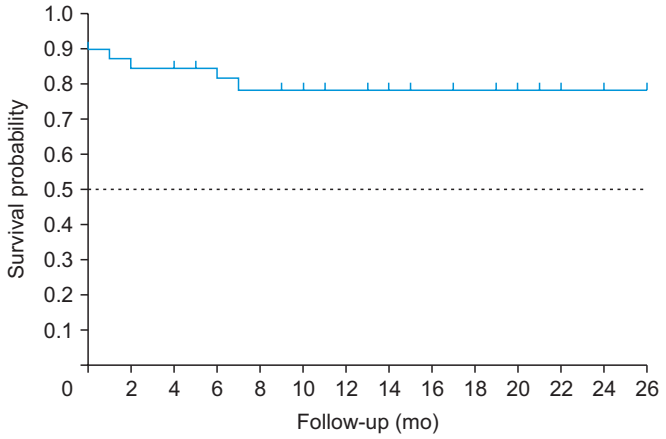

Fig. 3. Survival probability for liver transplant recipients over a 26-month follow-up period.

patient was admitted to the intensive care unit for acute cholangitis and received treatment with antibiotics and withdrawal from immunosuppression.

Mortality

During the observation period, eight patients died. The in-hospital mortality rate was 12.5%. The causes of death included sepsis in two patients, acute rejection in two patients, and liver failure due to PVT in one patient. Regarding the three cases of non-hospital mortality, the causes of death were coronavirus disease 2019 (COVID-19)–associated pneumonia, aspiration, and rejection in a non-compliant patient. Survival rates among the patients are represented in Fig. 3.

Donor Outcomes

The donors included 13 females and 27 males. The average body mass index was 23.2 kg/m^2. Regarding perioperative data, the median operative time for donors was 342.5 minutes (range, 230–440 minutes), and the estimated blood loss was 250 mL (range, 50–850 mL) (Table 3).

Complications experienced by donors are also detailed in Table 3. Specifically, wound seroma was noted in two cases. One donor experienced renal failure during antibacterial prophylaxis with sulperazone, presenting with oliguria, proteinuria, hematuria, edema, and pleural effusion. The administration of sulperazone was discontinued, and diuretic therapy was initiated, which alleviated the renal failure. Two donors experienced wound infections, necessitating extended dressing and antibiotic treatment. One individual developed hospital-acquired pneumonia, classified as Clavien-Dindo grade 2. Pleural effusion occurred in two patients, both of whom required drainage procedures. Bilomas developed in two patients and similarly required drainage. Additionally, two patients with bile leakage underwent open surgical revision. Another patient experienced bleeding due to a dislodged clip from the inferior vena cava, necessitating emergency surgery. The median hospital stay following liver resection was 10 days (range, 7–28 days). No late complications were observed among donors.

Table 3. Donor characteristics and clinical outcomes

Variable	Value (n=40)
Age (yr)	40 (18–56)
Sex	
Male	27 (67.5)
Female	13 (32.5)
Body mass index (kg/m^2)	23.2 (18.0–28.3)
Operation time (min)	342.5 (230–440)
Estimated blood loss (mL)	250 (50–850)
Complications (Clavien-Dindo)	
Grade 1	
Wound seroma	2
Grade 2	
Kidney failure	1
Pneumonia	1
Wound infection	2
Hemorrhage in drain	2
Grade 3a	
Pleural effusion	2
Biliary leakage	2
Grade 3b	
Bleeding from IVC	1
Biliary leakage	2
Median CCI among donors with complications	33.7 (8.7–50.1)
Length of stay (day)	10 (7–28)

Values are presented as median (range), number (%), or number only.
IVC, inferior vena cava; CCI, comprehensive complication index.

DISCUSSION

LDLT has become a life-saving option for patients with end-stage liver disease when cadaveric LT is not available [16]. Although LDLT has been successful, it carries inherent challenges and risks. Donors are subject to a major

surgical procedure that carries the risk of complications and necessitates a lengthy recovery period. Additionally, ethical issues are a concern, as the decision to donate part of one's liver requires careful consideration of both the altruistic intent and the potential risks to the donor's health [17]. In the Republic of Uzbekistan, no legal frameworks are in place to facilitate LT from deceased donors, making LDLT the sole opportunity for those with severe conditions necessitating transplantation.

LDLT is associated with a relatively high frequency of surgical complications posttransplantation, with hospital mortality rates after LDLT ranging from 3.6% to 18.9% [18–20]. In our study, the complications with the highest mortality were infection, acute rejection, and liver graft dysfunction due to PVT. In the two cases of graft rejection, the patients experienced uncontrolled increases in enzyme (alanine aminotransferase and aspartate aminotransferase) and bilirubin levels, with no signs of obstructive jaundice. We ruled out infections, such as acute cytomegalovirus infection, and vascular complications. The indications for transplantation in these patients were autoimmune hepatitis and viral hepatitis B. Despite treatment, including pulse therapy with methylprednisolone and extracorporeal detoxification, liver function was not restored in these patients.

The incidence of vascular complications in our series was slightly higher than that reported in the literature [11], which we attribute to the substantial learning curve associated with the first 15–20 LDLT cases [21,22]. During the observation period, three patients with arterial complications died. However, in all instances, the cause of death was unrelated to arterial impairment. Two months after LDLT, one patient with HAS contracted severe COVID-19 pneumonia and died from complications. The second patient, who experienced SASS, died from aspiration at home 1 month after discharge. Another patient, who had developed steal syndrome, died 2 months after LT due to ovarian apoplexy (sepsis), which was not diagnosed by local healthcare services.

Biliary complications remain a substantial challenge in LT, and these occur especially frequently among recipients of LDLT. The incidence of these complications varies across centers but can be as high as 30%, and with an associated mortality rate of 10%, they pose a considerable concern for patients after transplant [23]. In our cohort, most complications, specifically leakages, were observed in patients who had complex donor bile duct anatomy or arterial complications.

Our in-hospital mortality rate was 12.5%, which is comparable to data reported in the literature [18,20]. The survival rate during the 26-month follow-up period was 80%. The average incidence of complications in LDLT donors is around 25% [24], with some research indicating a complication rate as high as 40% [25]. Minor complications occur in 17% of cases, while major complications are seen in approximately 5.5%. In the present cohort, donor outcomes were consistent with the data reported in the literature.

As the Republic of Uzbekistan is a developing country, and since this represents our first meaningful experience with LT, it is particularly important to consider the challenges our team faced during the implementation phase of the LT program. For many years, the country lacked a regulatory framework governing organ transplantation and donation. This legislative foundation was only established in 2021, and the enactment was followed by a mandate from the national leadership to implement a transplantation program immediately. Consequently, we had a limited timeframe for implementation.

A second, and fundamental, aspect is the training of specialists. Our center was deficient in adequately trained medical professionals, including surgeons, hepatologists, intensivists, nurses, and others. Consequently, a substantial amount of time was invested into the ground-up training of specialists. A particular challenge was that this training had to occur concurrently with the launch of the program, even as operations were already underway, which may have impacted the outcomes. The training process was overseen at every stage by only two experienced physicians with extensive expertise in the field of LT. These physicians were responsible for training a diverse group of medical specialists, including surgeons, hepatologists, radiologists, intensivists, nurses, and endovascular surgeons. The training emphasized not only theoretical and practical knowledge in LT but also foundational principles such as aseptic and antiseptic techniques in the care of patients after transplantation. Additionally, fundamental education was provided on managing complications through minimally invasive methods whenever feasible [26]. The two physicians also provided round-the-clock supervision of the entire treatment process.

The technical equipment of the hospital is also crucial in determining surgical outcomes for both donors and recipients. For instance, our initial 30 procedures were conducted without access to high-quality liver retractor

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equipment for either party. Furthermore, for an extended period, our center did not possess an ultrasonic cavitation aspirator, which complicated the technical aspects of liver resection in donors. In our view, these elements, combined with the learning curve [21,22], had an impact on the results of the first LT operations at our center. Currently, the administration of our center has acquired most of the necessary surgical equipment.

Furthermore, we now understand that implementing an LT program necessitates the creation of a dedicated department. Within the general surgery and hepatobiliary surgery departments, the conditions for maintaining asepsis and using antiseptics were suboptimal, with frequent contact with infectious patients.

We also faced challenges in managing acute rejection. Although our center had the technical capacity to perform biopsies, we lacked the capability to interpret the results for the diagnosis of liver graft rejection. This limitation impeded our ability to diagnose rejection, necessitating empirical treatment. Currently, we are in the process of acquiring the requisite equipment for our hospital.

Additionally, at the patient selection stage, most individuals presented at our center with liver cirrhosis in advanced decompensation (Child-Pugh class C). These patients typically had not received treatment to stabilize their condition at local hospitals, nor had they been given antiviral therapy. Consequently, we were not presented with the option to select patients with less severe or less advanced stages of liver cirrhosis. Upon admission, we managed their care independently, preparing them for surgery, administering antiviral therapy, and proceeding with transplantation only after achieving a relative stabilization of their condition.

The selection of living donors also presented a challenge, largely because the local dietary habits led to a high prevalence of excess body weight and hepatic steatosis among the population. Consequently, many potential donors were disqualified due to hepatic steatosis. Those with borderline steatosis levels (S1 and S2, as determined by elastography data) were enrolled in a rehabilitation program that included physical exercise and dietary changes. Donors who demonstrated regression of steatosis upon follow-up were then considered eligible. Given the scarcity of related donors without hepatic steatosis, we were compelled to evaluate liver donors with complex biliary anatomy, which we believe could influence the rate of biliary complications in both donors and recipients. A more rigorous donor selection process appears to be warranted.

In the longer-term postoperative period, we encountered unexpected noncompliance among recipients with respect to their immunosuppressive medication regimen. Despite receiving education during their hospitalization, many patients ceased taking their immunosuppressants and medications for the prevention of viral hepatitis after discharge. Consequently, we implemented stringent outpatient monitoring, requiring patients to sign an agreement committing to regular medical follow-ups after LT. During these follow-up visits, the supervising physicians—primarily the liver transplant surgeons—personally reviewed blood test results, performed ultrasound examinations of the graft, and monitored the patient's adherence to their prescribed medication schedule.

Our experience with LDLT and the analysis of associated complications align with the international literature and are acceptable during the implementation phase of the LT program. Transplantation is a viable option in the Republic of Uzbekistan; however, surgical and therapeutic approaches require improvement to minimize the incidence of both early and late postoperative complications.

ARTICLE INFORMATION

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID

Konstantin Semash https://orcid.org/0000-0001-5830-5235
Timur Dzhanbekov https://orcid.org/0000-0002-8857-947X
Mirshavkat Akbarov https://orcid.org/0000-0002-7793-1810
Miraziz Mirolimov https://orcid.org/0009-0002-4776-9979
Azimjon Usmonov https://orcid.org/0009-0007-8025-1326
Navruz Razzokov https://orcid.org/0009-0004-6569-4397
Ziyodulla Primov https://orcid.org/0009-0008-0365-3644
Temurbek Gaybullaev https://orcid.org/0009-0001-9611-7160
Sardor Yigitaliev https://orcid.org/0009-0003-7741-7517

Author Contributions

Conceptualization: KS, TD, MA. Data curation: MM, AU, NR, ZP, TG. Formal analysis: SY. Methodology: TD, SY. Project administration: TD, KS, MA. Supervision: KS, TD. Visualization: KS. Writing–original draft: KS. Writing–review & editing: all authors. All authors read and approved the final manuscript.

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