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A FIVE-YEAR LIVER TRANSPLANT EXPERIENCE IN ROSTOV OBLAST

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Objective: to reflect on a 5-year experience in liver transplant surgery at the Rostov Regional Clinical Hospital. **Materials and methods.** Liver transplant was performed in Rostov Oblast in July 2015 for the first time. There were 52 liver transplant surgeries performed in the region by the end of February 2020. Cirrhosis due to viral hepatitis is the leading indication for liver transplantation in 33.3% of patients. The average age of recipients was 43.5 ± 15.8 years. Male recipients accounted for 59.6% of cases. Nine recipients got liver transplants from blood relatives, while 43 recipients received an organ from post-mortem donors. For two patients, liver graft was obtained by splitting the liver into two lobes using the *in situ* split technique. **Results.** The average duration of surgery was 5.14 ± 1.92 hours. Blood loss during surgery did not exceed 1400 ml. Up to 93% of lost blood was recovered using the reinfusion system. The need for red blood cell transfusion was observed in 48.1% of cases. Fresh frozen plasma was transfused in all cases. Early postoperative complications were observed in 15 patients (29.4%), and some of them had several complications simultaneously. Biliary and vascular complications, which were eliminated by minimally invasive methods and open surgeries, had a significant influence on liver transplant outcome. In-hospital mortality was 5.6%. The causes of death were intra-abdominal bleeding (1), portal vein thrombosis (1) and biliary sepsis (1). Four more people died in the long term after being discharged from hospital: lung cancer (1), graft rejection (1) and fungal sepsis (2). **Conclusion.** Liver transplant outcome depends on the skills and experience of the specialists implementing this program. Post-transplant in-hospital and long-term mortality depends on the presence and nature of complications, and on the possibility of early treatment.

Keywords: liver transplantation, surgical complications, hospital mortality.

INTRODUCTION

Today, environmental and socio-economic issues are playing major roles in the health of the population. Conditions of the digestive system, particularly cirrhosis, is among the major diseases leading to reduced working capacity, frequent hospitalization and rapid disability in adults [1].

Cirrhosis as the final stage of chronic liver disease comes with many complications, sometimes requiring urgent treatment, such as surgical interventions [2, 3]. But as practice has shown, it is not always possible to save a patient's life, being limited only by "half measures" – *f* palliative interventions aimed at eliminating the complications of portal hypertension, hepatic encephalopathy, hepatorenal syndrome and other life-threatening conditions [4].

At present, liver transplantation (LT) is the only effective treatment for cirrhosis in the final stages, when all other treatment methods have been unsuccessful. For more than half a century of existence, this operation has shown to be effective due to high 5-year survival rates of patients, reaching 80–90% [5, 6]. Nevertheless, active use of transplant surgery as a method of treating patients with end-stage cirrhosis all over the world is hampered by organ shortages [7]. This often increases the waiting time for operation, increases waitlist mortality, and those patients who survive often approach transplantation in a critical condition, which worsens surgery outcome both in the perioperative period and in the long-term post-transplant period [8].

Supportive therapy (immunosuppressive, antibacterial, etiotropic) and specific postoperative surgical complications remain the stumbling blocks on the way to achieving excellent transplantation outcomes [9]. First of all, these include problems associated with biliary anastomotic leak and decreased patency of blood vessels. Despite the fact that these complications take a small share in the overall structure, their specificity is often fraught with more serious consequences for the patient, primarily graft loss.

Considering the above, the purpose of the work was to conduct a retrospective generalized analysis of the outcomes of liver transplants performed by us over five years and assess the implementation of the regional program.

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MATERIALS AND METHODS

The first liver transplant performed in Rostov Oblast was at the Rostov Regional Clinical Hospital in July 2015. This event was preceded by multilateral organizational and practical training, generalization of the experience of domestic and foreign transplant centers, which resulted in the creation of a regional transplant center and beginning of implementation of the corresponding program.

At present, there are slightly above 3000 people observed for cirrhosis in Rostov Oblast. Waitlisted candidates for liver transplantation reached 350 in number.

As of the end of February 2020, 51 waitlisted candidates underwent liver transplantation. The indications for surgery were cirrhosis of various origins. However, viral hepatitis became the main cause of end-stage liver disease in patients – 17 (33.3%) cases (Fig. 1).

One patient underwent retransplantation due to graft dysfunction caused by hepatic vein thrombosis. So, a total of 52 liver transplants were performed.

The average age of recipients was 43.5 ± 15.8 years. Male recipients accounted for 59.6% (31 people) of cases. Forty-one patients (78.9%) received whole organs from deceased donors; 10 patients (19.2%) received the right lobe; 9 recipients got liver transplants from their blood relatives; there was 1 deceased donor; 1 patient received the left lobe of a cadaveric liver (1.9%). For 50 transplant cases, the liver or part of it was procured according to the standard protocol. For 2 patients, liver graft was procured by splitting the liver into two lobes using the *in situ* split technique (Fig. 2).

Before performing liver transplant operations, we, of course, carefully examined all patients. Laboratory tests, along with general clinical indicators, included an assessment of the functional state of the liver. We performed complete virological tests: HIV, hepatitis B, C,

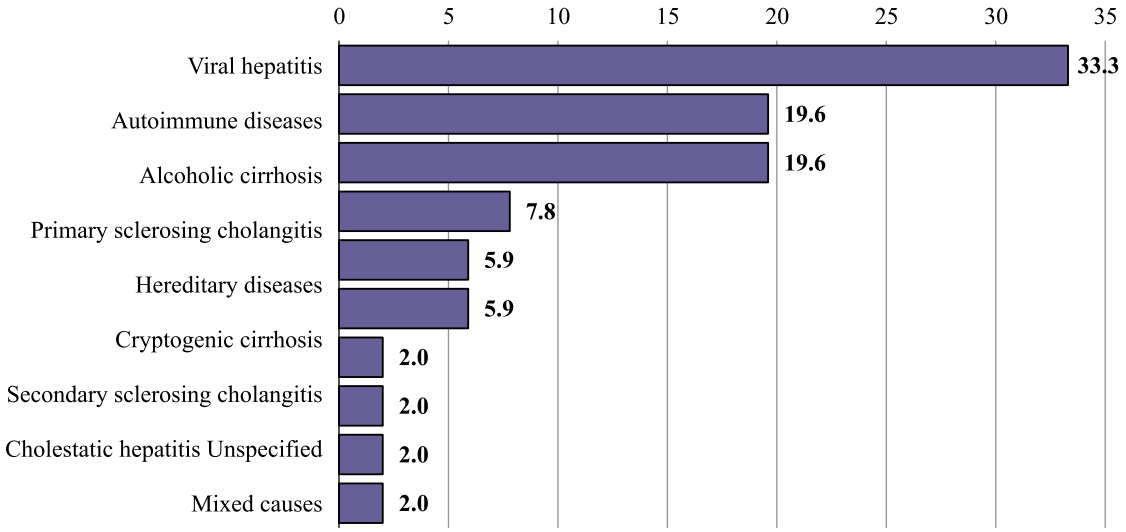

Fig. 1. Distribution of liver recipients according to the etiology of cirrhosis, %

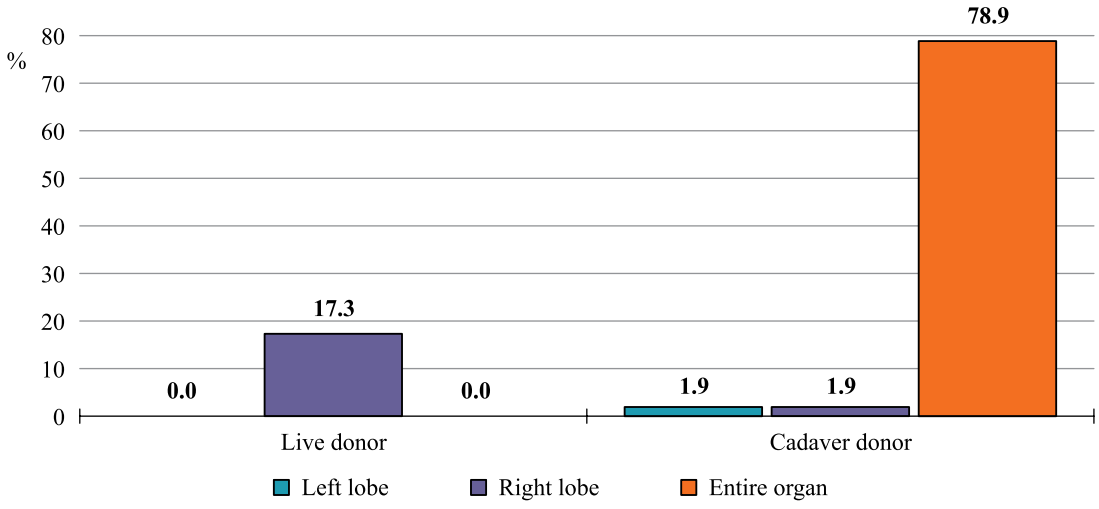

Fig. 2. Distribution of donor organs

D, G viruses, herpes viruses, cytomegalovirus (CMV), with detection of specific antibodies by ELISA and the activity of these viruses in PCR. Instrumental diagnostics included ECG, echocardiography, spirograph, esophagogastroduodenoscopy, chest CT scan, colonoscopy (irrigoscopy), triplex ultrasound of the veins and arteries of the lower limbs. In addition, clinical and instrumental diagnostic assessment of portal blood flow, liver structure assessment (ultrasound with dopplerography, triple-phase CT scan and magnetic resonance imaging (MRI) with bolus contrast, indirect liver elastometry) were performed.

After the surgery, CT scan, MRI, ultrasound scan, selective celiacography and minimally invasive diagnostic manipulations on the bile ducts were used, including transpapillary and percutaneous transhepatic interventions.

RESULTS

We performed liver transplant surgeries on all patients in accordance with ethical and legal standards. Average duration of operations was 5.14 ± 1.92 hours. Blood loss during surgery did not exceed 1400 mL (1076.1 ± 191.8 mL). Using the reinfusion system, we were able to recover up to 93% of lost blood (on average 996.5 ± 177.5 mL of blood), while 48.1% of cases required red blood cell transfusion during operation – an average of 238.7 ± 133.1 mL transfused blood in the next postoperative hours. In all cases, fresh frozen plasma was transfused with 1394.7 ± 303.1 mL in average transfusion volume.

Side-to-side cavo-caval anastomosis was performed in 35 (67.3%) cases, end-to-side cavo-caval anastomosis in 11 (21.2%) patients, piggyback anastomosis in 4 (7.7%) patients, and anastomosis using classical method was done in 2 (3.8%) cases. End-to-end arterial anastomosis was formed with common hepatic artery in 38 (73.1%) cases. A similar technique was used for lobar arterial anastomosis in 11 (21.2%) patients: right lobar arterial anastomosis in 10 patients, and left lobar arterial anastomosis in 1 patient. Due to the peculiarities of arterial blood supply to the graft, three cases (5.8%) required Y-shaped arterial reconstruction during anastomosis of the common hepatic artery and accessory hepatic artery. Portal reconstruction was carried out in a standard way, end-to-end. In 11 (21.2%) patients, the recipient's portal vein was anastomosed with the lobar vein of the graft. It should be noted that thrombectomy was performed in 3 recipients due to Yerdel's type I–II portal vein thrombosis (2 patients with Yerdel's type II portal vein thrombosis and 1 patient with type I).

End-to-end biliary anastomosis was formed in 39 (75.0%) cases. Roux-en-Y biliodigestive anastomosis was formed in 3 (5.8%) cases, including during retransplantation.

In the early postoperative period, surgical complications were noted in 15 (29.4%) patients, while several patients had several complications at once. In the "vascular" complications group, we often encountered intra-abdominal bleeding irrespective of the type of transplantation performed (Table 1).

Both minimally invasive techniques (41.7%) and relaparotomy (58.3%) were used for vascular complications management. In 2 clinical cases, common hepatic artery thrombosis developed on postoperative day 5 and day 7. When performing selective angiography of the celiac trunk in these patients, hepatic artery occlusion in the proximal third was determined, without hemodynamically significant stenosis of the trunk itself and the splenic artery with its branches (Fig. 3, a). Thrombolysis and stenting in these patients restored blood flow in the common hepatic artery (Fig. 3, b).

In 2 more cases, right hepatic artery stenosis was found, which has a significant effect on hemodynamics. This complication was eliminated by vascular stenting (Fig. 4).

Endovascular technique also helped to eliminate right hepatic vein stenosis in a patient after related liver transplant (Fig. 5).

Hepatic vein thrombosis in a patient after related transplantation led to graft dysfunction and death, which required retransplantation (Fig. 6).

Table 1

Characteristics of the vascular complications in different types of liver transplantation

Complication	Transplant				Total (n = 51)	
	Relative (n = 9)		Cadaver (n = 42)			
	n	%	n	%	n	%
Abdominal bleeding	2	22.2	2	4.8	4	7.8
Common hepatic artery thrombosis	1	11.1	1	2.4	2	3.9
Right hepatic artery coarctaction	0	0	2	4.8	2	3.9
Portal vein thrombosis	1	11.1	0	0	1	2.0
Inferior vena cava thrombosis	0	0	1	2.4	1	2.0
Transplant hepatic veins thrombosis	1	11.1	0	0	1	2.0
Right hepatic vein coarctaction	1	11.1	0	0	1	2.0
Total	**6**	**66.7**	**6**	**14.3**	**12**	**23.5**

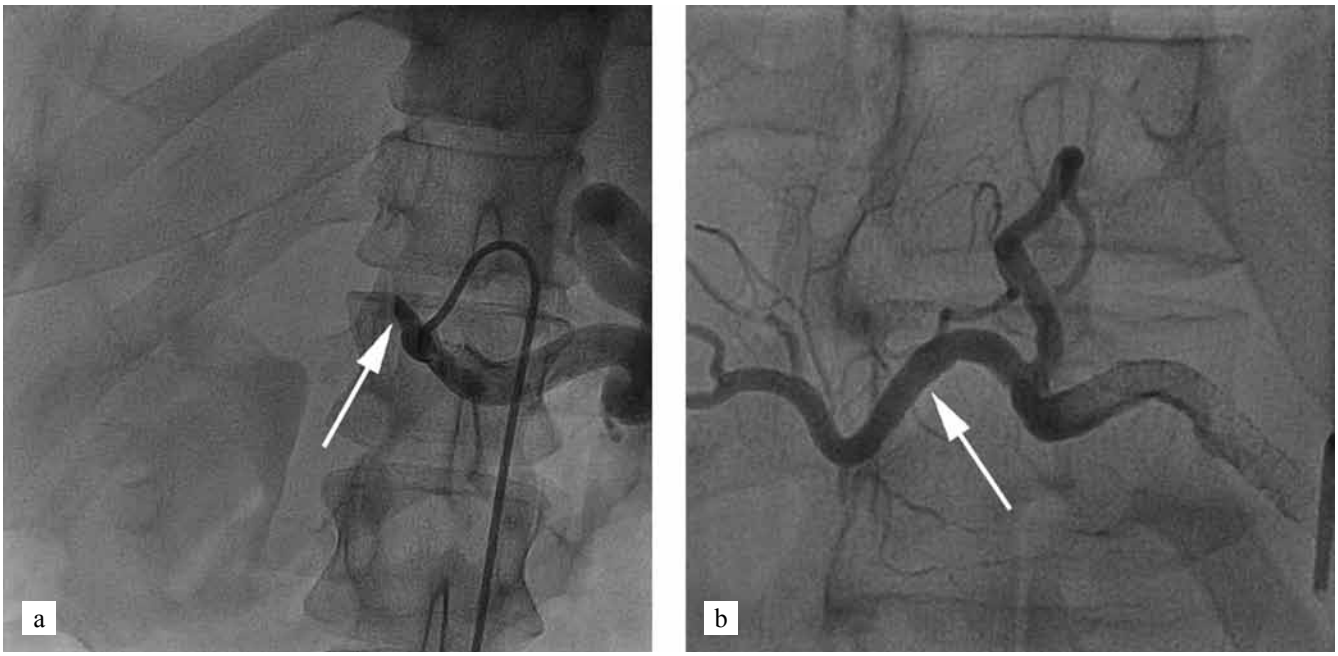

Fig. 3. The common hepatic artery thrombosis. Angiography: a – zone of occlusion; b – after stenting

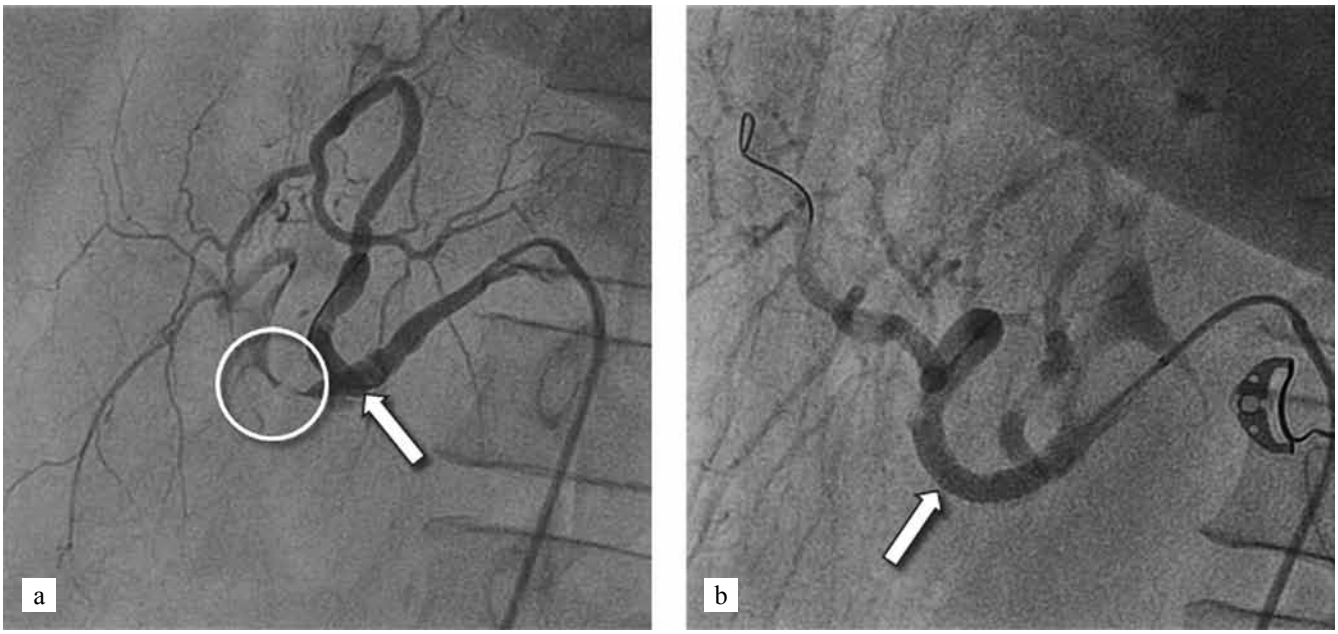

Fig. 4. The right hepatic artery stricture. Angiography: a – zone of stenosis; b – after stenting

Relaparotomy was done due to the technical failure of minimally invasive techniques in eliminating blood clots in the inferior vena cava and portal veins, as well as intra-abdominal bleeding (see Table 1).

Post-liver transplant biliary complications occurred in 8 (15.7%) patients (Table 2).

In 3 cases of biliary anastomosis incompetence, an ultrasound-guided percutaneous drainage of bilomas was carried out, of which percutaneous transhepatic cholangiostomy was additionally performed in one case. In one patient, partial biliary anastomosis incompetence was accidentally discovered during relaparotomy for intra-abdominal bleeding. Interestingly, there were no clinical signs of biliary incompetence at the time of re-intervention. In this case, anastomosis was dissociated, and a Roux-en-Y biliodigestive anastomosis was formed.

To eliminate biliary anastomotic strictures arising after the operation, we used various combinations of minimally invasive and open surgical interventions. For example, antegrade anastomosis was performed in one case, while in another two cases, antegrade anastomosis was supplemented with percutaneous transhepatic cholangiostomy. In another clinical case (after split transplantation), treatment was divided into two phases. At

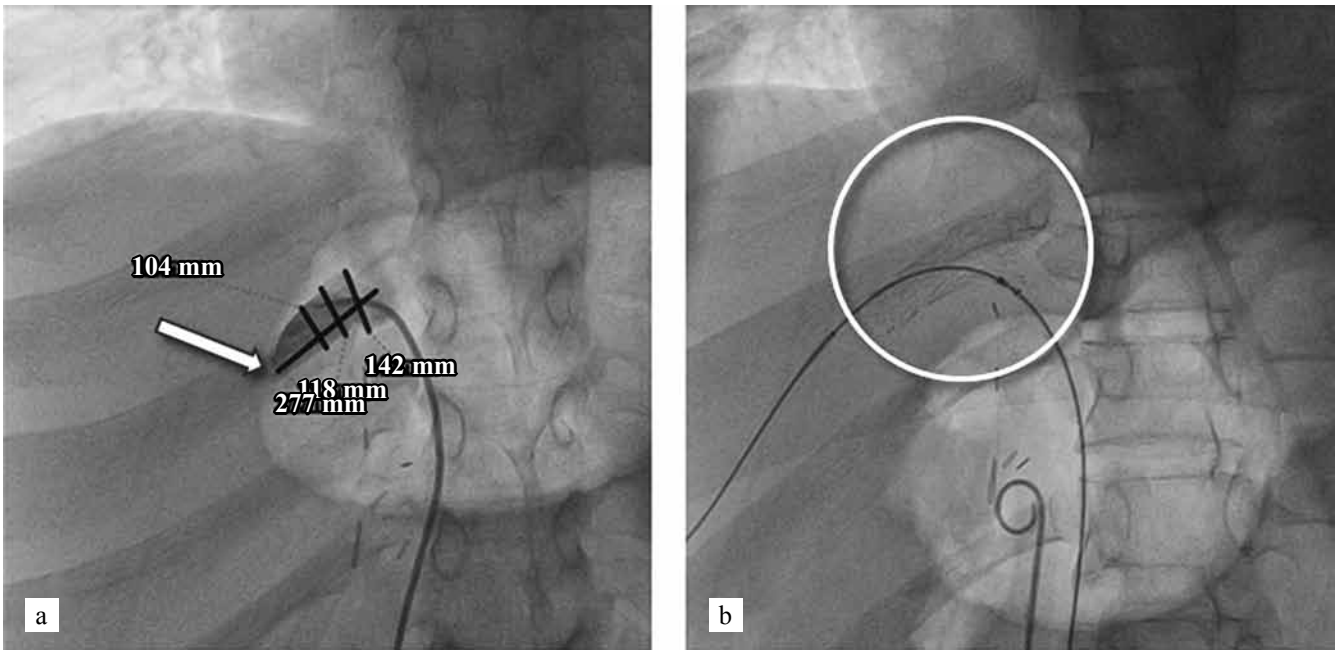

Fig. 5. The right hepatic vein stenosis. Angiography: a – zone of stenosis; b – stenting of the vein

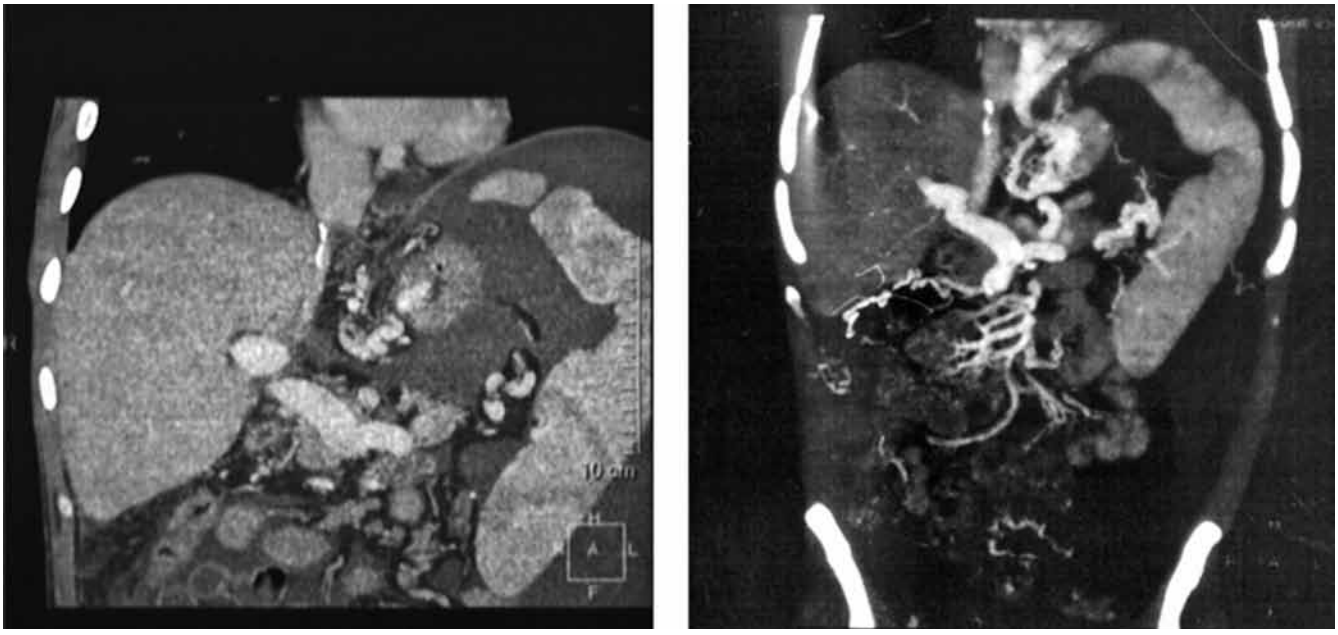

Fig. 6. CT with bolus contrast. The liver transplant acute failure on the background of hepatic vein thrombosis. The transplantation of the right lobe of the liver from a related donor due to liver cirrhosis in the outcome of mixed HBV + HDV infection, class C, decompensation stage. MELD 36. UNOS 1B

the first phase, we performed percutaneous transhepatic cholangiostomy (Fig. 7), and after reaching acceptable levels of bilirubinemia, we performed bile duct reconstruction, forming a biliodigestive fistula (Fig. 8).

Thus, timely measures taken to eliminate early postoperative complications saved the lives of 94.1% of liver transplant recipients. Unfortunately, three patients died from intra-abdominal bleeding (1), portal vein thrombosis (1), and biliary sepsis (1).

The average hospital stay after liver transplantation was 26.7 ± 2.2 days.

Speaking about the therapy given to recipients after organ transplantation, we note that immunosuppression was selected on an individual basis. In 89% of cases of related transplantation, monotherapy using calcineurin inhibitors (long-acting tacrolimus or cyclosporine) was administered. In the case of organ transplantation from a deceased donor, dual or triple therapy, which included calcineurin inhibitor, mycophenolic acid, and methyl-

Table 2

Characteristics of the biliary complications in different types of liver transplantation

Complication	Transplant				Total (n = 51)	
	Relative (n = 9)		Cadaver (n = 42)			
	n	%	n	%	n	%
Biliar anastomotic leak	4	44.4	0	0	4	7.8
Biliar anastomotis Biliar anastomotic	1	11.1	3	7.1	4	7.8
Total	**5**	**55.6**	**3**	**7.1**	**8**	15.7

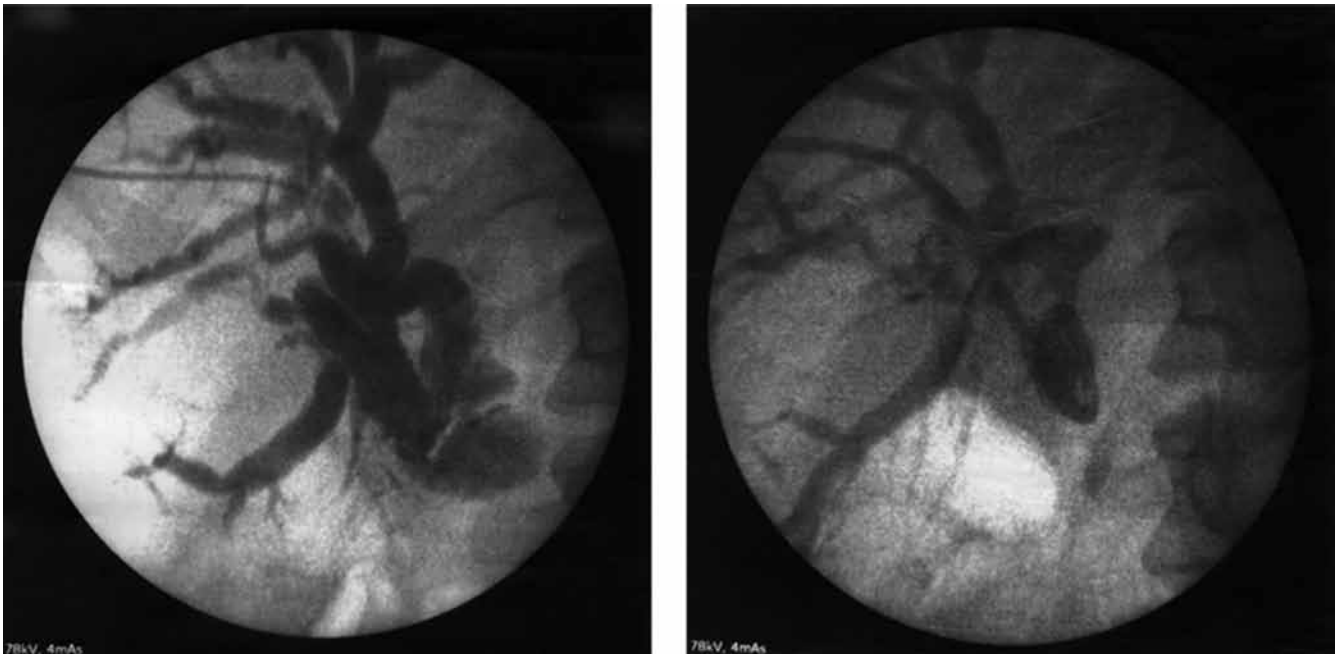

Fig. 7. Biliary anastomosis stricture with expansion of the intrahepatic ducts of the liver transplant in a patient after split transplantation of the right lobe. Transcutaneous transhepatic biliary drainage

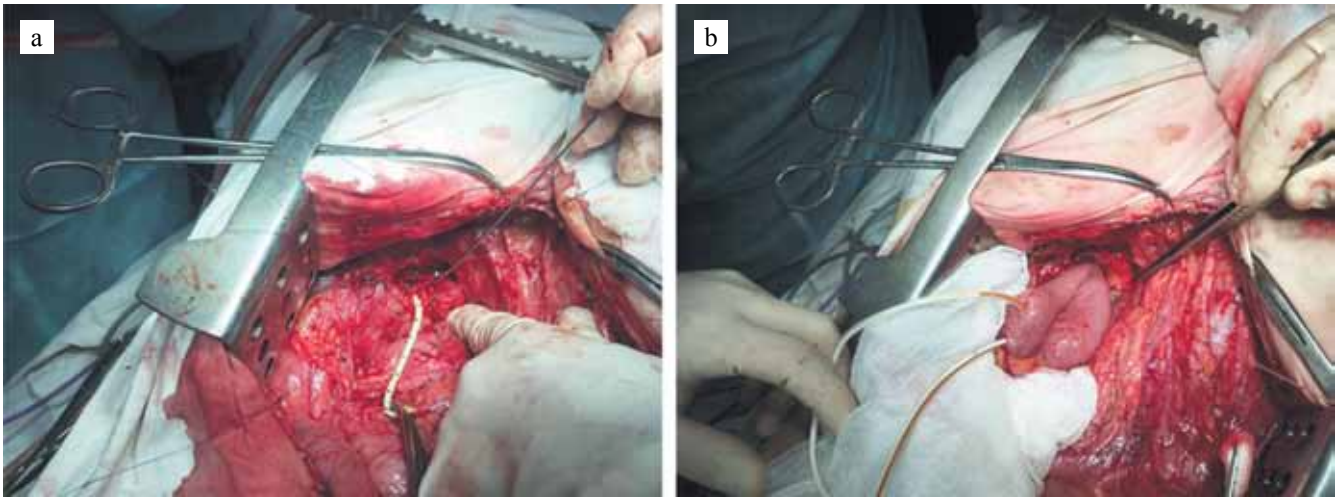

Fig. 8. Reconstruction of the biliary anastomosis: a – stage of separation of the anastomosis; b – the final type of operation (hepaticoejunostomy)

prednisolone, was administered. Pulse therapy with glucocorticosteroids was administered in 5.9% of cases due to graft rejection crisis. In 9 cases (17.6%), in connection with kidney failure and detected oncopathology, therapy was converted with the addition of an mTOR inhibitor (everolimus).

Currently, the follow-up for liver transplant recipients is from 1 month to 4.6 years. Among the long-term post-transplant complications experienced by patients were: autoimmune return (4), drug-induced nephropathy (9), arterial hypertension (7), drug-induced diabetes (5), obesity (5), generalized systemic atherosclerosis (1), lung adenocarcinoma (1), fungal sepsis (2), and testicular seminoma (1). Four more people died during this period from lung cancer (1), biliary sepsis (1), and fungal sepsis (2).

DISCUSSION

Transplantation is presently the only effective method for improving the survival rate in end-stage liver disease. However, despite the society's awareness of the necessity and justification of this technology, the stumbling block for further development of transplantation remains religious, moral and ethical issues, as well as the expediency of huge material costs. Lack of understanding among the public of the importance and humanity of transplant programs hinders rapid development of such programs, including in our region, Rostov Oblast.

A successful transplantation outcome depends not only on the transplant surgeon's skills, but also on the recipient's initial condition caused by underlying disease and associated pathology, as well as the "quality" and functional state of the donated organ. For example, we did not use organs from elderly donors. Therefore, we were able to avoid early graft dysfunction or non-function in almost all cases.

It should be noted that liver transplantation can become successful only with the active participation of a wide range of specialists at all stages of treatment. In this regard, a hepatologist managing the waiting list and monitoring the recipient's condition after liver transplantation, with constant correction of immunosuppressive and symptomatic therapy, plays an important role. Equally important is a qualified morphological and immunohistochemical graft assessment and diagnosis of complications.

The greatest concern on the effectiveness of liver transplantation comes from postoperative complications. Early postoperative vascular thrombosis is fraught with acute graft failure and loss. Biliary and bacterial-infectious complications, including fungal, often lead to patients' death, which has been the case in our practice.

CONCLUSION

Outcomes in liver transplantation depend on the skills and experience of the specialists implementing it. Post-transplant in-hospital and long-term mortalities depend on the presence and nature of complications, and on the possibility of early treatment.

The authors declare no conflict of interest.

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