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# TREATMENT OF VASCULAR COMPLICATIONS FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION. THE EXPERIENCE OF A REGIONAL CENTER

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**Objective:** vascular complications (VCs) following liver transplantation (LT) can pose a significant threat to the recipient's life – as the risk of graft loss increases significantly when blood flow in the graft is impaired. Diagnosis and early treatment of VCs seems to be a pressing issue in transplantology. The aim of this study is to evaluate the incidence, treatment and outcome of VCs in patients after orthotopic LT at the Center for Surgery and Donor Coordination, Rostov Regional Clinical Hospital. **Materials and methods.** Between July 2015 and April 2023, 100 orthotopic LTs were performed. VCs were retrospectively identified and analyzed. **Results.** The overall incidence of VCs was 24% (n = 24): hepatic artery stenosis, 5% (n = 5); intra-abdominal bleeding, 6% (n = 6); hepatic artery dissection, 2% (n = 2); intrahepatic venous thrombosis Budd–Chiari syndrome), 2% (n = 2); portal vein thrombosis, 1% (n = 1); inferior vena cava thrombosis/iliofemoral deep vein thrombosis, 2% (n = 2); inferior vena cava stenosis, 1% (n = 1); hepatic vein stenosis, 1% (n = 1); recurrent hepatic artery stenosis/thrombosis, 2% (n = 2); mesenteric vein thrombosis, 2% (n = 2). **Conclusion.** Most VCs following orthotopic LT occur in the early postoperative period and can lead to a high risk of graft dysfunction and patient death. Early recognition, diagnosis, and treatment of post-LT complications are critical to successful short- and long-term graft function and patient survival, even in patients with asymptomatic complications. Treatment options typically include surgical revascularization, percutaneous thrombolysis, percutaneous angioplasty, retransplantation, or, less commonly, a conservative approach.

*Keywords: liver transplantation, vascular complications.*

## INTRODUCTION

Orthotopic LT (OLT) is the most effective treatment modality for end-stage liver disease. Significant advances in surgical techniques for organ retrieval, introduction of potent immunosuppressive drugs, and improved peri- and postoperative patient care have resulted in increased patient survival after OLT to >90% [1]. However, VCs have life-threatening consequences for the patient as they impair blood flow in the graft. Most of these complications occur within the first month following OLT and require early detection, diagnosis, and immediate treatment [2]. Bleeding, stenosis and thrombosis can occur in any of the vascular anastomoses, as well as pseudoaneurysm in the arterial anastomosis [3, 4], with an overall reported incidence of 7.2% to 15% in adults (mainly arterial 5–10%, followed by portal 1–3% and caval <2%) [5–8]. However, the rate can be as high as 25% for hepatic artery thrombosis (HAT) and hepatic artery stenosis (HAS) [7].

**Hepatic artery thrombosis** (HAT) following OLT occurs in 1.9% to 16.6% of cases [8]. It is the most frequent and severe vascular complication following OLT. It accounts for more than 50% of all arterial complications and usually leads to graft loss [2, 9–14]. HAT is the main cause of biliary necrosis and massive liver necrosis accompanied by uncontrolled sepsis under immunosuppression, inevitably leading to patient death [15]. HAT occurring in the first month after LT is accompanied by mortality in 55% of cases; later stages of the thrombosis lead to death in 15% of cases [16]. In general, there are three treatment options for HAT: revascularization, retransplantation, and observation. The choice of any of these methods depends on the time of diagnosis [17]. Retransplantation rates are high in patients with untreated HAT (25–83%) compared to patients who receive graft revascularization (28%–35%) [9, 18, 19] and it provides the best survival outcomes. However, this option is subject to donor shortage and patient condition [9, 10, 20, 22].

**Hepatic artery stenosis (HAS)** is usually defined as a narrowing of the transverse diameter of the hepatic artery resulting in graft ischemia [9, 23–28]. HAS incidence

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is 2–13% according to different sources [9, 13, 23, 24, 26–28]. Percutaneous angioplasty is an alternative to surgical treatment for HAS [26]. If thrombectomy and angioplasty are ineffective, only LT can save the patient's life [17, 15].

**Hepatic artery pseudoaneurysm** (HAP) is a rare but life-threatening complication following OLT, occurring in approximately 0.27% to 3% of cases [13, 18, 31]. Ruptured extrahepatic aneurysm can lead to massive intraperitoneal bleeding and, as a consequence, to hemorrhagic shock. Color spectral Doppler, computed tomography, and selective angiography are useful diagnostic tests for differentiating complications [32].

**Venous complications**, compared with arterial complications, are less common, with an estimated overall incidence of less than 3% [5–7, 20, 35].

**Portal vein thrombosis (PVT)** and **portal vein stenosis (PVS)** complicate the postoperative period following OLT in 1–3% of cases [5–7, 20, 35]. The main methods in the early stages of treatment of PVT are thrombectomy and portal vein reconstruction combined with thrombolytic and anticoagulant drugs. If these methods are ineffective, urgent re-transplantation is the only method in most cases [36]. The treatment of choice for PVS is balloon angioplasty or stenting.

**Inferior vena cava or hepatic vein stenosis** are relatively rare complications arising after LT, with an incidence of less than 3% [2]. Clinical manifestations range from lower limb edema, hepatomegaly, ascites, pleural effusion, Budd–Chiari syndrome, hepatic and renal failure to low blood pressure leading to allograft loss and multiple organ failure [20, 36, 37]. Treatment of PVT includes systemic anticoagulant therapy, thrombolytic therapy by radiologic intervention with stent placement, portosystemic shunt, and re-transplantation in cases that are refractory to treatment [38].

## MATERIALS AND METHODS

During this study, the medical documentation of patients who underwent LT at the Center for Surgery and Donor Coordination, Rostov Regional Clinical Hospital, from July 2015 to April 2023, was reviewed. Analyzed were data on gender, age, and concomitant diseases of recipients; operations previously undergone by recipients; indications for LT; number and type of VCs; method used to diagnose complications; clinical course and treatment of patients; date and time of the operation. MS Office and Statistica software packages were used to analyze the data.

## RESULTS

A total of 100 (n = 100) OLTs were performed. The average age of the recipients was 43.5 ± 15.8 years. The indication for surgery was liver cirrhosis of various etiologies, the most common cause of end-stage liver disease in patients was viral hepatitis, 33% of cases (Fig. 1).

For 10 recipients, their close relatives were the liver donors, and 90 recipients received an organ from brain-dead donors. For two patients, the donor organ was obtained by splitting the liver into two lobes using the split in situ technique. LT in all patients was performed in accordance with ethical and legal standards.

The average duration of the surgical intervention was 5.14 ± 1.92 hours. Intraoperative blood loss did not exceed 1400 mL (1076.1 ± 191.8 mL). Using the reinfusion system, it was possible to return up to 93% of lost blood (996.5 ± 177.5 mL of blood on average), and the additional volume of erythrocyte mass transfused in 48.1%

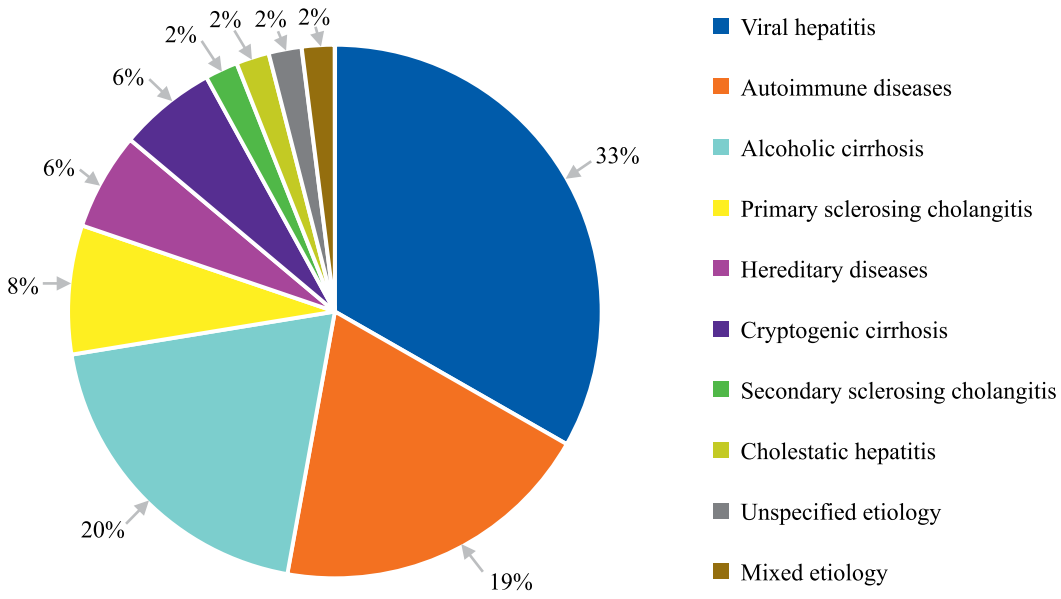


Fig. 1. Distribution of liver recipients by disease etiology

of patients during the operation and in the immediate postoperative hours was 238.7 ± 133.1 mL on average. In all cases, fresh frozen plasma was transfused with an average transfusion volume of 1394.7 ± 303.1 mL.

## Vascular complications

In the early postoperative period, VCs following OLT were diagnosed in 21/100 patients (21%), which is comparable to world literature reports [5–8, 42], while some patients had several complications at once, so the total number of VCs was 24 cases: hepatic artery stenosis and hepatic artery dissection (7%, n = 7), intra-abdominal bleeding (6%, n = 6), intrahepatic venous thrombosis (Budd–Chiari syndrome) (2%, n = 2), PVT (1%, n = 1), inferior vena cava/iliofemoral thrombosis (2%, n = 2), inferior vena cava stenosis (1%, n = 1), hepatic vein stenosis (1%, n = 1), recurrent HAS/HAT (2%, n = 2), mesenteric vein thrombosis (2%, n = 2) (Table).

## Characteristics of recipients who developed VCs after OLT:

- Recipient's gender: 16 males (69.6%) and 7 females (30.4%).
- Mean age at the time of surgery was (M ± SD) 46.46 ± 11.33 years.
- Mean body weight, (M ± SD) 75.52 ± 18.55.
- Mean body mass index (BMI), (M ± SD) 25.96 ± 4.16.
- 20 (95.2%) patients had comorbidities – arterial hypertension, thrombocytopenia, coagulopathy, chronic heart failure and morbid obesity.
- Child–Pugh classification: class B (Child B) 7–9 points in 8 cases (38.1%) and class C (Child C) 10–15 points in 12 cases (61.9%).
- MELD score and 3-month mortality:
  - in the range 30–39 points (52.6% mortality) in 3 cases (14.3%);
  - in the range 20–29 points (19.6% mortality) in 14 cases (66.7%);
  - in the range 10–19 points (6.0% mortality) in 3 cases (14.3%);
  - in the range <9 (1.9% mortality) in 1 case (4.8%).
- UNOS criteria:
  - status 1 (acute liver failure), 19 cases (90.5%);
  - status 2B (decompensated chronic liver disease), 2 cases (9.5%).
- METAVIR scale, F4 (Cirrhosis. Irreversible changes), 21 cases (100%).
- ABO blood group compatibility was the same in 21 cases (100%).

**Hepatic artery stenosis** with or without hepatic artery thrombosis occurred predominantly early after surgical intervention and during the patient's hospital stay. It occurred in 18/100 cases (18%). The diagnosis was established by Doppler ultrasound and angiography combined with laboratory investigation methods. Treatment priority was given to minimally invasive methods through endovascular technique, without exposing the patient to risks associated with thrombectomy and open reconstruction of the arterial anastomosis. From the right transradial access, catheterization of the celiac trunk was performed with a diagnostic angiographic catheter; selective catheterization of the common hepatic

Table

**Number of vascular complications following orthotopic liver transplantation at Rostov Regional Clinical Hospital and according to global reports**

| Vascular complication | Data from Rostov Regional Clinical Hospital | | | Data from world literature |
|---|---|---|---|---|
| | Number of cases | Percentage of all vascular complications (n = 24) | Percentage of total number of patients who underwent orthotopic liver transplantation (n = 100) | |
| Hepatic artery stenosis and hepatic artery dissections | 7 | 29.2 | 7 | 2–13% [9, 13, 23, 24, 26–28] |
| Intra-abdominal bleeding | 6 | 25.0 | 6 | 7.2–15% [5–8] |
| Intrahepatic venous thrombosis (Budd–Chiari syndrome) | 2 | 8.3 | 2 | The incidence is 1 per 100,000 population [40] |
| Portal vein thrombosis | 1 | 4.2 | 1 | 1–3% [5–7, 20, 35] |
| Inferior vena cava thrombosis/ iliofemoral deep vein thrombosis | 2 | 8.3 | 2 | <3% [2] |
| Inferior vena cava stenosis | 1 | 4.2 | 1 | <3% [2] |
| Hepatic vein stenosis | 1 | 4.2 | 1 | <3% [2] |
| Recurrent hepatic artery stenosis/ thrombosis | 2 | 8.3 | 2 | No data |
| Mesenteric vein thrombosis | 2 | 8.3 | 2 | 11% of all forms of visceral deep vein thrombosis [41, 42] |

artery was performed; a coronary conduit was placed in its distal parts through the thrombus and the stenosis zone of the arterial anastomosis (Fig. 2); 15 mg of the drug Actilyse was injected through a microcatheter into the thrombosis zone using an infusion pump at a rate of 1 mg/min; a 20-minute exposure was carried out, after which a coronary stent, coated with the drug Everolimus, was implanted in the area of the stenosed anastomosis of the common hepatic artery with the donor liver artery with a length exceeding the length of the stenosis, and angiographic control was performed in the stenting zone (Fig. 3) [15].

Treatment failed in 3/100 cases (3%), accompanied by progression of liver failure, which required repeated hepatic artery angioplasty and stenting; subsequently, one patient underwent organ retransplantation; one patient died against the background of multiple organ and intra-abdominal bleeding.

**Portal vein thrombosis** developed in 1/100 patients (1%) during a 5-day hospital stay. The diagnosis was established by ultrasound and then confirmed by angiography. Treatment was performed by open thrombectomy from the portal vein, but the patient died on the background of graft failure.

Hepatic vein thrombosis occurred in 2/100 cases (2%) within 4–10 months after hospital discharge. The pathology was diagnosed by Doppler ultrasound followed by spiral CT phlebography. One patient underwent partial splenic vein embolization and was subsequently listed for liver retransplantation. One patient underwent organ retransplantation 9 months after primary transplantation (5 months after hepatic vein thrombosis).

**Hepatic vein stenosis** was noted in 1 patient. The diagnosis was established by ultrasound and then confirmed by direct cavography. The hepatic vein was stented. Subsequently, against the background of graft failure, the patient died.

**Stenosis of the inferior vena cava** in the anastomosis zone, extending in the cranial direction, was noted in 1 patient; balloon angioplasty of the artery was performed 24 hours later. Pressure gradient in the area of stenosis was measured before and after angioplasty to confirm patency. Partial thrombosis of the inferior vena cava was noted in one patient, conservative therapy was performed. Iliofemoral deep vein thrombosis complicated by pulmonary embolism with subsequent placement of a cava filter was noted in 1 patient.

All patients with stenotic and thrombotic vascular complications were treated with anticoagulant therapy (heparin or low molecular weight heparin) at the calculated dosage in combination with selective thrombolysis in patients with X-ray image-guided endovascular reconstructions. Heparin infusion up to 180–200 IU/kg/day, adjusted according to the activated partial thromboplastin time (target levels, 50–70 seconds).

**Bleeding** episodes were reported in 5 patients after OLT, of which 2 episodes occurred after hepatic artery stenting and selective thrombolysis.

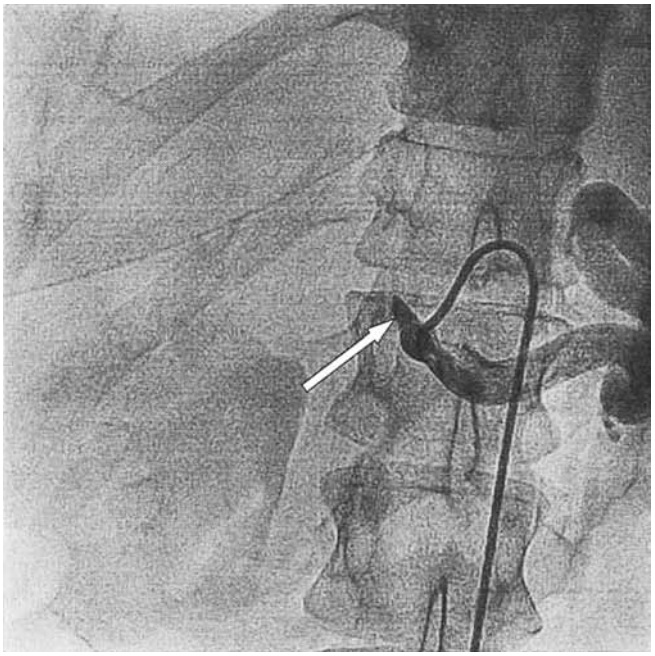

Fig. 2. Selective angiography of the common hepatic artery after liver transplantation. Thrombotic prestenotic occlusion in the proximal part – contrast break, arterial anastomosis stenosis

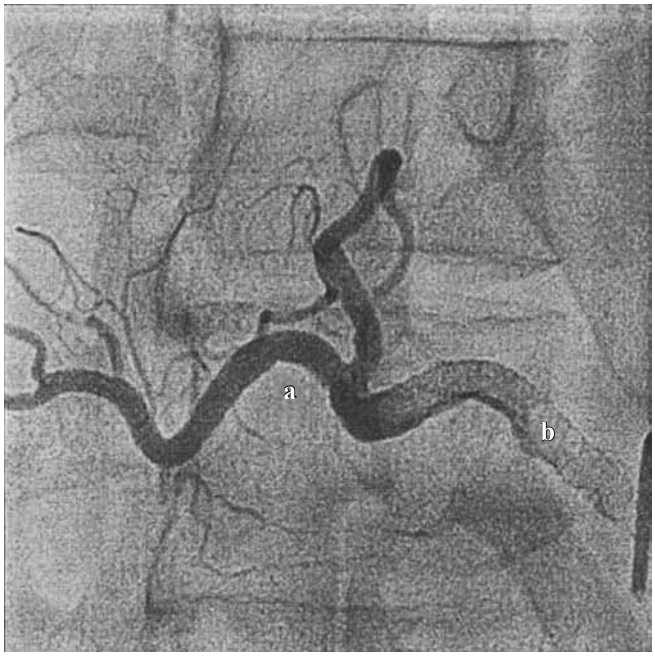


Fig. 3. Selective angiography of the common hepatic artery after liver transplantation: a, restoration of blood flow in the liver after selective thrombolysis; b, the hepatic artery anastomosis area is stented

## DISCUSSION

The frequency of vascular complications described in the literature varies greatly according to world and Russian literature. Despite technological advances, VCs are still an important factor in allograft loss, increasing postoperative morbidity and mortality.

Arterial complications are more common, occur in the early postoperative period, and are associated with a high incidence of graft loss and patient mortality. Conversely, venous complications are less frequent, occur in the late postoperative period and do not have a significant impact on graft loss or mortality.

The most common risk factors of arterial complications in LT are technical difficulties and errors at the stage of arterial anastomosis. This is because of the anatomical features of the graft, as well as previous reconstructions at the back table stage, atherosclerotic lesion of the organ artery in expanded criteria donors, significant difference in the diameter of the anastomosed arterial stumps, arterial spasm, and previous surgical interventions on abdominal organs in the recipient. The most common risk factors for venous complications in LT are previous thrombosis in the portal vein system, splenectomy, a significant difference in the diameter of the portal vein sections being sutured, a high MELD score, and the etiologic nature of the recipient's liver damage. Unfortunately, the impact of most of the described factors can only be prevented by improving surgical technique and working with the selection of patients on the waiting list. Identification of the above risk factors, prevention of technical complications and early diagnosis of VCs can reduce mortality, morbidity and the need for repeat transplantation.

Current trends have shown an increasing use of endovascular interventions initially to treat VCs after LT with good outcomes.

When endovascular procedures fail, open surgical repair still plays a role.

## CONCLUSION

Most VCs following OLT occur in the early postoperative period (up to 1 month) and can lead to a high risk of graft dysfunction and patient death.

LT outcome depends on the competence and skills of the specialists.

Early detection, diagnosis, and treatment of post-OLT complications are critical for successful short- and long-term graft function and patient survival, even in asymptomatic patients.

The leading methods for detecting and diagnosing VCs at early and late stages of treatment after OLT, included in most study protocols, are Doppler ultrasound and CT/selective angiography, which allows for early detection of VCs.

Treatment options typically include surgical revascularization, percutaneous thrombolysis, percutaneous angioplasty, retransplantation, or, less commonly, a conservative approach.

A combined approach to resolving post-OLT VCs can achieve a positive outcome with minimal surgical trauma to the patient.

VCs following OLT are a formidable and potentially dangerous complication. Therefore, further accumulation and systematization of experience in the diagnosis and treatment of this condition is important.

*The authors declare no conflict of interest.*

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