DOI: 10.15825/1995-1191-2020-3-99-106

INITIAL EXPERIENCE IN DIRECT GRAFT PERFUSION ASSESSMENT FOLLOWING ORTHOTOPIC LIVER TRANSPLANT

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Objective: classical methods of determining arterial blood supply of the graft following orthotopic liver transplantation (OLT) reflect the presence of blood flow in the trunk and large branches of the *A. hepatica*, without the characteristic of completeness of blood filling of peripheral sections, which is very important for objective evaluation of function. The aim of this study is to establish the diagnostic value of a direct perfusion study (IFlow) of the graft. **Materials and methods**. From 1998 to 2019, 245 OLTs were conducted. From 2015 to 2019, arterial changes were detected in 24 (23%) patients after 104 OLTs. A perfusion study was performed in 9 patients with suspected arterial graft failure. According to the IFlow study, liver hypoperfusion due to stenosis and/or splenic steal syndrome was detected in 8 cases and became an indication for therapeutic intervention. **Results.** Hepatic stenting and/or splenic artery embolization was performed to improve arterial blood supply to the liver. Endovascular procedures performed restored the perfusion index from 0.24 (0.01–0.89) to 0.61 (0.35–0.98). **Conclusion**. Absence of ultrasound and multispiral computed tomography signs of arterial complications does not rule out the need for perfusion angiography. Perfusion angiography allows to objectify the angiography data and perform corrective intervention in good time.

Keywords: orthotopic liver transplantation, blood flow, stenting, splenic artery embolization, graft perfusion angiography.

INTRODUCTION

The main indication for orthotopic liver transplantation (OLT) is terminal cirrhosis of various etiologies. The formation of cirrhosis leads to hemodynamic changes in the pancreatobiliary zone: depletion of the arterial flow to the liver and its simultaneous increase in the left gastric, gastroduodenal and splenic arteries. This creates unfavorable conditions for the blood supply to the donor organ [1].

During OLT, ligation of aberrant hepatic arteries is performed, leaving the common hepatic artery as the only source of blood supply to the organ parenchyma and bile ducts. Classical methods for determining the arterial blood supply of the graft after OLT (ultrasound, ultrasound, computed tomography, CT and angiography) display the presence of blood flow in the trunk and large branches of *A. hepatica*, without characterizing the completeness of blood filling in its peripheral parts, which seems to be quite important for an objective assessment of the graft function [2].

The **purpose** of the present study is to establish the diagnostic value of direct perfusion investigation of the graft by the IFlow program of the angiographic complex in patients with clinical, laboratory and radiological suspicion of liver hypoperfusion.

MATERIALS AND METHODS

In the Granov Russian Scientific Center of Radiology and Surgical Technology (St. Petersburg, Russian Federation) from 1998 to 2019, 245 OLTs were conducted. In 1998–2014, classical subtraction diagnostic angiography was performed only when vascular complications were detected using non-invasive (CT and / or ultrasound) methods (Fig. 1).

Fig. 1:

– a–c: MSCT of the abdominal organs with intravenous contrast, arterial phase: the diameters of the splenic (white arrow) and common hepatic arteries (black arrow) are comparable, = 3 mm (a); the right hepatic artery (arrow) is patent (b); segmental liver arteries (arrow) are defined (c);
– d: celiacography 2 days after MSCT; depleted intrahepatic arterial architectonics: no segmental vascular pattern as a sign of insufficient inflow (thick white arrows); the diameter of the dilated splenic artery (black arrow) is twice the common hepatic artery (white arrow): steal syndrome;
– e: control celiacography after embolization of the splenic artery trunk (under the same conditions for the introduction of a contrast agent); restored intrahepatic arterial architectonics, the vascular pattern can be traced to the subsegmental level (white arrows); stenosis of the common hepatic artery, the hemodynamic significance of which cannot be assessed without

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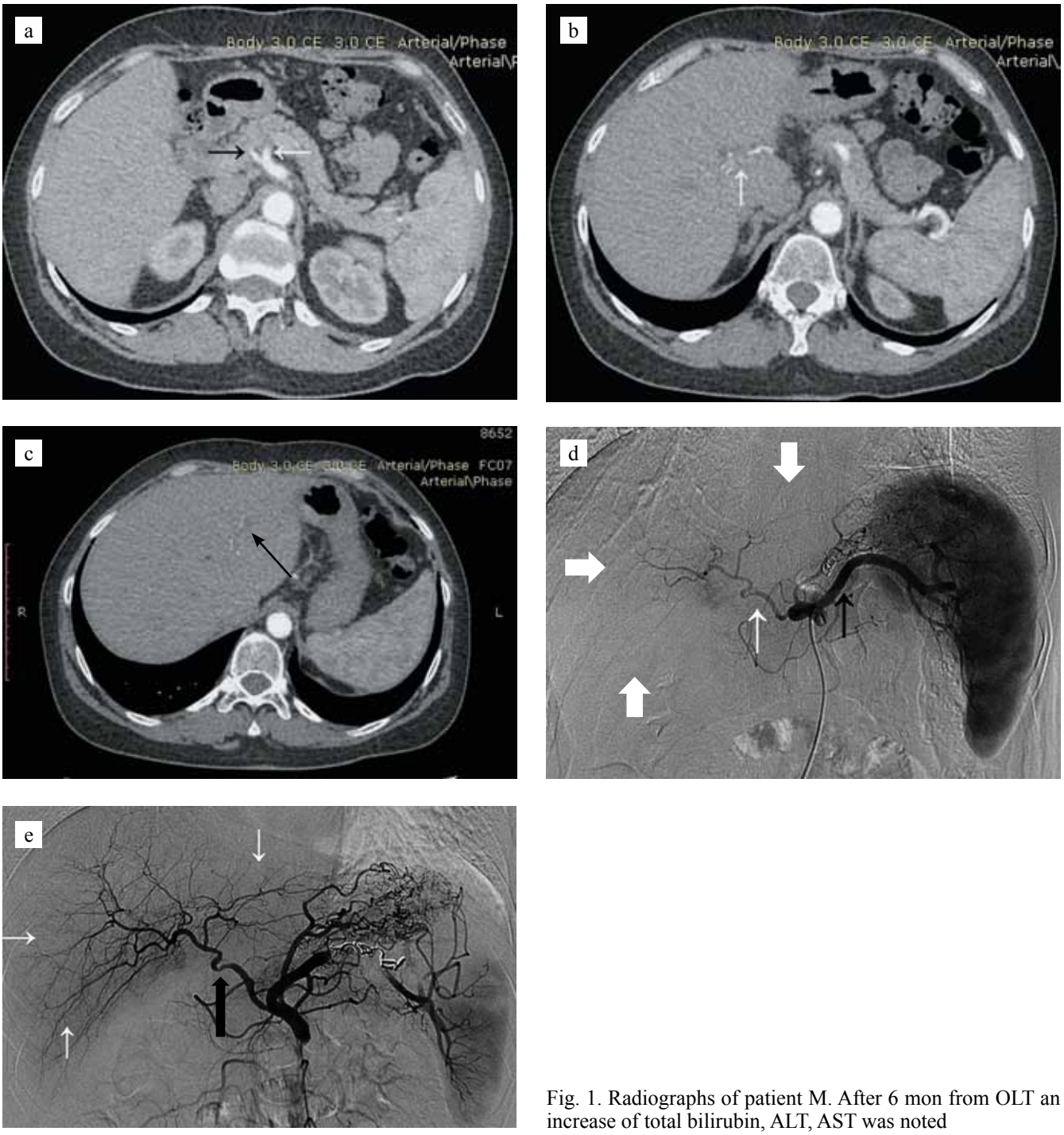

Fig. 1. Radiographs of patient M. After 6 mon from OLT an increase of total bilirubin, ALT, AST was noted

iFlow (black arrow); after 2 weeks. after endovascular intervention, biochemical parameters returned to normal, observed 4 years after OLT without biliary complications.

Since 2015, all patients with suspected liver hypoperfusion according to clinical and laboratory data have underwent angiography. In 2015–2019, arterial changes after 104 OLT were detected in 24 (23%) patients.

Classical diagnostic angiography was performed on a modern angiographic complex Siemens Artis Zee Biplane (Germany) with the IFlow function. Femoral artery puncture was performed under local anesthesia with 1% lidocaine solution using a 5F (1F = 0.33 mm) introducer sheath. Next, a Hook 5F catheter (Cook/Cordis, USA) was sequentially placed in the superior mesenteric artery and celiac trunk, subtraction angiography was performed using a syringe injector and 35 ml of contrast agent (Omnipak-350 or Ultravist-370) was injected at a rate of 4 ml/s.

The perfusion study was performed in 9 patients (Table). The difference in contrast agent concentration in the reference area (Ref AUC) and control areas (ROI AUC) was determined, where Ref AUC (referral area under curve) is the area of reference value under the curve,

Table

Analysis of perfusion values after OLT

Nos., age (years)	Timing of angiography after OLT	Interventions	Initial perfusion in S_{VI}, S_{VIII}, S_{II}	Final perfusion in S_{VI}, S_{VIII}, S_{II}	Ischemic biliary complications
1. K., 49	47 months	SAE SAE	0.08 0.10 0.22	0.40 0.65 0.40	–
2. S., 26	19 days	DA DA	0.89 0.81 0.89	0.89 0.81 0.89	–
3. K., 29	2 months	SAE + St SAE + St	0.20 0.25 010	0.55 0.50 0.53	+
4. Ch., 36	2 months	St St	0.15 0.20 0.10	0.60 0.28 0.33	+
5. K., 50	1 days	St St	0.01 0.02 0.01	0.45 0.40 0.35	+
6. S., 47	1 months	BAp BAp	0.50 0.55 0.30	0.70 0.75 0.65	–
7. K., 38	3 months	SAE + St SAE + St	0.02 0.30 0.25	0.45 0.55 0.35	+
8. Ch., 53	4 days	SAE + St SAE + St	0.12 0.11 0.35	0.80 0.81 0.83	–
9. G., 49	9 days	SAE SAE	0.08 0.05 0.16	0.81 0.89 0.98	–

Note. OLT – orthotopic liver transplantation, DA – diagnostic angiography, SAE – splenic artery embolization, St – stenting, BAp – balloon angioplasty.

and ROI AUC (region of interest area under curve) – the area of the control area under the curve. The reference area is the vessel (usually the celiac trunk) with maximum contrast medium filling during angiography. The control areas are the areas of the liver segments of interest (the most peripheral: SVI, SVIII, SII). The obtained angiograms were evaluated in the IFlow program. For this purpose, celiacography was selected at the workstation for 6–8 s of the series, when the vascular pattern of the liver was traced as far as possible along the segments. In the image tab, we switched to the IFlow mode, in the appeared dialog box, the duration video was set at the second when the subtraction celiacography was stopped. Then we went to the total contrast ROI selection dialog box with the subsequent selection of the circle value of the control area (circle ROI). The reference area was installed in the celiac trunk, giving it a value equal to the cross-sectional area of the vessel. Three control areas for measuring blood flow were set in the projection of the donor organ with the same values of their area, within 150–400 mm^2, and were located in the segments farthest from the reference point (SVI, SVIII, SII). The obtained tabular and graphical images displayed the completeness of filling the parenchyma with a contrast agent and the rate of reaching the peak concentration of the contrast agent, which in numerical value objectified the results obtained (Fig. 2, observation No. 1, Table). Adequate perfusion index (ROI AUC/REF AUC) was considered to be ≥0.65, the reference value was 1.0.

Fig. 2:

– a: celiacography, picture of depleted intrahepatic arterial architectonics. The diameter of the enlarged splenic artery (black arrow) is twice the common hepatic artery (white arrow): steal syndrome;
– b: perfusion study; the reference area, the size of which is equal to the cross-sectional area of the celiac trunk (value = 1) – circle Ref; areas of interest, areas of all circles in mm^2 – white circles 2, 3 and 4 (arrows in the upper table); the graph (at the bottom of the figure) displays the degree of filling of the studied areas (circles 2, 3 and 4) with a contrast agent over time, at 7 s: 5, 10 and 10%, respectively (thick arrow); the perfusion parameters of the studied areas are reduced (curved arrows);
– c: control celiacography after embolization of the splenic artery trunk to eliminate steal syndrome: in-

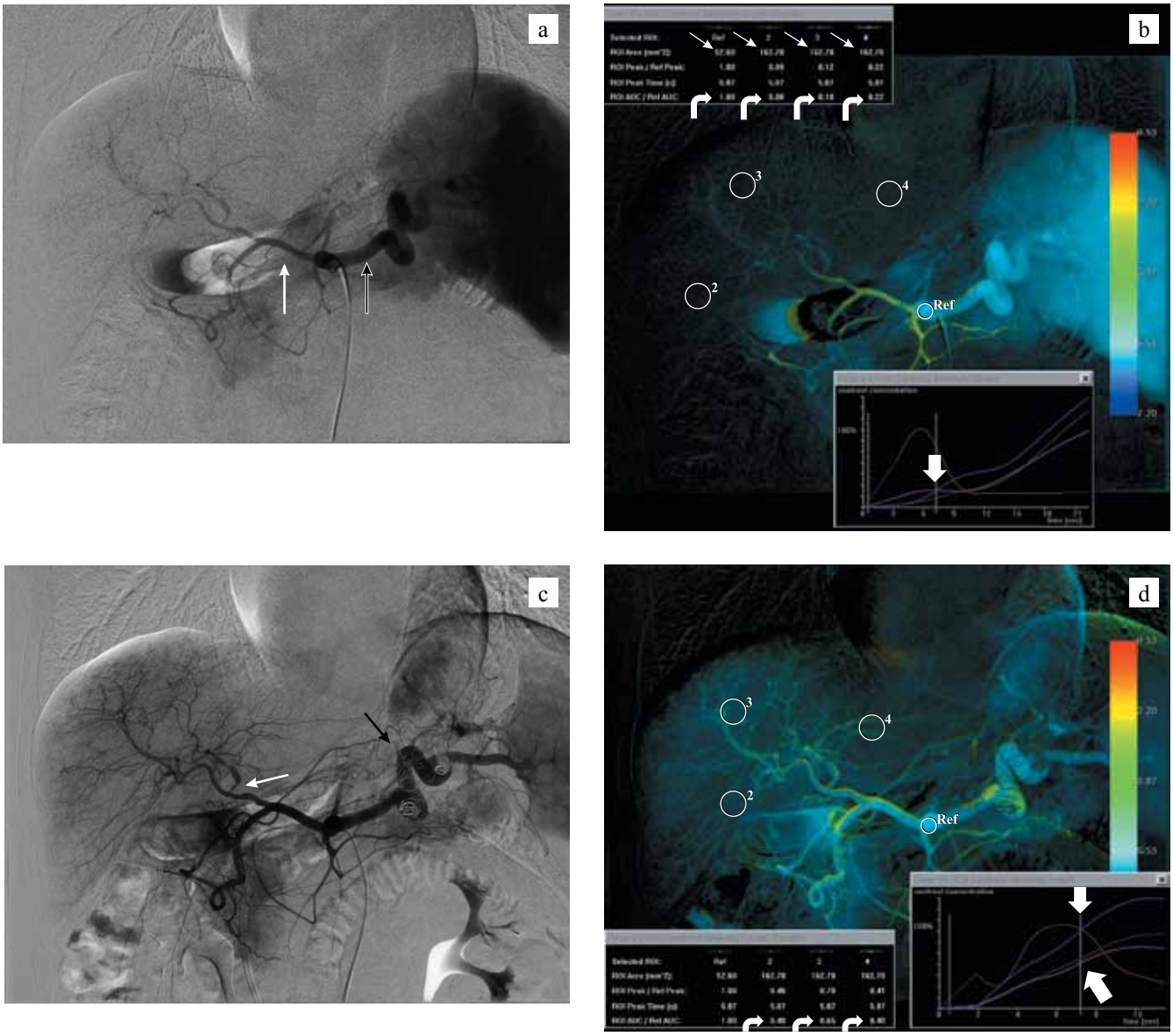

Fig. 2. Angiograms of patient K. 47 mon after OLT (case 1). The increase of ALT and AST was noted against adequate immunosuppressive therapy

trahepatic arterial architectonics can be traced in all segments; stenosis of the left hepatic artery (white arrow); metal coils in the trunk of the splenic artery (black arrow).

– d: perfusion study of the same patient after embolization, the perfusion index increased by 5, 6 and 2 times, respectively (curved arrows); the filling of the areas under study with a contrast agent increased by 7 s to 40, 40 and 70% (thick arrows); despite the unevenness of the contours of the left hepatic artery, the perfusion index of the left lobe of the liver is satisfactory, additional intervention is not required; the patient is observed 5.5 years after OLT without biliary complications.

RESULTS

There were no complications associated with diagnostic angiography. Initial angiograms and liver perfusion were satisfactory in one case (Fig. 3, observation No. 2, Table). Based on the obtained angiographic and perfusion data, therapeutic intravascular interventions were required in 8 patients (Table).

Fig. 3:

– a: cholangiography; X-ray picture of “burnt tree” of the left lobe of the liver, class C according to C. Buis (black arrows); complete block at the level of the biliary anastomosis (white arrow); cholangiostomy (thick white arrow);
– b: at celiacography, the contours of the hepatic artery are even, the diameters of the splenic and common hepatic arteries are comparable, arterial architectonics

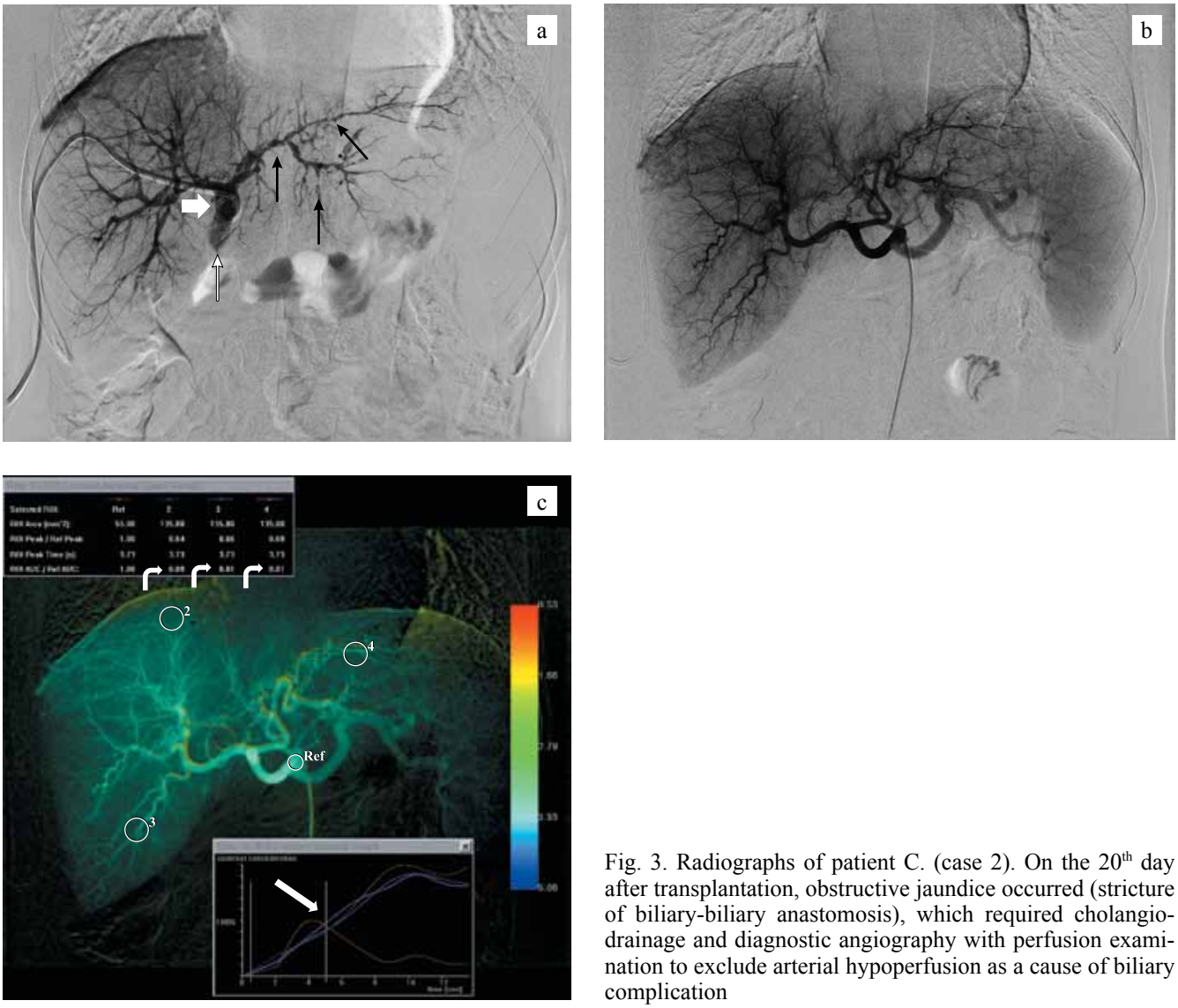

Fig. 3. Radiographs of patient C. (case 2). On the 20th day after transplantation, obstructive jaundice occurred (stricture of biliary-biliary anastomosis), which required cholangiodrainage and diagnostic angiography with perfusion examination to exclude arterial hypoperfusion as a cause of biliary complication

can be traced to the subsegmental level; there were no angiographic signs of hypoperfusion;

– c: perfusion study; a reference area, the size of which is equal to the cross-sectional area of the celiac trunk (value = 1) – circle Ref; the areas under study (white circles 2, 3, 4), the perfusion index of which in SVI, SVIII, SII = 0.89; 0.81; 0.81 (curved arrows); the graph (at the bottom of the figure) displays the percentage of filling the areas under study with a contrast agent over time, for 5 s: up to 45% (white arrow); perfusion indicators are more than 0.65, and the curve of filling the studied areas with a contrast agent over time is equated to the reference value; hypoperfusion was not detected; the biliary stricture is recognized as anastomotic, balloon plasty of the biliary-biliary anastomosis is performed.

The mean baseline perfusion value in the presence of splenic artery steal syndrome and / or hepatic artery stenosis was 0.24 (0.01–0.89). As a result of the therapeutic measures (stenting of the hepatic artery and / or embolization of the splenic artery trunk), the segmental perfusion index was restored to 0.61 (0.35–0.98) in all 8 patients. In four patients, the perfusion index did not exceed 0.6; later, biliary non-anastomotic strictures of class C and D according to Buis developed [3, 4]. The perfusion study avoided embolization of the left gastric artery to enhance the flow to the liver and objectified the need for hepatic artery stenting despite a satisfactory angiographic picture in one patient (Fig. 4, observation 8). Upon reaching a perfusion value of ≥0.65, no therapeutic actions were performed.

Fig. 4:

– a: celiacography: steal syndrome of the liver by the splenic artery (black arrow); kink of the non-anastomotic part of the hepatic artery (white arrow) was regarded as hemodynamically insignificant; depleted intrahepatic arterial architectonics;
– b: perfusion study; the reference area, the size of which is equal to the cross-sectional area of the celiac trunk (value = 1) – circle Ref; the areas under study

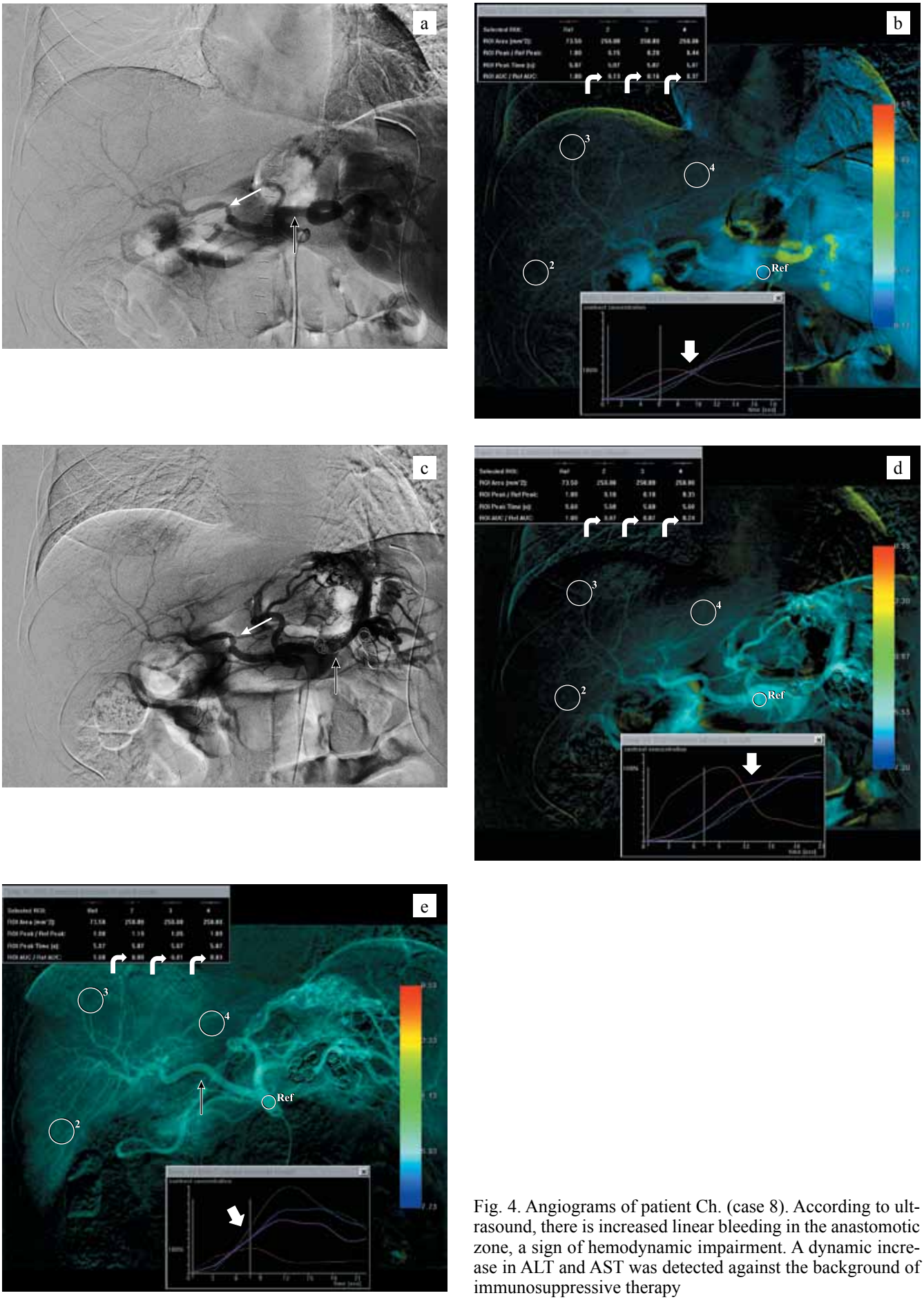

Fig. 4. Angiograms of patient Ch. (case 8). According to ultrasound, there is increased linear bleeding in the anastomotic zone, a sign of hemodynamic impairment. A dynamic increase in ALT and AST was detected against the background of immunosuppressive therapy

(white circles 2, 3, 4), the perfusion index of which in SVI, SVIII, SII = 0.13; 0.16; 0.37 (curved arrows); the graph (at the bottom of the figure) displays the percentage of filling the areas under study with a contrast agent over time, for 9 s: up to 30% (thick arrow); IFlow picture of pronounced hypoperfusion;

– c: celiacography after embolization of the splenic artery trunk: depleted intrahepatic arterial pattern is preserved, with moderately positive dynamics, bending of the hepatic artery (white arrow); reduced blood flow in the trunk of the splenic artery (black arrow);
– d: perfusion index in the studied areas 0.07; 0.07; 0.24, below original values (curved arrows); the filling of the studied areas with a contrast agent only for 13 s reaches 30–35% (thick arrow); IFlow picture of pronounced hypoperfusion, negative dynamics despite embolization of the splenic artery; the decision was made to stent the hepatic artery;
– e: perfusion study after hepatic artery stenting (black arrow); the perfusion index in the studied areas increased by 11, 11 and 4 times and amounted to 0.80; 0.81; 0.83 respectively (curved arrows); the filling of the study areas with a contrast agent decreased to 7 s and increased to 40, 40 and 50%, respectively (thick arrows); endovascular treatment was found to be effective, ALT and AST indices returned to normal on the 10th day.

DISCUSSION

We share the opinion of the authors who consider angiography a priority method for detecting vascular changes after OLT. Complications associated with diagnostic angiography do not exceed 1%, we did not have such complications [5, 6].

The present study showed that the presence of ultrasound and / or CT signs of intrahepatic arterial blood supply does not exclude transplant hypoperfusion [7].

The programs available in modern angiographic complexes help not only to suspect, but also to objectively identify the cause of the hypoperfusion state of the graft, which, with its timely and adequate elimination, can reduce the risk of biliary ischemic complications [2].

The obtained data are of great importance in the choice of tactics for the restoration of adequate graft perfusion. Embolization of the splenic or left gastric arteries performed without indications can lead to septic complications leading to a cascade of pathological mechanisms, especially against the background of mandatory immunosuppressive therapy [8]. Unnecessary stenting of the hepatic artery condemns the patient to lifelong antiplatelet therapy, and in case of thrombosis leads to the death of the organ and the patient [5]. According to D. Seehofer et al. [4], the formation of nonanastomotic strictures of the bile ducts in the graft is based on arterial hypoperfusion at all levels. It is associated either with a defect in the collection of the organ, or with its inadequate perfusion after the start of arterial blood flow. According to our data, there is a clear relationship between low perfusion values (<0.65) and ALT and AST indices with the subsequent development of biliary strictures.

CONCLUSION

The absence of ultrasound and CT signs of arterial complications does not exclude the need for angiography in case of suspected transplant hypoperfusion according to clinical and laboratory data. Angiography in combination with IFlow supplements the data of non-invasive diagnostic methods, allowing an objective assessment of the indications and efficacy of endovascular X-ray interventions in patients after OLT. Further study of graft hypoperfusion is required using the results of IFlow and MSCT perfusion.

The authors declare no conflict of interest.

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The article was submitted to the journal on 1.06.2020