

Endovascular Reduction of Splenic Blood Flow in the Treatment of Patients with Liver Cirrhosis

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Authors' contributions

This work was carried out in collaboration between all authors. Author UM designed the study, performed data collection, wrote the initial manuscript and revisions. Author SK wrote the protocol. Author BA performed the literature review and managed the literature searches. Author MK helped with the writing manuscript. Author TN helped with the statistical analyses. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: Defining the effectiveness of the embolization of the splenic artery (ESA) in the treatment of patients with liver cirrhosis.

Materials and Methods: We have analyzed the results of treatment 318 patients with cirrhosis who were hospitalized in the 2-clinic of the Tashkent Medical Academy in 2007-2014. Most of the patients (201) were males, mean age was 35.1±17.7 years. For the purpose of monitoring performed comprehensive study, including clinical, laboratory and special instrumental methods of research. To assess the severity of the Hepatic Failure (HF) used classification of Child-Turcotte-Pugh (CTP). Bleeding from the esophagus and stomach varices history was noted in 207 (65.1%) patients, in 151 (47.5%) of them had been made endoscopic ligation varices of esophagus and stomach and 56 (17,6%) patients was successfully performed percutaneous transhepatic embolization coronary vein and short gastric vein using the technique described by Lunderquist et al. Pronounced hemodynamic disorder on the background of anemia accompanied by deteriorated metabolic and functional status of the liver and other organs. Therefore, 32.0% detected HF class-A by CTP, at 45.6% - Class-B and 22.4% -Class C. The indications for ESA are splenomegaly with

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hypersplenism, and without it, varices of esophagus and stomach, high portal pressure (PP). Contraindications were severe general condition of the patient, the high activity of cirrhotic process, which was estimated at the level of bilirubin and ALT, AST.

Results: The effectiveness of endovascular interventions we evaluated on the following criteria: changes in general clinical and biochemical parameters of blood, portal blood flow dynamics and the state of varices of esophagus and stomach, the incidence of bleeding, the overall mortality rate and life expectancy. Laboratory analysis was carried out after stabilization of the patients in terms from 1 to 3 months, revealed an increase in cellular composition and the level of hemoglobin. The number of leukocytes increased to $6.8 \pm 0.24 \times 10^9/L$, platelet – to $176.3 \pm 15.8 \times 10^9/L$, the hemoglobin level was 94.7 ± 12.4 g/l. The increase in arterial blood supply of the liver caused by the redistribution of blood flow after ESA, accompanied by an improvement of the functional state of the liver, which evaluated by a number of clinical and laboratory parameters in 37 the at 1 month, 3 months, 6 months and 12 months. Results of the study of the portal system show that in the period of 3 months after the ESA with a decrease of PP $428,7 \pm 10,2$ to $342,3 \pm 12,6$ mm of water.

Conclusion: Splenic artery embolization after endoscopic band ligation varices of esophagus and stomach or transhepatic embolization coronary vein and short gastric vein reduces the risk of rebleeding and maybe use as method for improve liver function and decrease of portal hypertension.

Keywords: Portal hypertension; liver cirrhosis; esophageal varices; liver insufficiency; splenic artery embolization.

1. INTRODUCTION

Portal Hypertension (PH) is one of the most severe complications of liver cirrhosis. Violation of adequate blood flow from the portal vein system at PH disorders characterized by regional and general hemodynamics, which leads to disruption of metabolism, water and electrolyte metabolism, a significant reduction in the functionality of vital organs. Particularly pronounced changes occur in the stage of decompensation of the disease, with the development of serious complications such as bleeding varices (BV), esophagus and stomach, ascites, Hepatic Failure (HF) [1-3].

PH arises against liver cirrhosis, usually leads to splenomegaly, which is the main factor in the development of hypersplenism and hence thrombocytopenia, anemia and leukopenia [4]. Reduced hematological indices, taking into account the presence of patients with liver failure has significant clinical implications, since further increases the risk of bleeding from the esophagus and stomach [5]. Recurrent bleeding occurs more than 70% of patients with PH bleeding from the esophagus and stomach varices history [6,7]. It is a common belief that all patients had a history of bleeding from varices esophagus and stomach are in need of further treatment to prevent rebleeding [8,9].

Endoscopic methods of stopping the bleeding from varices of esophagus and stomach are various. Following the development of

techniques of endoscopic ligation (EL) varices was made possible not only to stop, but the to prevent of bleeding. However, endoscopic intervention do not solve the problem of portal hypertension and hepatic failure. Given that splenectomy in patients with liver cirrhosis often leads to serious complications and death, percutaneous intervention opened a promising new approach to reduce the pressure in the portal vein, reducing the number of complications and deaths, as well as improving the quality of life of patients by recovering from liver failure [10-12].

Embolization of the splenic artery (ESA) has been developed as an alternative to portocaval bypass surgery. After ESA portal pressure is reduced to 100-150 mm water column activated cholinesterase and increased serum albumin that relieves symptoms of hepatic insufficiency. This proves the effectiveness of the ESA in portal hypertension with splenomegaly for treatment and prevention of recurrence of bleeding from varices esophagus and stomach [13-16].

1.1 Purpose

Defining the effectiveness of the ESA in the treatment of patients with liver cirrhosis.

2. MATERIALS AND METHODS

We have analyzed the results of treatment 318 patients with cirrhosis who were hospitalized in the 2-clinic of the Tashkent Medical Academy in 2007-2014. Most of the patients (201) were

males; mean age was 35.1 ± 17.7 years. For the purpose of monitoring performed comprehensive study, including clinical, laboratory and special instrumental methods of research.

To assess the severity of the HF used classification of Child - Turcotte - Pugh (CTP). Bleeding from the esophagus and stomach varices history was noted in 207 (65.1%) patients, in 151 (47.5%) of them had been made endoscopic ligation varices of esophagus and stomach and 56 (17,6%) patients was successfully performed percutaneous transhepatic embolization coronary vein and short gastric vein using the technique described by Lunderquist et al. [17,18]. Splenic and coronary venograms were obtained to portal venous anatomy and localize all venous supplies

to the esophageal varices (Fig. 1A). Whenever more than one major blood supply was demonstrated, each was selectively catheterized and embolized with using combinations of 0.035 metallic coils (Cook, Inc., Bloomington, Ind.) and 70% alcohol 10 ml to occlude esophageal veins (Fig. 1B). The portal pressure was measured using a with water manometers through inserted catheter into the portal vein after transhepatic embolization of coronary vein and short gastric vein.

To assess the severity and prevalence varices of esophagus and stomach we used the classification proposed by the World Gastroenterology Organisation Global Guidelines (2014). In endoscopy varices of esophagus and stomach were found in 219 (81.0%) patients,

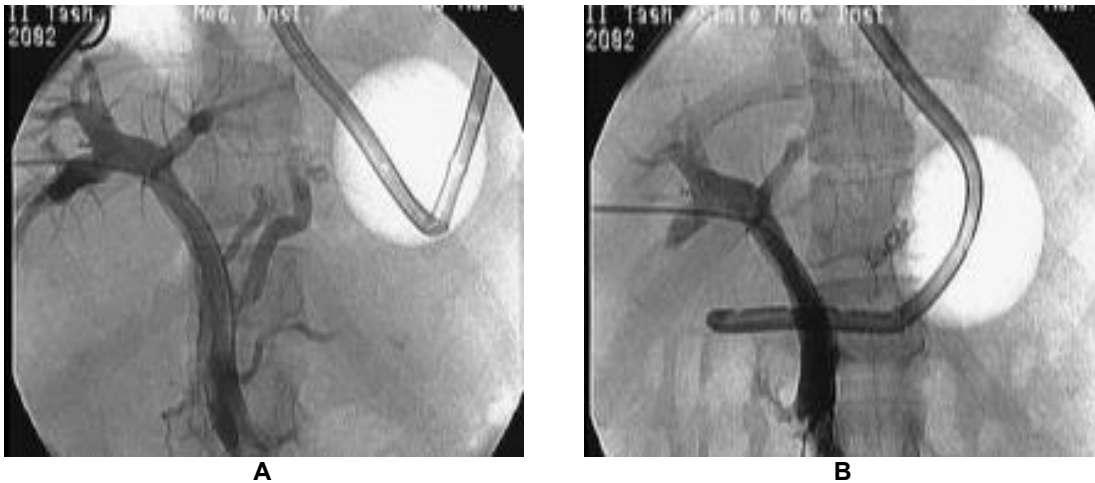


Fig. 1. A- Percutaneous transhepatic portal and coronary venograms. B- Percutaneous transhepatic embolization coronary vein

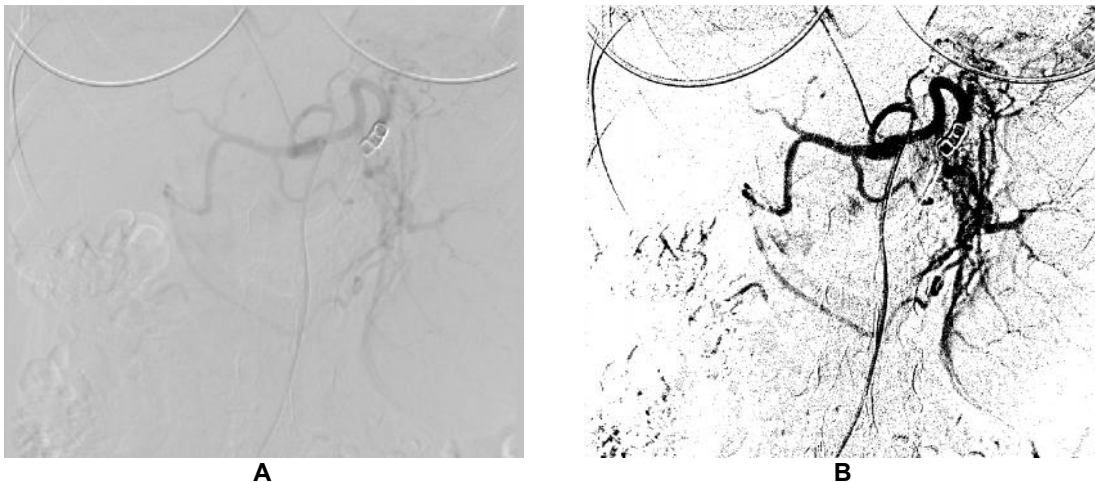


Fig. 2. The development of additional collateral after ESA

including from 102 - I degree, 39 - II and 78 - III degree. In 136 of these observed phenomenon of portal gastropathy with varying severity.

In the laboratory analysis showed a reduction of the blood component (Table 1). Pronounced hemodynamic disorder on the background of anemia accompanied by deteriorated metabolic and functional status of the liver and other organs. Therefore, 32.0% detected HF class-A by CTP, at 45.6% - Class-B and 22.4% - Class C.

Table 1. Clinical characteristics of patients, n = 318

Patient characteristics	The number of patients
Sex (male/female)	201/117
Age	35,1±17,7
Laboratory data:	
Hemoglobin, g/l	78,4±16,8
Erythrocytes 10 ¹² /L	2,5±0,6
Leukocytes 10 ⁹ /L	2,9±0,7
Platelets, 10 ⁹ /L	102,6±15,6
Bilirubin, mol/l	23,2±4,1
Totalprotein, g/l	57,7±9,6
HF by CTP (A/B/C)	102/145/73
Degree varices of esophagus and stomach	
I	102
II	39
III	78

*CTP-classification of Child - Turcotte – Pugh

The indications for ESA are splenomegaly with hypersplenism, and without it, varices of esophagus and stomach, high portal pressure (PP).Contraindications were severe general condition of the patient, the high activity of cirrhotic process, which was estimated at the level of bilirubin and ALT, AST.

The main goal of endovascular therapy was considered to achieve correction of the changes of portal-hepatic circulation for the prevention and treatment of complications of PH, primarily profuse bleeding from varices of esophagus and stomach.

2.1 The Technique of Embolization of the Splenic Artery

The procedure was having performed after local anesthesia by the Siemens Artis Zee angiography under. Access is via the femoral artery catheter 5F by Seldinger technique. Celiac arteriography and splenoportography performed to determine the point of origin of the arteries of the spleen and the availability of collaterals.

After defining the anatomy of the celiac trunk and Splenic Artery (SA) catheter was cannulated in the proximal part of it, and then introduce embolic agent using combinations of 0.018 inch or 0.035 inch metallic coils, such as the Nester and Micro Nester coils (Cook Medical, Bloomington, IN, USA). Embolic agent selectively introduced before the hilum of the spleen. The procedure on embolization, was 35-50 minutes.

Endovascular treatments were carried out in parallel with targeted conservative therapy include the complex pathogenic events, depending on the severity of various disorders.

3. RESULTS

The effectiveness of endovascular interventions we evaluated on the following criteria: changes in general clinical and biochemical parameters of blood, portal blood flow dynamics and the state of varices of esophagus and stomach, the incidence of bleeding, the overall mortality rate and life expectancy.

In the postoperative period, 97/30.5% experienced pain of varying intensity, which localized in the left half of the abdomen, which was due to ischemia of the splenic parenchyma. The pain persisted for 3-5 days after the procedure stopped receiving non-narcotic analgesics.

Increased body temperature, which usually lasted for 3-7 days, observed in 164 patients. In 270/85%, it was associated with the release of pyrogen agents from the infarct area of spleen. In 35.5% body temperature rises above 38°C, which was due to a significant portion of splenic ischemia due to acute reduction of blood flow through the splenic artery (Table 2).

Pneumonia, atelectasis and pleural effusion occur frequently on the left side. When congestion in the pleural cavity more than 500 ml, the effusion was aspirated with puncture the pleural cavity.

In 75% of patients with encephalopathy symptoms regressed in the early postoperative period.

In 169 (53.1%) patients who had ascites and taking diuretics, and non-selective β-blockers, there was a decrease in the amount of ascites fluid from the abdominal cavity, while 27.0% without them, which was accompanied by an increase in the daily volume of urine output.

Table 2. The nature of complications after ESA

Complication	The number of patients (%)
Increase in body temperature (> 38)	113 (35.5)
Severe pain in the abdomen	97 (30.5)
Pneumonia	54 (16.9)
Pleuritis	41 (12.8)
Splenecosis	1 (0.3)
Compromised renal function	4 (1.2)
Compromised liver function	7 (2.2)
Portal vein thrombosis	5 (1.5)

Laboratory analysis was carried out after stabilization of the patients in terms from 1 to 3 months, revealed an increase in cellular composition and the level of hemoglobin. The number of leukocytes increased to $6.8 \pm 0.24 \cdot 10^9/l$, platelet- to $176.3 \pm 15.8 \cdot 10^9/l$, the hemoglobin level was 94.7 ± 12.4 g/l. The increase in arterial blood supply of the liver caused by the redistribution of blood flow after ESA, accompanied by an improvement of the functional state of the liver, which evaluated by a number of clinical and laboratory parameters in the at 1 month, 3 months, 6 months and 12 months (Table 3).

Thus, in the early period after ESA total protein serum has not changed, then at the 3rd month, it was increased from 57.7 ± 9.6 to 62.6 ± 12.3 g/l, reaching a statistically significant level to 12th month (68.4 ± 12.3 g/l).

In some cases, there are no increasing the activity of alanine amino transferase and aspartate amino transferase and total bilirubin level, increasing the concentration of prothrombin index, and an increase in activity of

cholinesterase testified necrobiotic termination processes.

There was an increase in hemoglobin levels to 114 ± 13.8 g/l, the amount of erythrocytes to 3.32 ± 0.9 ($10^{12}/l$), platelets to 187.6 ± 16.7 ($10^9/l$) leukocytes to 5.4 ± 1.2 ($10^9/l$).

Despite the increase in these parameters in the average group, a statistically significant increase observed in 233 (73.2%) patients, whereas in 85 patients specific changes in the composition of blood cells was observed. By the 3rd month 246 of 261 patients noted improvement in general well-being, which has been seen by us as satisfactory, the disappearance of weakness and fatigue, abdominal pain.

According to ultrasonography reducing the area of the spleen to 172.2 ± 32.4 to 117.3 ± 19.4 cm² was observed in 202 (63.5%) patients. Persistent disappearance of ascites was observed in 86 (27.0%) patients.

Embolization of the splenic artery led to a reduction of splenic blood flow, which was accompanied by a decrease in portal pressure by 75-90 mm of water (an average of 76.4 ± 9.3 mm of water). Results of the study of the portal system show that in the period of 3 months after the ESA with a decrease of $PP 428.7 \pm 10.2$ to 342.3 ± 12.6 mm of water (Table 4). In the period of 6 months of Portal Pressure (PP) again rose to 388.6 ± 14.2 mm of water, which was associated with the occurrence of recanalization SA and collateral blood flow to the spleen. The diameter of the portal and splenic veins after isolated ESA did not undergo significant changes.

In the study of long-term results of embolization SA 47.1% of the patients showed dilation of the

Table 3. Changes of laboratory parameters after ESA (M±m)

	Before performing ESA	After ESA			
		1 month	3 months	6 months	12 months
The number of patients	318	294	261	237	218
Hemoglobin, g/l	78.4 ± 16.8	$94.7 \pm 12.4^*$	$114 \pm 13.8^*$	$98 \pm 12.6^*$	$104 \pm 13.2^*$
Erythrocytes $10^{12}/L$	2.5 ± 0.6	$3.24 \pm 0.9^*$	$3.32 \pm 0.9^*$	$3.10 \pm 0.7^*$	$3.46 \pm 0.9^*$
Leukocytes $10^9/L$	2.9 ± 1.7	$6.8 \pm 1.2^*$	$5.4 \pm 1.2^*$	$3.2 \pm 1.3^*$	$4.7 \pm 1.3^*$
Platelets, $10^9/l$	102.6 ± 15.6	$176.3 \pm 15.8^*$	$187.6 \pm 16.7^*$	$124.6 \pm 14.6^*$	$202.3 \pm 16.7^*$
Bilirubin, mol/l	23.2 ± 4.1	$22.6 \pm 5.8^*$	$21.4 \pm 3.4^*$	$19.2 \pm 4.6^*$	$18.4 \pm 4.8^*$
Total protein, g/l	57.7 ± 9.6	$60.7 \pm 12.4^*$	$62.6 \pm 12.3^*$	$64.6 \pm 12.4^*$	$68.4 \pm 12.3^*$
AST, mmol / lh	0.70 ± 0.15	$0.42 \pm 0.13^*$	$0.56 \pm 0.15^*$	$0.67 \pm 0.15^*$	$0.52 \pm 0.13^*$
ALT mmol / lh	0.82 ± 0.17	$0.64 \pm 0.12^*$	$0.57 \pm 0.11^*$	$0.62 \pm 0.13^*$	$0.58 \pm 0.14^*$
Prothrombin index, %	64.8 ± 12.8	$78.6 \pm 13.2^*$	$74.4 \pm 12.8^*$	$70.4 \pm 11.9^*$	$76.8 \pm 12.6^*$

Note. * - $P < 0.05$

Table 4. The value of PP, the diameter of the portal and splenic veins, the size of the liver after ESA

Index	Before embolization	3 months	6 months	12 months
PP mm of water.	428,7±10,2	342,3±12,6*	388,6±14,2*	394,8±16,5*
The diameter of the portal vein,	1,98±0,24	1,97±0,33*	1,95 ± 0,18*	1,90 ± 0,31
The diameter of the splenic vein,	1,67±0,13	1,64±0,17*	1,58±0,13*	1,58±0,25*

Note.* - $P < 0.05$.

arteries of the liver and improve its blood supply, which had a positive impact on its functionality. At the same time, SA recanalization was observed in 33.9% of patients. In 28 patients with splenic artery was stenosis in the previously inserted a coil. In these cases, as well as complete occlusion of an artery to form various arterial collaterals the spleen (Fig. 2).

Most of collaterals were developed through the left gastric artery (31.3%), gastric and left gastroepiploic artery (27.7%) and the gastroepiploic artery (15.5%), at least - through the left gastric, gastrointestinal and pancreatic stuffing artery (7.2%), the left gastric, gastroepiploic artery and right gastric (11.5%). In these cases carried re-embolization of SA (Fig. 3), were performed if necessary - embolization of collaterals (Fig. 4).

The best clinical effect after ESA due in a period of 3 months. He was shown a decrease in the area of the spleen with $172,24 \pm 32,43$ to $117,36 \pm 19,46$ cm² and arterialization of liver, expansion of its own hepatic artery (OHA) from $3,5 \pm 0,6$ to $4,6 \pm 0,7$ mm (Fig. 5).

In subsequent periods, after 6 and 12 months, the results are worse: the size of the spleen and the diameter of the OHA approaching source

(respectively 117 ± 12.33 cm² and 0.37 ± 0.08 cm). The deterioration at 6 and 12 months was due to recanalization of the artery and the occurrence of arterial flows on the extended left gastric artery (from 3.8 ± 0.9 to 5.9 ± 1.1 mm) and gastro-omental arteries (2.3 ± 0.7 to 0.9 ± 4.2 mm) (Fig. 6).

Identified by repeated angiography the characteristic changes in angioarchitecture of celiac trunk were observed such as the development of collateral network, restoring blood flow in the portal vein and to maintain a high PP, pointed to the need for appropriate re-embolization artery involved in the exchange flow of blood to the spleen to consolidate the effect. In these cases, we conducted additional embolization of the left gastric artery, which not only enhances the effect of embolization SA, but also reduces the threat of esophageal bleeding due to a sharp increase in blood flow in cardioesophageal zone.

When the control endoscopy was performed most patients showed varices of esophagus with collapsed state, or no tendency to increase. New varicose veins in the esophagus, within one year were formed in 127 (39.9%) patients. These patients were performed endoscopic ligation (EL).

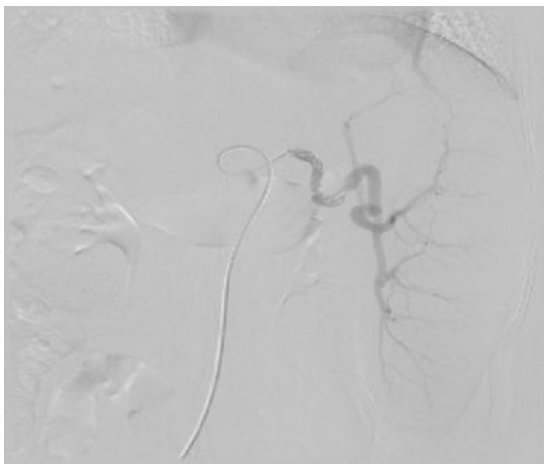


Fig. 3. Re-embolization of SA



Fig. 4. Embolization of gastro-omental artery



Fig. 5. The total reduction of splenic blood flow after embolization SA, left gastric and gastro-omental artery

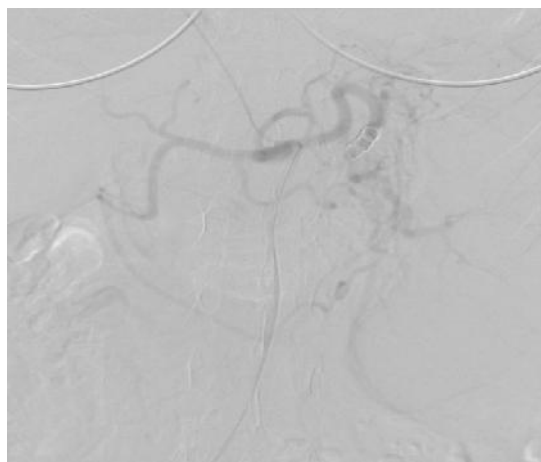


Fig. 6. Recanalization SA and the occurrence of arterial flows on the enlarged left gastric artery

In the follow-up within one year a recurrence of bleeding occurred in 18 (4.4%) patients, 3 of whom bleeding was stopped using Blackmore tube, others made the EL. In 2 patients due to profuse bleeding from varices of fundus Sugiura is operation was performed. 3 patients died due to hemorrhagic shock.

The decrease of portal blood flow and an increase in the number of platelets leads to the development of hypercoagulable that was the cause of portal vein thrombosis, which is docked appointment of antiplatelet therapy in 7 patients.

Complications were observed. In the late period 1 patient developed an abscess of the spleen due to prolonged ischemia. Although performed splenectomy, the patient died from acute organ failure. In 13 patients had acute ischemia of more than 80% of the splenic parenchyma, which was determined by ultrasound scanning. Massive splenic parenchyma ischemia resulted in ESA function and progression of liver disease, which is associated with the redistribution of blood flow, release of endotoxin in portal vein due to necrosis of the spleen and kidney hypoperfusion.

Especially difficult recovery after ESA was observed in patients with HF Class-C by CTP. They were managed with anti-inflammatory therapy with albumin transfusion, but 3 patients died within three months due to acute liver failure.

4. DISCUSSION

Portal hypertension - threatening complication of cirrhosis of the liver, which leads to the development of a number of complications,

which resulted in more than one third of patients die within 6 weeks after admission. Among the most dangerous complications are bleeding of varices atesophagus and stomach, and HF [19-21].

An effective method of stopping and prevention of bleeding from esophageal and gastric varices is endoscopic ligation, but the number of relapses and deaths remain high. EL does not solve the problem of increased portal vein pressure and liver failure, and hypersplenism. In this condition it is necessary to supplement EL endovascular treatments [22-31].

The effect of endovascular embolization of the splenic artery is preserved in more than one year, noting the improvement of the functional reserve of the liver in Indocyan test 46-62.5% of patients; it's connected with the hemodynamic effects of embolization. Our study revealed a number of positive hemodynamic changes of the portal-hepatic blood flow after ESA. Thus, the size of the spleen decreased from 172.24 ± 32.43 to 117.36 ± 19.46 cm², Portal Pressure (PP) decreased from 428.7 ± 10.2 to 342.3 ± 12.6 mm of water, arterialization of the liver, i.e. the increase of the own hepatic artery, increased from 3.5 ± 0.6 to 4.6 ± 0.7 mm. However, to achieve a lasting effect it is necessary reembolization of SA and its flows in the long-term. In our case, after double and triple reduction of splenic blood flow efficiency was 85.5%, which was reflected in subjective improvement of the patients, and in clinical and biochemical parameters: there was a significant increase in the number of blood corpuscles with normalization of enzymes and bilirubin.

Decrease in the blood flow in the splenic artery after its occlusion with 436.1 ± 66.5 to 213.1 ± 29.1 ml/min, while in hepatic artery it was increased from 99.5 ± 7.4 to 150.8 ± 13.9 ml/min. the pressure in the portal vein decreased from 3.6 ± 0.25 to 2.9 ± 0.23 k Pa. In an effort to occlusion 50-70% in traorganic bloodstream by introducing a small emboli, gelatin, heloma, PTFE microspheres, the author observed an exacerbation of hepatic failure in 8-12% of patients, the formation of abscesses of the spleen from 2-3.5%. Complications were the cause of deaths in 8.3% of patients. In this regard, we prefer the stem embolization using metal coils, and long occlusion of the splenic artery.

The positive effect of embolization of the SA, as measured by improvement of clinical and biochemical parameters, increasing of life expectancy. A positive result was observed 62 (85.3%) patients. Poor results the authors attributed to the presence of in patients with decompensated liver cirrhosis, severity of disease, frequency and duration of high activity of cirrhotic process, the development of complications.

For reducing the number of relapses and deaths the use of a combination of endoscopic and endovascular treatment of patients with PH that simultaneously achieves regression of liver failure can be favored, and reduce the risk of bleeding from the BV esophagus and stomach. However, the problem of treatment of patients with severe edematous-ascitic syndrome, decompensated portal hypertension are still not resolved. Resistance to diuretics ascites, presence of BV stomach in patients with decompensated liver cirrhosis and portal hypertension dictate the need for more benign or minimally invasive endovascular methods of reduction of portal hypertension [32-39].

5. CONCLUSIONS

Splenic artery embolization after endoscopic band ligation varices of esophagus and stomach or transhepatic embolization coronary vein and short gastric vein reduces the risk of rebleeding and maybe use as method for improve liver function and decrease of portal hypertension.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hyder A, Dilshad MA, Sarwar S, Alam A, Khan AA, Butt AK. Comparison of single verses multiple session band ligation for the treatment of bleeding oesophageal varices. *J Ayub Med Coll Abbottabad*. 2015;27(1):212-5. PMID: 26182779
2. Martínez J, Albillos A. *Gastroenterol Hepatol*. 2014;37(Suppl 2):68-73. Spanish. PMID: 25087715
3. Solà E, Ginès P. Challenges and management of liver cirrhosis: Pathophysiology of renal dysfunction in cirrhosis. *Dig Dis*. 2015;33(4):534-8. Epub 2015 Jul 6. PMID:26159270
4. Gangireddy VG, Kanneganti PC, Sridhar S, Talla S, Coleman T. Management of thrombocytopenia in advanced liver disease. *Can J Gastroenterol Hepatol*. 2014;28(10):558-64. Epub 2014 Sep 15. Review. PMID: 25222481.
5. Wang WJ, Tang Y, Zhang Y, Chen Q. Prevention and treatment of hemorrhage during laparoscopic splenectomy and devascularization for portal hypertension. *Huazhong Univ Sci Technolog Med Sci*. 2015;35(1):99-104. Epub 2015 Feb 12. PMID: 25673201.
6. Trasancos Escura C. Stomalvarices: An unusual cause of bleeding in patients with portal hypertension. *Rev Esp Enferm Dig*; 2015. PMID: 26177364.

7. Liu J, Zou Y, Chang W. Esophageal and gastric variceal bleeding in the prevention of early rebleeding given enteral nutrition value after endoscopic variceal ligation and treatment. *Zhonghua Gan Zang Bing ZaZhi*. 2015;23(1):46-9. Chinese. PMID: 25751386.
8. Sass DA, Chopra KB. Portal hypertension and variceal hemorrhage. *Med Clin North Am*. 2009;93(4):837-53. Review. PMID: 19577117.
9. Puente A, Hernández-Gea V, Graupera I, Roque M, Colomo A, Poca M, Aracil C, Gich I, Guarner C, Villanueva C. Drugs plus ligation to prevent rebleeding in cirrhosis: An updated systematic review. *Liver Int*. 2014;34(6):823-33. Review.
10. Leite LA, PimentaFilho AA, Ferreira R-de C, da Fonseca CS, dos Santos BS, Montenegro SM, Lopes EP, Domingues AL, Owen JS, Lima VL. Splenectomy improves hemostatic and liver functions in hepatosplenic schistosomiasis mansoni. *PLoS One*. 2015;10(8):0135370. eCollection 2015. PMID: 26267788
11. Kawanaka H, Akahoshi T, Kinjo N, Harimoto N, Itoh S, Tsutsumi N, Matsumoto Y, Yoshizumi T, Shirabe K, Maehara Y. Laparoscopic splenectomy with technical standardization and selection criteria for standard or hand-assisted approach in 390 patients with liver cirrhosis and portal hypertension. *J Am Coll Surg*. 2015;221(2):354-66. Epub 2015 Apr 23. PMID: 26206637.
12. Chu HB, Zhang TG, Zhao JH, Jian FG, Xu YB, Wang T, Wang M, Tang JY, Sun HJ, Li K, Guo WJ, Zhu XJ. Assessment of immune cells and function of the residual spleen after subtotal splenectomy due to splenomegaly in cirrhotic patients. *BMC Immunol*. 2014;15:42. PMID: 25293512.
13. Charissa Y Chang, Ashwani K Singal, Sri V Ganeshan, Thomas D Schiano, Robert Lookstein, Sukru Emre. Use of splenic artery embolization to relieve tense ascites following liver transplantation in a patient with paroxysmal nocturnal hemoglobinuria. *Recanati Miller Transplant Institute and Department of Interventional Radiology, Mount Sinai Hospital, New York, NY, Liver Transplantation*. 2007;13:1532-1537.
14. Mitchell Smith, Charles E Ray. Splenic artery embolization as an adjunctive procedure for portal hypertension. *Semin Intervent Radiol*. 2012;29(2):135-139.
15. Dwivedi MK, Pal RK, Dewanga L, Nag P. Efficacy of partial splenic embolisation in the management of hypersplenism. *Indian J Radiol Imaging*. 2002;12:371-4
16. Amr A Nassef, Ayman A Zakaria, Mohamed S AbdElBary. Partial splenic artery embolization in portal hypertension patients with hypersplenism: Two interval-spaced sessions' technique. *The Egyptian Journal of Radiology and Nuclear Medicine*. 2013;44:531-537.
17. Ríos Castellanos E, Seron P, Gisbert JP, BonfillCosp X. Endoscopic injection of cyanoacrylate glue versus other endoscopic procedures for acute bleeding gastric varices in people with portal hypertension. *Cochrane Database Syst Rev*. 2015;5:CD010180.
18. Xingshun Qi, Guohong Han, Chuangye He, Zhanxin Yin, Hongbo Zhang, Jianhong Wang, Jielai Xia, Hongwei Cai, Zhiping Yang, Ming Bai, Kaichun Wu, Daiming Fan. For the PVT-TIPS Study Group Transjugular intrahepatic portosystemic shunt may be superior to conservative therapy for variceal rebleeding in cirrhotic patients with non-tumoral portal vein thrombosis: A hypothesis *Med Sci Monit*. 2012;18(8):HY37-HY41. Published online 2012 Aug 1.
19. Yong-Song Guan and Ying Hu. Clinical application of partial splenic embolization. *Scientific World Journal*. 2014;2014: 961345. Published online 2014 Nov 3.
20. Chikamori F, Kuniyoshi N, Kawashima T, Takase Y. Short-term portal hemodynamic effects of partial splenic embolization for hypersplenism. *Hepato-Gastroenterology*. 2007;54(78):1847-1849. [PubMed]
21. Ito K, Ozasa H, Noda Y, Horikawa S. Splenic artery ligation ameliorates hepatic ischemia and reperfusion injury in rats. *Liver International*. 2006;26(2):254-260. [PubMed][Cross Ref]
22. Ito K, Ozasa H, Noda Y, Koike Y, Arii S, Horikawa S. Splenic artery ligation improves remnant liver function in partially hepatectomized rats with ischemia/reperfusion injury. *Liver International*. 2007;27(3):400-407. [PubMed][Cross Ref]
23. Xu J, Yang Z, Zeng J. Role of NF-kappaB in liver ischemia reperfusion injury of rats. *Journal of Huazhong University of Science and Technology—Medical Science*. 2003; 23(2):158-160. [PubMed][CrossRef]

24. Tajiri T, Onda M, Yoshida H, Mamada Y, Taniai N, Kumazaki T. Long-term hematological and biochemical effects of partial splenic embolization in hepatic cirrhosis. *Hepato gastroenterology*. 2002;49:1445–1448. [PubMed].
25. Hayashi H, Beppu T, Okabe K, Masuda T, Okabe H, Ishiko T, Baba H. Therapeutic factors considered according to the preoperative splenic volume for a prolonged increase in platelet count after partial splenic embolization for liver cirrhosis. *J Gastroenterol*. 2010;45:554–559. [PubMed].
26. Hidaka H, Kokubu S, Saigenji K, Isobe Y, Maeda T. Restoration of thrombopoietin production after partial splenic embolization leads to resolution of thrombocytopenia in liver cirrhosis. *Hepato Res*. 2002;23:265. [PubMed].
27. Bárcena R, Moreno A, Foruny JR, Moreno A, Sánchez J, Gil-Grande L, Blázquez J, Nuño J, Fortún J, Rodríguez-Gandía MA, et al. Improved graft function in liver-transplanted patients after partial splenic embolization: Reversal of splenic artery steal syndrome? *Clin Transplant*. 2006;20:517–523. [PubMed].
28. Hiromitsu Hayashi, Toru Beppu, Ken Shirabe, Yoshihiko Maehara, Hideo Baba. Management of thrombocytopenia due to liver cirrhosis. A review *World J Gastroenterol*. 2014;20(10):2595–2605. Published online 2014 Mar 14.
29. Mitchell Smith, Charles E Ray. Splenic artery embolization as an adjunctive procedure for portal hypertension. *Intervent Radiol*. 2012;29(2):135–139.
30. Pålsson B, Hallén M, Forsberg AM, Alwmark A. Partial splenic embolization: Long-term outcome. *Langenbecks Arch Surg*. 2003;387(11–12):421–426. [PubMed].
31. Koconis KG, Singh H, Soares G. Partial splenic embolization in the treatment of patients with portal hypertension: a review of the English Language literature. *J Vasc Interv Radiol*. 2007;18(4):463–481. [PubMed].
32. Miyaaki H, Ichikawa T, Nakao K, et al. Portal hypertensive gastropathy with portal thrombosis successfully treated with partial splenic embolization. *Clin J Gastroenterol*. 2009;2(3):218–221.
33. Orlando R, Lirussi F, Basso SM, Lumachi F. Splenomegaly as risk factor of liver cirrhosis. A retrospective cohort study of 2,525 patients who underwent laparoscopy. *In Vivo* 2011;25:1009-1012. [PMID: 22021698]
34. Ogata T, Okuda K, Sato T, Hirakawa Y, Yasunaga M, Horiuchi H, Nomura Y, Kage M, Ide T, Kuromatsu R, Kinoshita H, Tanaka H. Long-term outcome of splenectomy in advanced cirrhotic patients with hepatocellular carcinoma and thrombocytopenia. *Kurume Med J*. 2013;60:37-45. [PMID: 24064764]. DOI: 10.2739/kurumemedj.MS62010]
35. Kim H, Suh KS, Jeon YM, Park MS, Choi Y, Mori S, Hong G, Lee HW, Yi NJ, Lee KW. Partial splenic artery embolization for thrombocytopenia and uncontrolled massive ascites after liver transplantation. *Transplant Proc*. 2012;44:755-756. [PMID: 22483487]. DOI: 10.1016/j.transproceed.2012.01.066
36. Elmonem SA, Tantawy HI, Ragheb AS, Matar NEH, Tantawi I. The outcome of partial splenic embolization for hypersplenism in cirrhotic patients. *Egypt J Radiol Nuc Med*. 2011;42:35-42. DOI: 10.1016/j.ejrn.2011.01.002
37. Smith M, Ray CE. Splenic artery embolization as an adjunctive procedure for portal hypertension. *Semin Intervent Radiol*. 2012;29:135-139. [PMID: 23729984]. DOI: 10.1055/s-0032-1312575
38. Pandey R, Garg R, Darlong V, Punj J, Kumar A. Role of splenic artery partial embolization in a patient with portal hypertension and pancytopenia undergoing hysterectomy under anesthesia. *AANA J*. 2012;80:96-98. [PMID: 22586877]
39. Gowda NK, D'Souza D, Golzarian J. Partial splenic artery embolization. *Endovascular Today*. 2012;11:74-76.

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