UDC 616.149-008.341.1
DOI https://doi.org/10.32782/2226-2008-2024-4-6

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CLINICAL AND PATHOPHYSIOLOGICAL ASPECTS OF SPLENECTOMY AND SELECTIVE SPLENIC ARTERY LIGATION IN PATIENTS WITH DECOMPENSATED PORTAL HYPERTENSION

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The research aims to demonstrate the difference in approaches to correcting hypersplenism in portal hypertension of various etiology.

Materials and methods. The approach of splenectomy (SE) and splenic artery ligation (SAL) without removal of the spleen during porto-azygos disconnection in patients with upper variceal bleeding was compared. Differences in hematological changes and portal hemodynamics in the postoperative period were evinced. Participants: patients (n=37) with decompensated portal hypertension complicated by variceal bleeding, who underwent porto-azygos dissection and splenectomy formed group 1 (n=20), those who underwent porto-azygos dissection and splenic artery ligation formed group 2 (n=17). The comparative characteristics of surgical interventions in the two groups were performed.

Results. Diameter of the portal vein, blood flow and congestion index were correlated with spleen size and type of surgical intervention ($p < 0.005$). The increase in thrombotic activity after splenectomy was characterized by an increase in the number of platelets and changes in blood coagulation. Complications in the form of thrombosis of the portal and superior mesenteric veins were observed in patients after splenectomy with concomitant Covid-19 infection. In the patients of the second group, thromboembolic complications were not observed, instead, there were purulent-septic complications in the form of splenic infarction, subdiaphragmatic and intrapleural accumulation of pathological contents.

Conclusions. In the studied cohort of patients, the performance of splenectomy indicates a clinically significant improvement in portal hemodynamics. Decrease of intrahepatic blood flow due to reduction of splenic blood flow leads to improvement of liver function. Any type of reduction in splenic blood flow leads to an increased risk of thrombosis in the portal vein system.

Key words: portal hypertension, variceal bleeding, splenectomy, splenic artery ligation.

УДК 616.149-008.341.1

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КЛІНІКО-ПАТОФІЗІОЛОГІЧНІ АСПЕКТИ ВИКОНАННЯ СПЛЕНЕКТОМІЇ ТА СЕЛЕКТИВНОГО ЛІГУВАННЯ СЕЛЕЗІНКОВОЇ АРТЕРІЇ У ХВОРИХ ІЗ ДЕКОМПЕНСОВАНОЮ ПОРТАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

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Порівняно підходи спленектомії та перев'язки селезінкової артерії без видалення селезінки під час порто-азигального роз'єднання у пацієнтів із варикозною кровотечею з верхніх відділів шлунково-кишкового тракту. У пацієнтів після спленектомії із супутньою інфекцією COVID-19 спостерігались ускладнення у вигляді тромбозу ворітної та верхньої брижових вен. У хворих другої групи тромбоемболічних ускладнень не спостерігалося, натомість мали місце гнійно-септичні ускладнення у вигляді інфаркту селезінки, піддіафрагмального та внутрішньоплеврального скупчення рідинного вмісту. У досліджуваній популяції пацієнтів виконанню спленектомії слідувало клінічно значуще покращення портальної гемодинаміки. Зниження портального кровотоку за рахунок зменшення селезінкового призводить до поліпшення функції печінки. Будь-який тип зниження кровотоку у селезінці призводить до підвищеного ризику тромбозу у системі ворітної вени.

Ключові слова: портальна гіпертензія, варикозна кровотеча, спленектомія, лігування селезінкової артерії.

Introduction. In the coagulation system of patients with liver cirrhosis, procoagulant and anticoagulant factors are in a dangerous balance, they are too complex and delicate to find a balance between bleeding or thrombosis [1; 2]. Disturbances in the balance between procoagulation and anticoagulation factors can be caused by splenectomy, infection, acute renal failure, etc. [3]. Portal vein thrombosis (PVT) is a common complication after splenectomy, which can negatively affect the prognosis of patients with liver cirrhosis [4]. Many factors are associated with the occurrence of postoperative PVT, such as hemodynamic changes, splenomegaly, splenectomy, coagulation and anticoagulation disorders, liver cirrhosis, platelet count, D-dimer level, infection, inflammation, and other factors [5]. It is believed that prolonged prothrombin time is an independent factor in the occurrence of postoperative PVT [6]. An enlarged spleen secretes related factors that inhibit the release of platelets from the bone marrow and decrease thrombopoietin in cirrhosis [7]. After splenectomy, suppression and clearance of platelets disappear, megakaryocytes proliferate in the bone marrow, causing a short-term platelet spike, and PVT may be associated with a rapid increase in platelet counts after surgery [8]. Thrombocytosis is considered an independent risk factor for portal vein thrombosis after splenectomy [9]. Partial splenic artery embolization has been used to increase platelet counts and has been combined concurrently or heterochronously with retrograde transvenous obliteration with balloon occlusion (B-RTO) resulting in improved liver function [10]. All this indicates the difficulty of assessing and the possibility of correcting hemodynamic disorders in the portal system aimed at improving the functional capabilities of the liver in patients with decompensated portal hypertension (PH).

The aim. The present study was performed to determine the effect of splenectomy or splenic artery ligation in patients with splenomegaly and hypersplenism on portal hemodynamics and liver function in patients with decompensated portal hypertension.

Materials and methods. Hemodynamic features of the portal system were studied in 37 patients with decompensated PH who were operated on for variceal upper gastrointestinal bleeding, hypersplenism, and splenomegaly. The study was conducted at Kyiv Emergency Hospital from 2019–2024. Based on retrospectively analyzed clinical material of treatment of 46 operated patients from 2010 to 2015, an algorithm for surgical reduction of splenic blood flow was formed. In 20 patients included in the first group, esophagogastric devascularization, transection of the esophagus and splenectomy were performed, and in 17 patients in the second group, esophagogastric devascularization and transection of the esophagus were supplemented with splenic artery ligation to correct hypersplenism.

Among the patients of the first group, there were 6 (30%) women and 14 (70%) men. The age of patients among women ranged from 30 to 68 years, an average of 45.33±13.32 years ($p<0.1$), among men from 29 to 65 years, an average of 49.15±10.71 years ($p<0.1$). In the second group there were 6 (35.3%) women and 11 (64.7%) men. The age of patients among women ranged from 29 to 65 years, an average of 47.00±11.71 years ($p<0.1$), among men from 32 to 52 years, an average of 47.45±9.26 years ($p<0.1$).

Patients underwent Doppler and contrast-enhanced computed tomography (CT) to assess splenic volume, portal hemodynamics, collateral screening, and splanchnic vein thrombosis before and 7–14 days after surgery. Endoscopy of the upper parts of the gastrointestinal tract to assess the severity of esophageal varices was performed before and within 1 month after surgery. The severity of PH was assessed according to the Child-Pugh scale. CT in a patient with sinistral portal hypertension revealed isolated gastric varices of the first type according to the Sarin classification with collaterals in the form of posterior and short gastric veins.

During endoscopic examination, varicose veins of the third degree were detected in 11 (55%) patients of the first group and 6 (35.3%) of the second group. In addition, the stigmata of probable recurrence as red spots, which were observed after the bleeding stopped, determined indications for surgical treatment.

Doppler ultrasonography imaging was performed to determine blood flow in the portal vein (ml/min) with calculation of velocity (cm/s) and cross-sectional area (cm^2). The cross-sectional area of the portal vein was calculated using the formula: cross-sectional area of the portal vein = π (R2/4) (where R is the diameter of the portal vein). The "congestion index" is used to mean the ratio between the cross-sectional area (cm^2) and the blood flow velocity (cm/sec) of the portal vein, as determined by a duplex Doppler system. There was a statistically significant difference between the congestion indices from the normal subject group and indices obtained from patients with chronic hepatitis, cirrhosis, and idiopathic portal hypertension.

The Child Pugh scale made it possible to assess the severity of the patient's condition, carry out preoperative preparation corresponding to the indicators of the scale, and predict the peculiarities of the postoperative period course.

Among the patients of the first group, according to the Child Pugh scale, 18 (90%) patients were classified as B-class, 2 (10%) C patients, and in the second group, 16 (94.1%) had B class and 1 patient C class (5.9%).

Hemostasis was performed medically and using an interventional method by ligating varices n=3 and installing a Sengstaken-Blakemore probe n=7 in the first group, and in n=2 and n=5 in the second, respectively.

Indications for ligation of the splenic artery were the size of the spleen, which did not exceed 20 cm, and the number of platelets was > 50x10^9. If the size of the spleen was >20 cm in length and/or thrombocytosis <50x10^9, splenectomy was performed.

Intraoperative blood loss was minimized by using a laparoscopic surgical approach using the Covidien ValleyLab LigaSure© electroligation tool. In the postoperative period, no patient received transfusion of blood components.

Blood tests were performed on a LabAnalyt 3000 Plus hematology analyzer.

Ultrasound examination was carried out using the ALOKA© SSD 5000 –Ultrasound device.

The endoscopic examination was performed on the Stryker© endoscopic stand.

The study did not include patients who did not give written consent to participate in the study, patients with non-compliance, cases of portal hypertension caused by

malignant liver neoplasms and patients with a history of hematological diseases.

The principles of the Code of ethics of the World Medical Association (Declaration of Helsinki) were followed during the research. Conducting an ethical commission and observing ethical norms was carried out as part of the scientific work of the Department of Surgery, Faculty of Dentistry, Bogomolets National Medical University "Application of the latest technologies in emergency abdominal surgery" 2020–2024. State registration No. 0116U000121. The research materials were checked by the ethical commission of the Bogomolets National Medical University with expert opinion No. 140 dated 12/21/2020.

Processing of clinical indicators was carried out in the statistical package MedStat v.5.2, Statistica 10 and Microsoft Excel 2016. Sample characteristics were evaluated using typical descriptive statistics. Frequency and percentage were used to describe categorical variables. Average and standard deviation (or medians and ranges where appropriate) were used to describe continuous variables. Checking the distribution of data for normality was implemented using the Shapiro-Wilk test. Hypotheses were tested using the following criteria: Student, Wilcoxon with a two-sided critical area. $p<0.05$ with a research power of 80% was considered a statistically significant result.

Results. Preoperative preparation in the first and second groups was aimed at improving the indicators of patients who belonged to class C according to the criteria of the Child-Pugh scale, which made it possible to operate on these patients with Child-Pugh criteria corresponding to class B.

Preoperative comparison of the two operational groups. There was no significant difference between first and second groups of the preoperative database including age, gender, Child-Pugh's score and biochemical tests ($p>0.05$). The two groups were well balanced in the distribution of prognostic factors and other characteristics.

The time of surgical intervention in the first group was 284.5±19.44 min. ($p>0.1$), and in the second 210.9±24.51 min. ($p<0.1$).

In the first group, intraoperative blood loss was 687.3 ±169.3 ml ($p<0.05$), and the volume of hemotransfusion depended on the possibilities of blood reinfusion, including blood deposited in the spleen. In the second group, intraoperative blood loss was 385.6 ±85.3 ml ($p<0,05$).

A restrictive strategy of hemotransfusion support was observed – transfusion of erythrocytes was carried out at hemoglobin < 70 g/l. Thus, in the first group, hemotransfusion of two doses of erythrocytes was performed for 4 patients, and one – for 3, in the second hemotransfusion of erythrocyte mass was performed for 5 patients who had a preoperative decrease in hemoglobin within 80 g/l and intraoperative blood loss exceeding 1000 ml.

In the first group of patients, esophagogastric devascularization was performed laparoscopically, and esophageal transection and splenectomy were laparoscopically assisted. In the second group, esophagogastric devascularization was performed by open method in 5 and laparoscopically assisted method in 12, combining them with splenic artery ligation. In the postoperative period, starting from the first day, in order to prevent thromboembolic complications, anticoagulant therapy with low molecular weight heparins was performed.

Table 1 presents data on changes in hematological parameters and liver function after splenic artery ligation and splenectomy.

In the patients of the first group, the number of leukocytes and platelets was significantly higher 2 weeks after splenectomy compared to the preoperative values and indicators of the patients of the second group. None of the 20 patients had encephalopathy after splenectomy. Thus, none of them had deterioration of liver function and patients in Child-Pugh class B had improvement. In three patients who bordered on Child-Pugh class C and who had 9 points, the mean concentration of total bilirubin decreased from 36.8 (CI 95% 24.5–47.8) to 29.3 (CI 95% 23.2–37.7) μmol/L, albumin increased from 21 (CI 95% 19–23) to 31 (CI 95% 29–32) g/L, prothrombin time decreased from 2.16±0.98 sec ($p<0.005$) to 1.98±0.87 sec ($p<0.05$), and Child-Pugh score decreased from 9 (CI 95% 8–9) to 6 (CI 95% 6–7).

Two patients of the second group had thromboembolic complications, which were the cause of death, in the form of thrombosis of the superior mesenteric vein and thrombosis of the portal vein, which occurred on the 21st and 28th day after the operation in the presence of COVID-19 pneumonia.

There is no significant difference between the number of leukocytes in the patients of the first and second groups, in the same time platelets count was higher 2 weeks after splenic artery ligation compared to the preoperative values, but lower compared to the patients of the first group (Table 1). Improvement of total bilirubin and albumin concentration was observed in patients of the second group and slightly in patients of the first group. The encephalopathy observed in 3 patients did not significantly decrease. Thus, no deterioration of liver function was observed. The average concentration of total bilirubin decreased from 34 (CI 95% 23.2–46) to 27.4 (CI 95% 21–32) μmol/L, albumin increased from 22 (19–24) to 30 (28–32) g/L, prothrombin time increased from 2.17±0.39 to 2.07±0.37 ($p<0.005$), and Child-Pugh score decreased to 6 (6–7) in the second group.

Hemodynamic changes in the portal vein are shown in fig.1–4. Although portal vein velocity did not change significantly after splenectomy, blood flow, cross-sectional area, and congestion index decreased. The initial mean values of the diameter of the portal vein in the SE group were 15 (95% CI 14.5–16.5) mm and did not differ between the initial values of the SAL group 15 (95% CI 14–16) mm ($p=0.897$). A significant difference was found between the indicators before SE and after SE 13 (95% CI 12–14) mm ($p=0.0002$), indicators before SAL and after SAL 13 (95% CI 13–14) mm ($p=0.0026$). No significant difference was found between the indicators after SE and after SAL ($p=0.628$), which indicates a ecrease in the size of the portal vein with any type of reduction of splenic blood flow.

The average values of the minute volume of blood flow in the portal vein in the SE group were 1025 (95% CI 990–1050) ml/min, in the SAL group 1010 (95% CI 1000–1080) ml/min and did not differ significantly among themselves ($p=0.988$). A significant difference was found between the parameters before SE and after SE 940 (95% CI 895–980) ml/min ($p=0.0001$), indicators before SAL and after SAL 905 (95% CI 875–930) ml/min ($p=0.0001$).

Table 1

Changes in hematological indicators and liver function after splenic artery ligation and splenectomy

Indicator \ Approach	Splenectomy		Splenic artery ligation	
	Before surgery Me	2 weeks after surgery	Before surgery	2 weeks after surgery
Leukocytes Me (CI 95%) (10^9/L)	5.8 (5.1–8.2)	8.9 (6.2–10.1)	5.6 (4.4–8.0)	8 (7.5–8.2)
Platelets (10^9/L) p<0.05	43.12±9.49	974.1±129.9	59.21±24.77	474.1±84.7
Total bilirubin Me (CI 95%) (μmol/L)	36.8 (24.5–47.8)	29.3 (23.2–37.7)	34.7 (23.2–46)	27.4 (21–32)
Serum albumin Me (CI 95%) (g/L)	21 (19–23)	31 (29–32)	22 (19–24)	30 (28–32)
PT INR p<0,05	2.16±0.98	1.98±0.87	2.17±0.39	2.07±0.37
Ascites	yes / no	yes / no	yes / no	yes / no
	16 / 4	6 / 14	14 / 3	4 / 13
Child-Pugh (scores)	9 (8–9)	6 (6–7)	8 (7–8)	6 (6–7)

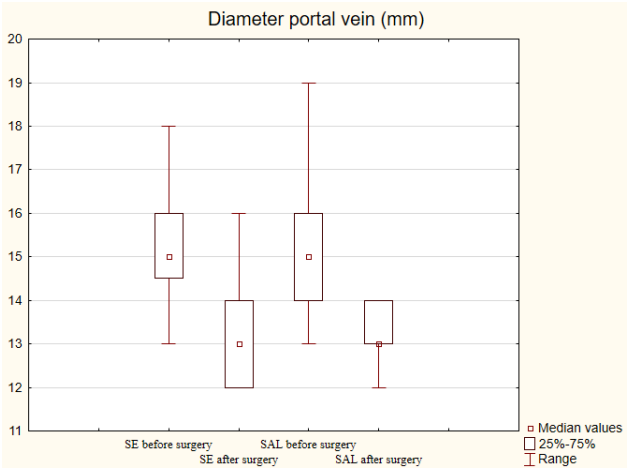

Fig. 1. Diameter portal vein in both groups

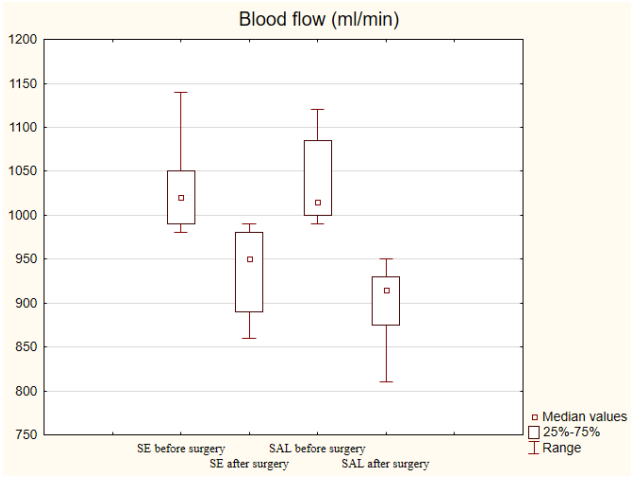

Fig. 2. Blood flow in both groups

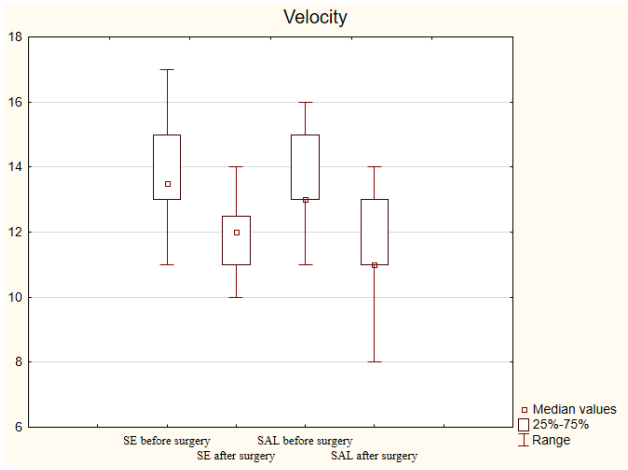

Fig. 3. Velocity in both groups

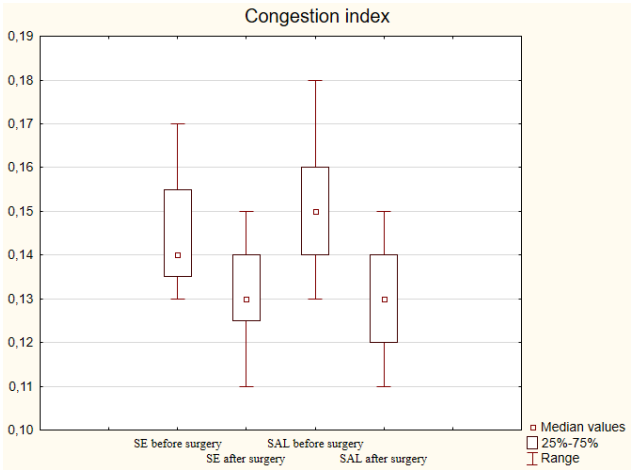

Fig. 4. Congestion index in both groups

There was no significant difference between the indicators after SE and after SAL (p=0.533), which indicates a decrease in the minute volume of blood flow in the portal vein with any type of reduction of splenic blood flow.

The average values of the linear velocity of blood flow in the portal vein in the SE group were 13.5 (95% CI 13–15) cm/sec, in the SAL group 13 (95% CI 13–15) cm/sec and did not reveal a significant difference between them (p=0.542). The difference between indicators before SE and after SE was 12 (95% CI 11–12.5) cm/sec (p=0.0002), indicators before SAL and after SAL 11.5 (95% CI 11–13) cm/ sec (p=0.0004). There was no significant difference

between the indicators after SE and after SAL (p=0.229). However, they indicate a decrease in the linear velocity of blood flow in the portal vein both in SE and in PSA.

After calculating the "congestion index" and summarizing the obtained data, the mean values in the SE group were 0.14 (95% CI 0.135–0.155) and were not statistically different between the SAL group indicators 0.15 (95% CI 0.14–0.16), (p=0.289.). The difference between the indicators before SE and after SE was found to be 0.13 (95% CI 0.125–0.14), (p=0.0004); indicators before SAL and after SAL 0.13 (95% CI 0.125–0.14), (p=0.0004). No significant difference was found between the indicators after SE and after SAL (p=0.950).

Thus, hemodynamic changes in patients with PH, which were observed after surgical interventions aimed at the correction of both portal hemodynamics and hematological parameters, contributed to the improvement of the course of the disease, and two fatal cases (11.8%), which, despite anticoagulation therapy, occurred in patients of the second group were associated with accompanying viral pathology.

Discussion. Splenectomy is considered to be one of the main factors contributing to the high rate of postoperative venous thrombosis [11]. Based on the specific pathophysiological characteristics of slow portal vein blood flow velocity caused by sinusoidal portal hypertension, the velocity becomes even lower after splenectomy. In addition, the number of platelets increases sharply, which due to thrombocytosis, which improves the coagulation function, can lead to their agglutination and thrombosis. As the pressure in the portal vein and the size of the spleen increase, its function to deposit and destroy blood elements by the spleen itself increases [12]. Platelets are not only crucial for the blood clotting process, but also accelerate liver regeneration in chronic liver diseases such as fibrosis [13].

Patients with cirrhosis and portal hypertension have been reported to have improved platelet counts and platelet aggregation function after laparoscopic splenectomy with azygoportal dissection compared with patients without surgery [14].

Splenectomy not only lowers pressure in PH, but also has a positive effect on liver metabolism. A two-year prospective study proved that when liver function indicators such as albumin, total bilirubin, and international normalized ratio are improved, the degree of liver fibrosis also decreases [15; 16].

Patients who underwent total splenectomy showed a significant increase in total lymphocytes, including B lymphocytes, total T lymphocytes, and their subsets, resulting in improved immune function [17].

It is also believed that the spleen plays a central role in the regulation of the immune system, a metabolic asset involved in endocrine function, and infectious complications after splenectomy lead to death in 50% [18; 19].

A meta-analysis showed that low-molecular-weight heparin in combination with low-molecular-weight dextran is the most effective agent for the prevention of portal vein thrombosis after splenectomy in patients with liver cirrhosis [20].

Thus, the studies conducted regarding the function of the spleen and its absence in patients with PH have partial contradictions, which necessitates further study of this issue.

Conclusions. In patients with PH, splenectomy changes hemodynamics in the portal system, and splenic artery ligation, like splenectomy, increases platelet levels. Reduction of intrahepatic blood flow due to elimination of blood flow in the spleen after splenectomy leads to a decrease in intrahepatic vascular resistance and promotes splanchnic hemodynamics and improves liver function. Ligation of the splenic artery helps to increase the number of platelets and, like splenectomy, improves liver function. Prescribing anticoagulants in the form of low-molecular-weight heparin is the prevention of thromboembolic complications in patients after operations, which are accompanied by thrombocytosis and threaten thromboembolic complications. Concomitant diseases, regardless of anticoagulant therapy, increase the risk of thromboembolic complications.

Conflict of interest. Authors have no conflict of interest to declare.

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Надійшла до редакції 23.02.2024 р.
Прийнята до друку 28.11.2024 р.
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