

Analysis of Variceal Bleeding Recurrence Rate After Various Interventions in Extrahepatic Portal Hypertension

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Abstract

Purpose: To conduct a comparative analysis of the incidence rate and period of gastric and esophageal varices bleeding recurrence associated with extrahepatic portal hypertension after different interventions.

Materials and Methods: The study included 131 patients with various forms of extrahepatic portal hypertension; who underwent operative therapy of extrahepatic portal hypertension in the Republican Specialized Scientific and Practical Medical Center of Surgery named after academic V. Vakhidov (RSSPMCS) for the period from 2006 to 2020. Most patients were adolescents (41.2%) and young age (45.0%). Total gastroesophageal basin disconnection was performed in 57 (43.5%) patients, portosystemic shunting - in 51 (38.9%) patients, and endoscopic interventions - in 23 (17.6%).

Results: The comparative incidence rate of bleeding recurrence showed that the most effective intervention is portosystemic shunting. Significantly low efficiency is observed after endoscopic interventions, in which the incidence of hemorrhagic syndrome is 65.2% on average after 13.5 ± 2.9 months. While after a total disconnection of the gastroesophageal collector, a relapse-free course was noted in 35.1% ($p = 0.014$) of cases lasting 25.9 ± 4.4 months ($p < 0.05$), which in terms of timing did not differ significantly from relapses after portosystemic shunting - 41.4 ± 8.2 months, but significantly lower in the occurrence of variceal bleeding during decompression operations - 17.6% ($p < 0.001$).

Conclusion: The most effective surgical intervention is portosystemic shunting with a bleeding recurrence freedom rate in 82.4% ($p = 0.014$) of patients. The most long-term recurrence period is within 41.4 months ($p < 0.05$), and with a 5-year persistent remission in 75.0% of patients. After disconnection operations, bleeding recurrence was noted in 35.1% of patients; the recurrence period averaged 19.6 months.

Keywords: Extrahepatic Portal Hypertension; Operative Treatment; Gastric and Esophageal Varices Bleeding; Immediate and Long-Term Results

Introduction

Extrahepatic portal hypertension (EPH) is defined as a syndrome of portal hypertension (PH) that is not associated with non-

cirrhotic and non-oncological lesions of the hepatic parenchyma while including a sufficiently wide range of diseases of various eti-

ologies and pathogenesis affecting the vascular system of the liver at different levels: from microvasculature to the great vessels [1-3]. At the same time, up to 30% of the portal vein (PV) thrombosis is particularly related to extrahepatic thrombosis, which is the cause of gastric and esophageal varices (GEV) bleeding in 25 - 30% of cases, and in childhood up to 68-84% of cases [3-6].

There has been a significant improvement in the results of surgical treatment of extrahepatic portal hypertension in recent years, which is facilitated by the selection of patients and, accordingly, the choice of the most optimal method for correcting extrahepatic portal hypertension. Endoscopic ligation (EL) and endoscopic sclerotherapy (ES) should be used as the main methods of primary and secondary prevention of gastric and esophageal varices bleeding. Ineffectiveness of endoscopic hemostasis (8 - 12%), according to most authors, is an indication for operative therapy [3,5,6]. Porto-systemic shunting (PSS), splenorenal or mesentericocaval, is the most effective among the surgical treatment strategies. It is effective in 84 - 100% of cases and in the absence of the risk of thrombosis, it can totally save the patient from PH and its complications [6-8].

Purpose of the Study

To conduct a comparative analysis of the rate and period of bleeding recurrence from gastric and esophageal varices on the background of extrahepatic portal hypertension after different interventions.

Materials and Methods

The study included 131 patients with different forms of extrahepatic portal hypertension who underwent various options of surgical preventive measures for bleeding recurrence from gastric and esophageal varices at the Republican Specialized Scientific and Practical Medical Center of Surgery named after academic V. Vakhidov for the period from 2006 to 2020. There were 58.0% of male and 42.0% of female patients. Mostly, patients of adolescence (41.2%) and young age (45.0%) prevailed. Patients of mature and elderly age made up only 13.7% in total.

History taking showed that acquired thrombophilia occurred in 4 (3.0%) patients of young age with confirmed hematological status was - an increased level of coagulation factor VIII. Hereditary thrombophilia associated with a mutation of the methylene-

tetrahydrofolate reductase gene and antithrombin deficiency was observed in two (1.5%) and one (0.76%) cases, respectively. The progression of extrahepatic portal hypertension associated with the pathological course of pregnancy was observed in 3 (2.3%) patients, and in 5 (3.8%) patients, it was associated with long-term use of contraceptive drugs and changes in the endocrine profile of the body. Most of the adolescent (42/32.0%) and young (31/23.6%) patients with a history of extrahepatic portal hypertension had previous umbilical sepsis-associated in most cases with exchange transfusions in the neonatal period and improper management of the umbilical cord.

Concomitant Crohn's disease (3/2.3%) and ulcerative colitis (2/1.5%), which could cause extrahepatic portal hypertension, were observed in 5 (3.8%) patients with extrahepatic portal hypertension. Two patients (1.5%) were on specific treatment for tuberculous mesenteric disease for a long time. In 19 (14.5%) patients, extrahepatic portal hypertension was interpreted on the background of idiopathic liver fibrosis and in the remaining cases (10/7.6%) as a cryptogenic etiology.

Isolated "portal vein thrombosis" and "splenoportal bed thrombosis" were diagnosed in 49 and 50 (38.1%) patients, respectively. "Thrombosis of the portal system" and isolated "thrombosis of the splenic vein" was observed in 5 (3.8%) and 7 (5.3%), respectively. In other cases, there was a "cavernous transformation of the portal vein".

There were 24 (18.3%) patients with total gastric and esophageal varices; the extension of the process in the area of gastric cardia was observed in 94 (71.8%) patients. At the same time, patients with the maximum varix dilatation predominated.

The most common complaints during planned hospitalization of patients with extrahepatic portal hypertension in the hospital were: general weakness, nosebleeds, pain, and heaviness in the left hypochondrium. An enlarged spleen was observed according to the ultrasound examination data in 119 (90.8%) patients.

All patients were admitted to the Republican Specialized Scientific and Practical Medical Center of Surgery named after academic V. Vakhidov for operative therapy. The allocation of patients by the nature of the surgical intervention showed that total disconnection of the gastroesophageal collector (TDGEC) was performed in 57

(43.5%) patients, portosystemic shunting - in 51 (38.9%) patients and endoscopic surgery (ES) - in 23 (17.6%). At the same time, patients with "portal thrombosis" underwent only total disconnection of the gastroesophageal collector (5/3.8%).

Most of portosystemic shunting was performed in patients with "portal vein thrombosis" and its "cavernous transformation" - 36 (27.5%) and 11 (8.4%), respectively. In contrast, 35 (26.7%) patients with thrombosis of the "splenoportal bed" underwent total disconnection of the gastroesophageal collector, and only 3 (2.3%) patients underwent portosystemic shunting.

Endoscopic sclerotherapy was performed as an independent aid in 23 (17.6%) cases in the absence of indications for one of the types of open surgeries in 18 (13.7%) cases and in 5 (3.8%) cases when the patient refused surgery. Endoscopic sclerotherapy was performed using sclerotherapy techniques for esophageal varices in 7 and ligation in 16 patients.

Variants of PSS were: the imposition of distal splenorenal anastomosis (DSRA), which was performed in 16 (12.2%) patients, splenosuprarenal anastomosis (SSRA) - in 14 (10.7%), laterolateral splenorenal anastomosis (LLSRA) - in 5 (3.8%); mesocaval shunt with H-insert (MCS with H-insert) - in 7 (5.3%); mesorenal shunt with H-insert (MRS with H-insert) - in 3 (2.3%); proximal splenorenal anastomosis (PSRA) - in 2 (1.5%); H-shaped splenorenal anastomosis (H-shaped SRA) - in 4 (3.1%). Most DSRA (11/8.4%) was performed in portal vein thrombosis.

The research materials were statistically processed using parametric and nonparametric analysis methods in Microsoft Office

Excel 2016 spreadsheets and using the STATISTICA 13.3 program (developed by StatSoft.Inc).

Quantitative indicants were assessed for compliance with the normal distribution (Kolmogorov-Smirnov test).

The student's t-test was calculated when comparing the mean values in normally distributed sets of quantitative data. The obtained values of the student's t-test were evaluated by comparison with the critical values. Differences in indicants were considered statistically significant at a significance level of $p < 0.05$.

Comparison of nominal data was carried out using the Pearson χ^2 test, which allowed us to assess the significance of differences between the actual quantity of outcomes or qualitative characteristics of the sample falling into each category and the theoretical quantity that can be expected in the studied groups if the null hypothesis is valid. Freedom from bleeding recurrence was assessed using the Kaplan-Meier method.

Results and Discussion

The analysis of the structure and cause-and-effect relations of the bleeding recurrence development after different interventions is detailed in table 1-3.

So, after total disconnection of the gastroesophageal collector (Table 1), bleeding recurrence was noted in 35.1% of patients. What is more, this complication was typical for any of the nosological forms of extrahepatic portal hypertension, and the recurrence period varied within 3 - 92 months, on average 19.6.

Cause of EPH	Amount	Recurrence		Recurrence period after surgery (months)				Without bleeding	
		abs.	%	Min-max	M	δ	m	abs.	%
Portal system thrombosis	5	2	40,0%	16-31	23,5	10,6	7,5	3	60,0%
Portal vein thrombosis	8	4	50,0%	14-92	42,5	34,2	17,1	4	50,0%
Thrombosis of the splenoportal bed	35	10	28,6%	3-57	22,7	15,3	4,8	25	71,4%
Cavernous transformation of PV	3	2	66,7%	11-25	18,0	9,9	7,0	1	33,3%
Splenic vein thrombosis	6	2	33,3%	15-23	19,0	5,7	4,0	4	66,7%
Total	57	20	35,1%	3-92	25,9	19,6	4,4	37	64,9%

Table 1: Bleeding recurrence rate after TDGEC in EPH.

Recurrence of esophageal bleeding after portosystemic shunting (Table 2) was observed in 17.6% of patients, with the highest relapse rate (66.7%) in patients who underwent portosystemic

shunting on the background of portal and splenic vein thrombosis. The average rate of recurrence onset varied within 24.6 months.

Cause of EPH	Amount	Recurrence		Recurrence period after surgery (months)				Without bleeding	
		abs.	%	Min-max	M	δ	m	abs.	%
Portal system thrombosis	0	0	0,0%	-	-	-	-	0	0
Portal vein thrombosis	36	6	16,7%	11-88	47,0	28,5	11,6	30	36
Thrombosis of the splenoportal bed	3	2	66,7%	18-47	32,5	20,5	14,5	1	3
Cavernous transformation of PV	11	1	9,1%	33	33,0	-	-	10	11
Splenic vein thrombosis	1	0	0,0%	-	-	-	-	1	1
Total	51	9	17,6%	3-92	41,4	24,6	8,2	42	51

Table 2: Bleeding recurrence rate after PSS in EPH.

The highest recurrence rate (Table 3) was observed in patients after endoscopic sclerotherapy (65.2%), practically regardless of the cause of extrahepatic portal hypertension. The average devel-

opment time of this complication was 13.5 months, which once again makes it necessary to focus the attention of clinicians on the fact that this aid is mainly effective at the stages of performing more radical methods of gastric and esophageal varices eradication.

Cause of EPH	Amount	Recurrence		Recurrence period after surgery (months)				Without bleeding	
		abs.	%	Min-max	M	δ	m	abs.	%
Portal system thrombosis	0	0	0,0%	-	-	-	-	0	0
Portal vein thrombosis	5	3	60,0%	6-12	8,7	3,1	1,8	2	5
Thrombosis of the splenoportal bed	12	8	66,7%	3-42	17,1	14,6	5,2	4	12
Cavernous transformation of PV	6	4	66,7%	6-15	10,0	3,9	2,0	2	6
Splenic vein thrombosis	0	0	0,0%	-	-	-	-	0	0
Total	23	15	65,2%	3-42	13,5	11,3	2,9	8	23

Table 3: Bleeding recurrence rate after EV in EPH.

A more informative presentation of assessing the effectiveness of different techniques is reflected in the diagrams in figure 1-3.

The initial values were: the number of observations - 131, recurrence rate - 44 (33.59%), $\chi^2 = 33.85937$, $df = 2$, $p < 0.001$.

As can be seen from figure 2, the indicant of freedom from esophageal bleeding recurrence regardless of the causes of extrahe-

patic portal hypertension has maximum value after portosystemic shunting and the best values at all stages of follow-up and with a 5-year persistent remission in 75.0% of patients. Cumulative proportion of bleeding recurrence in patients with extrahepatic portal hypertension associated with portal vein thrombosis (number of observations - 49, recurrence - 13 (26.53%), recurrence-free - 36 (73.47%), $\chi^2 = 15.34263$, $df = 2$, $p = 0.00047$) (Figure 3) or its cav-

Figure 1: Indicant of freedom from bleeding recurrence from GEV in EPH after different interventions.

Figure 2: Indicant of freedom from bleeding recurrence from GEV in EPH on the background of portal vein thrombosis after different interventions.

ernous transformation (number of observations - 20, recurrence - 7 (35.00%), recurrence-free - 13 (65.00%), $\chi^2 = 8.721781$, $df = 2$, $p = 0.01277$ (Figure 4) show the effectiveness of portosystemic shunting in comparison with total disconnection of the gastro-esophageal collector and endoscopic sclerotherapy.

Figure 3: Indicant of freedom from bleeding recurrence from GEV in EPH on the background of cavernous transformation of the portal vein after different interventions.

Despite satisfactory indicants of the effectiveness of portosystemic shunting in the above nosological forms, the rate of freedom from bleeding recurrence from gastric and esophageal varices in thrombosis of the splenoportal bed (number of observations - 50, recurrence - 20 (40.00%), recurrence-free - 30 (60.00%), $\chi^2 = 6.504186$, $df = 2$; $p = 0.03871$) (Figure 4) after this type of intervention is the worst, with 50% bleeding recurrence during the first year after surgery.

Figure 4: Indicant of bleeding recurrence freedom from GEV in EPH on the background of splenoportal thrombosis after different interventions.

Summing up when comparing the incidence of bleeding recurrence from gastric and esophageal varices on the background of extrahepatic portal hypertension with different prevention measures, which is reflected in the diagrams in figure 5 and 6, we can conclude that the most effective intervention is portosystemic shunting with freedom from bleeding recurrence indicant in 82.4% ($\chi^2 = 6.045$, Df = 1, p = 0.014) of patients and the most long-term recurrence period within 41.4 months (t = 2.35; p < 0.05).

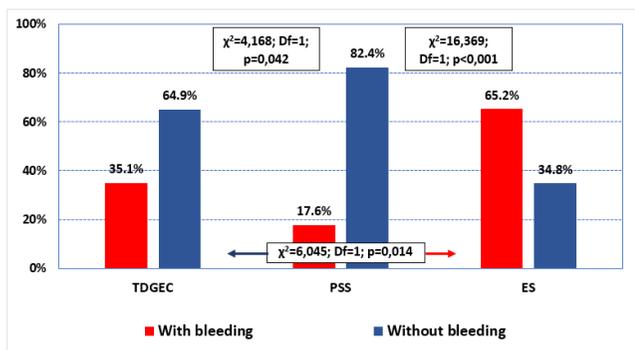


Figure 5: Comparative rate of bleeding recurrence from GEV on the background of EPH in the course of different preventive measures.

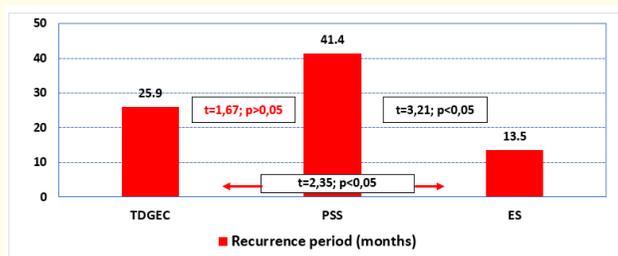


Figure 6: Comparative rate of bleeding recurrence from GEV on the background of EPH in the course of different prevention measures.

Conclusion

The comparative incidence of bleeding recurrence from gastric and esophageal varices on the background of extrahepatic portal hypertension showed a significantly low efficiency of endoscopic sclerotherapy, in which repeated episodes of hemorrhagic

syndrome developed in 65.2% of patients on average after 13.5 ± 2.9 months. total disconnection of the gastroesophageal collector, in turn, provided delaying time to recurrence lasting 25.9 ± 4.4 months (t = 2.35, p < 0.05) in 35.1% of cases ($\chi^2 = 6.045$, Df = 1, p = 0.014), which in terms of timing did not differ significantly from recurrences after portosystemic shunting - 41.4 ± 8.2 months (TDGEC: t = 1.67, p > 0.05 and ES: t = 3.21; p < 0.05), but significantly lower in occurrence of this complication during decompressive surgeries - 17.6% (TDGEC: $\chi^2 = 4.168$, Df = 1, p = 0.042 and ES: $\chi^2 = 16.369$, Df = 1, p < 0.001).

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