



Efficacy of Endoscopic Interventions in Prevention of Gastroesophageal Bleeding in Patients with Liver Cirrhosis

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ABSTRACT: To analyze the survival of patients with liver cirrhosis, and to assess the effectiveness of endoscopic interventions in the prevention of portal genesis bleedings. To evaluate the efficacy of endoscopic interventions, our study included 449 liver cirrhotic patients with portal hypertension in the period from 1996 to 2015, admitted with bleeding from variceal bleedings or the threat of its recurrence. All patients were divided into 2 groups of the study. The main group included 239 patients treated between 2008 and 2015 in the control group - 210 patients in the period from 1996 to 2007. The analysis showed that the percentage of patients without recurrence of variceal bleeding when performing only endoscopic interventions was 27% (33 patients) in the control group and 54.2% (64) in the main group. With the phased tactics of portosystemic shunt performance after endoscopic interventions this figure amounted to 32.4% (45) and 109 (61.6%). In the structure of mortality of patients without cirrhosis in the long-term period (81 patients) with endoscopic interventions recurrence of bleeding were observed in 40.7% (33) cases in the control group and 68.1% (64 of 94) in the main group. In turn, when combined endoscopy and portosystemic shunting in the structure of the patients, without counting deaths from progressive liver cirrhosis, the proportion of absence of recurrence was 45.9% (in 45 of 98 patients) and 71.2% (in 102 out of 153 tracked in the remote period excluding deaths from cirrhosis). In the group of patients that do not carry out any endoscopic intervention and the patients received only conservative therapy only in 3 (10.7%) cases it was possible to avoid recurrence of bleeding, which determines the therapeutic ineffectiveness isolated attempts to reduce the risk of recurrence of hemorrhagic syndrome. Modern possibilities of endoscopic technologies have significantly improved the results of treatment and prevention of varicose bleeding or the threat of its recurrence, and the commitment to the phased tactics, with a combination of minimally invasive and traditional decompressive surgery, allowed to increase the survival rates of patients with 80% to 88% - up to 1 year and from 42% to 64% - to 3 years of follow-up.

Author Keywords: Liver Cirrhosis, Portal Hypertension Syndrome, Bleeding From Esophageal And Gastric Varices, Portosystemic Shunting, Endoscopic Ligation, Endoscopic Sclerotherapy.

INTRODUCTION

In modern hepatology chronic diffuse liver diseases are still relevant socio-epidemiological and clinical health problem [1, 2]. Bleeding from varicose veins of the esophagus and stomach (VVES) occurs in 80% of patients with liver cirrhosis (LC) with portal hypertension (PH) and is the most common and life-threatening complications [3, 4, 5]. The risk of its development during the first two years after the identification of the transformation of varicose veins of the esophagus is 30%, while the annual hemorrhagic syndrome develops in 12-15% of patients with VVES [6]. Mortality from the first bleeding ranges from 30 up to 60%, and within decompensated liver function reaches 76-100% [7,8].

The only radical treatment method is a liver transplantation, but in the absence of indications for transplantation, or because of impossibility of its performance within social and law issues, the main focus of the surgical treatment of these patients is the prevention of bleeding [9, 10].

Among the entire spectrum of surgical interventions, used in treatment and prevention of bleeding, minimally invasive technologies are of special interest. In this series, the most promising and competitive are the various techniques of endoscopic interventions on VVES. The development of these technologies brought them

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into the category of "first-line method", as in bleeding altitude so do in patients with high risk for its development [13, 14].

MATERIALS AND METHODS

The study included 449 patients with LC and PH admitted with bleeding from VVES or with the threat of its recurrence. Observation period was held from 1996 to 2015. All patients were divided into 2 groups of the study. The study group included 239 patients who received treatment between 2008 and 2015 in the control group - 210 patients which were observed between 1996 and 2007. In the main group endoscopic procedures have been used much more widely, both for prevention and for emergency indications. Endoscopic sclerotherapy (ES) was applied in 332 (73.9%) patients. Endoscopic ligation (EL) in 117 (26.1%) patients.

In the control group 102 patients were admitted in emergency order, and 119 - in the main group. Routinely hospitalized 108 and 120 patients, respectively. Age ranged from 19 to 66 years. The median age was 31.2 years. The men were 289 (64.3%), women - 160 (35.7%). During the emergency endoscopy esophageal varices was the source of bleeding in 81 (79.4%) patients in the control group and in 91 (76.5%) patients in the study group. Gastric cardia variceal bleeding (GC) was determined in 21 (20.6%) and 28 (23.5%) cases, respectively. In the early posthemorrhagic period 76 portosystemic shunt (PSS) were carried out in both groups, 19 - in the control group and 57 in the main. All patients had 1-2 sessions of endoscopic interventions with effective hemostasis and subsequent preoperative preparation to perform PSS in terms of 6 to 25 days after the bleeding.

The majority of patients had selective anastomosis performed - the distal splenorenal anastomosis (DSRA) - 49 (64.5%). Central anastomosis where performed in 27 (35.5%). In the group of central shunts performed splenosuprarenal anastomosis, laterolateral splenorenal, and H-shaped graft anastomosis with inserting of the internal jugular vein were performed.

RESULTS

In our observations, an effective endoscopic hemostasis was achieved in 76 (74.5%) patients in the control group, and in 84.9% (101 patients) in the study group, (Table. 1). In the GC bleeding group effective hemostasis elevated in 42.9% (9 of 21 patients) in the control group and 71.4% (20 of 28) in the main group. Operated 9 (42.9%) and 7 (25%) patients, respectively. Overall mortality was 7 (33.3%) and 4 (14.3%) cases.

In order to prevent bleeding after endoscopic hemostasis patients additionally had 1-3 sessions of EC or EL. The average re-ES sessions were carried out in 3-4 days. The progression of the various complications led to the transfer of 19 (18.6%) patients in the control group and 16 (13.4%) in the study group from functional class "B" to the class "C". The main reasons were growing of edematous-ascitic syndrome and progression of hepatocellular insufficiency. The class "C" progression of these complications observed in 14.7% (15 patients) and 6.7% (8), but it should be noted that by day 10-12 post-hemorrhagic rehabilitation from Class "C" in class "B" translated into 8 (7.8%) and 19 (16%) patients. In general, groups of improvement identified in 21.6% of patients in the control group and 33.6% in the study group, the deterioration to the 41.2% and 23.5% of cases, stable at 37.3% and 42.9% of patients.

In our observations Child-Pugh scale in the class "A" amounted to $6,2 \pm 0,1$ points, on a scale of MELD (Model for End-Stage Liver Disease) - $9,1 \pm 0,2$ points. In the class "B» - $8,4 \pm 0,3$ and $12,4 \pm 0,3$ points, respectively. In the class "C" - $11,6 \pm 0,3$ and $18,2 \pm 0,4$ points. Determination of the MELD was performed in 69 patients (from 2011), and was of fundamental importance in defining the terms for radical treatment. In our study, these figures reflect the condition of patients in period of development of hemorrhagic syndrome. Class "A" - 11 (15.9%) patients, class "B" - 36 (52.2%) and Class "C" - 22 (31.9%).

In 68.1% of cases the development of hemorrhagic syndrome in patients with LC is noted on the background of compensated and subcompensated disease with high short-term prognosis (3-month) survival ($P < 0,001$), defined on a scale of MELD, and corresponds to the class "A" Child -Pugh - 15,9% of patients with index $9,1 \pm 0,2$ points (MELD), class "B" - 52,2% ($12,4 \pm 0,3$ points). At maintaining the functionality reserve of the hepatocytes on the background of cirrhosis (MELD < 15 ; "A" and "B" Child-Pugh) leads to a favorable long-term prognosis without transplantation survival ($P < 0,001$), while the rate of mortality even at the first episode of bleeding in this group reaches 11,1%, followed by a multiple increase in this index at relapse.

Further the results of endoscopic interventions in the group of patients who were admitted in planned order were observed. In the control group 100% (108 cases) of interventions were carried out on the esophageal veins. In the main group in 6 of 120 (5%) cases routine vein ligation of the cardia of the stomach was performed. Bleeding after intervention noted in 6 (5.6%) of cases in the control group and in 2 (1.7%) in the study group.

Emergency surgery was required only in 2 (1.9%) and 1 (0.8%) patients. Mortality in the control group was 0.9%, and in the there was no lethal outcome in the main group.

Summing up the results of all interventions following can be noted. Endoscopic procedures efficiency was 82.4% (173 of 210 patients) in control group and 90% (215 of 239) in the main group. Emergency operation after endoscopic manipulation was performed in 23 (11%) and 15 (6.3%) patients. Overall mortality was 10.5% (22 patients) and 5% (12), respectively (Fig. 1).

Table 1. The efficacy of endoscopic hemostasis and mortality rate, depending on the Child- Pugh functional class

Index	Control				Main			
	Functional class			Total	Functional class			Total
	«A»	«B»	«C»		«A»	«B»	«C»	
Total amount	18	48	36	102	19	55	45	119
	17.6%	47.1%	35.3%	100%	16.0%	46.2%	37.8%	100%
Effective hemostasis	16	38	22	76	18	47	36	101
	88.9%	79.2%	61.1%	74.5%	94.7%	85.5%	80.0%	84.9%
Ineffective endoscopic hemostasis, or inability of intervention	2	10	14	26	1	8	9	18
	11.1%	20.8%	38.9%	25.5%	5.3%	14.5%	20.0%	15.1%
Mortality	0	4	10	14	0	3	6	9
	0.0%	8.3%	27.8%	13.7%	0.0%	5.5%	13.3%	7.6%
Dissection surgery's	2	10	9	21	1	8	5	14
	11.1%	20.8%	25.0%	20.6%	5.3%	14.5%	11.1%	11.8%
Mortality (after surgery)	0	2	5	7	0	1	2	3
	0.0%	20.0%	55.6%	33.3%	0.0%	12.5%	40.0%	21.4%
General mortality	0	6	15	21	0	4	8	12
	0.0%	12.5%	41.7%	20.6%	0.0%	7.3%	17.8%	10.1%

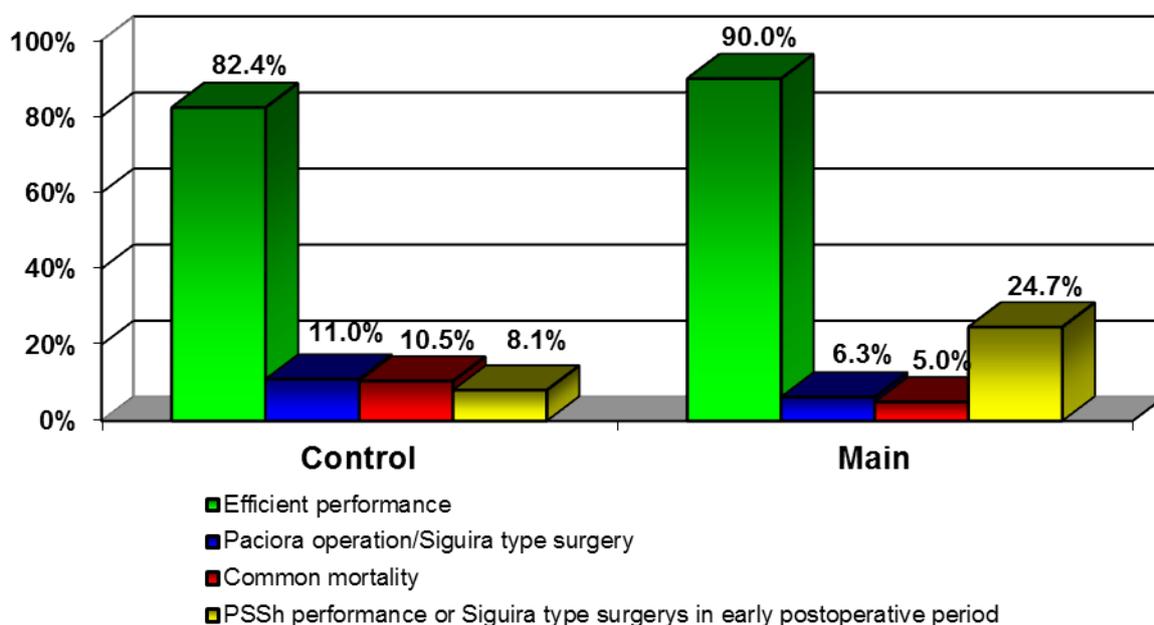


Figure 1. Short-term results of endoscopic interventions

It should be noted that in the study group good hemostatic effect and tactics undertaken by post-hemorrhagic rehabilitation allowed to expand a greater degree opportunities for the use of combined-stage tactics. After only three weeks after the hemorrhage episode with an effective endoscopic hemostasis performed PSS was performed in 17 (8.1%) patients in the control and 59 (24.7%) in the study group.

In the late period 319 patients were observed in both groups. Also, from the analysis of long-term results observation patients who were on a background of ineffective endoscopic hemostasis were performed various options for emergency uncoupling operations. In general 72 patients were excluded from the study.

The main parameter for evaluating long-term results was the analysis of the haemorrhage recurrence. In view of decompressive effect of performed PSS in some patients, they were not included in to the study. Within one month after discharge 10 (8.2%) of 122 patients from the main group and 5 (4.2%) patients in of 118 in the study group were admitted to different clinics (Fig. 2).

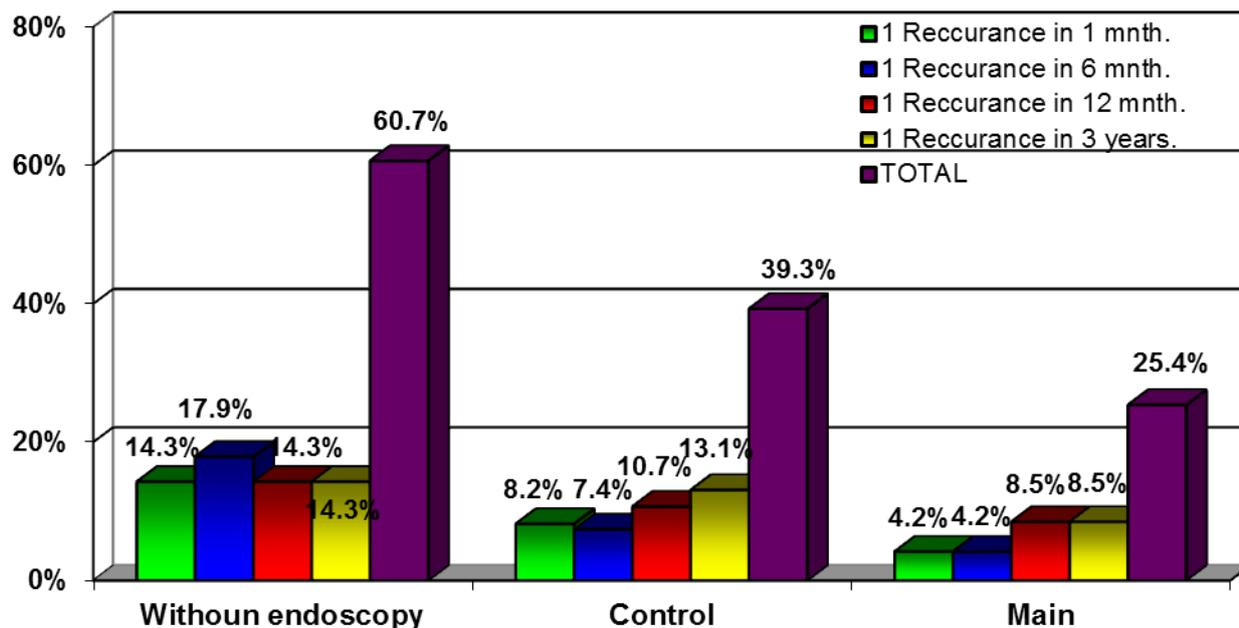


Figure 2. Frequency of rebleeding after endoscopic interventions

Analysis of patients with conservative, including a Blackmore-Segstaken tube hemostasis is of a special interest. Of these 28 patients, bleeding in the three-year period of observation developed in 17 (60.7%), including 13 (46.4%) in the periods up to a year after the initial episode.

Due to mortality in the remote period, patients were divided into those with LC progression and ones with recurrence of hemorrhagic syndrome. In the various periods of follow up because of increasing liver failure died 5 (4.1%) 15 (12.3%) in the control group and 3 (2.5%) 10 (8.5%) in the study group. Bleeding from 4 (3.3%) to 9 (7.4%) and 2 (1.7%) to 4 (3.4%), respectively. In general, in control group in the remote period of up to 3 years, 41 (33.6%) patients died due to increasing liver failure and 22 (18%) patients from hemorrhage. In the main group, the figures were lower and amounted to 24 (20.3%) and 1 (9.3%) patients, respectively. Mortality among patients with bleeding was 45.8% in the control group (22 deaths out of 48 patients) and 36.7% in the study group (11 out of 30 died).

The analysis showed that: the proportion of patients with effective hemostasis within three years without recurrence only with performance of endoscopic procedures was 27% (33 patients) in the control group and 54.2% (64 patients) in the study group. In the phased tactics with the performance of PSS after endoscopic interventions mentioned rates were: in the main group - 61.6% (109 patients) In the structure "no mortality" in patients with LC in the remote period (81 patients) with endoscopic interventions there was no recurrence of bleeding observed in 40.7% (33) cases in the control group and 68.1% (64 of 94) in the main group. In turn, in patients with combined endoscopy plus PSS, not including those who died from progressive LC, absence of bleeding recurrence was 45.9% (in 45 of 98 patients) and 71.2% (102 out of 153 tracked at a remote period, excluding died from LC complications). In the group of patients that did not underwent any endoscopic procedures, and were receiving only conservative therapy only in 3 (10.7%) cases it was possible to avoid recurrence, this determines the therapeutic ineffectiveness of isolated attempts in the risk of recurrence reduce.

DISCUSSION

Stage care in the tactics of management of patients with LC with the threat of hemorrhagic syndrome encouraged by many hepatological schools. In countries with developed transplant service minimally invasive intervention, such as endoscopic or endovascular manipulation, can extend the waiting period for a liver transplantation, as

mortality from hemorrhagic syndrome on the waiting list exceeds 25%. For countries with a lack of opportunity of radical treatment, the risk of rebleeding dictates necessity of optimization of therapeutic and preventive measures without considering the probability of liver transplantation in the future. Studies have shown that the modern arsenal of endoscopic technologies ensures adequate hemostasis. But to improve the long-term results over a third of patients required to take additional preventive measures, as even a phased implementation ligation or sclerotherapy does not achieve complete eradication of veins. Against this background and different technical capabilities, combining preventive methods are used. In particular, endoscopic procedures are used as a means of influencing directly on the source of the bleeding, but decompressive effect is achieved by performance of different portocaval bypass surgeries. These operations are divided into two groups: traditional and endovascular. The essence of transjugular intrahepatic shunting (Transjugular intrahepatic portosystemic shunting - TIPS) is in the combination of intrahepatic branches of the portal vein to the hepatic vein. Alternatively PSS, and TIPS can also be attributed to as partial, due to the possibility of creating different shunt diameters. In our view, PSS should still continue to be considered as an option method of portal decompression, especially in patients with ineffective pharmacologic and endoscopic treatment, and in the absence of indications for liver transplantation. The use of different options of endoscopic interventions, even with the dynamic control and with the use of additional ligation sessions or sclerotherapy, allowed to achieve 78% annual survival rate. In the group of patients with PSS mentioned rates were: 88%. Survival at 24 months was only 54% in the endoscopy group, while the combined tactics improved this index up to 78%. In terms to 3 years of observation, the figures were 34% versus 64% ($P < 0,001$).

In general, PSS should be carried out only by certain indications. For functional class "C" patients endoscopy remains a priority method of hemostasis and bleeding prevention. Assuming stabilization of patients state and transfer to functional classes A and B, the question of decompressive operations will be opened. In other cases it is advisable to use only minimally invasive techniques. In particular, endoscopic and endovascular interventions, since this group of patients due to severity of LC, are already regarded as potential candidates for radical treatment.

CONCLUSIONS

In 68.1% of cases hemorrhage development in cirrhotic patients is observed on the background of compensated and subcompensated course of the disease with a high forecast short-term (3-month) survival ($P < 0,001$). Mentioned is defined by MELD scale. Class "A" on the Child-Pugh - corresponds to 15.9% of patients with index $9,1 \pm 0,2$ points, class "B" - 52,2% ($12,4 \pm 0,3$ points).

Maintained hepatocytes functional reserve on the background of cirrhosis (MELD < 15 points and classes "A" and "B" on the Child-Pugh) leads to a favorable long-term prognosis of "without transplantation" survival ($P < 0,001$), while the mortality rate on the first episode of bleeding in this group of patients reaches 11.1%, followed by a multiple increase in this index at relapse.

Prognostic value of prophylactic endoscopic interventions is determined by the reduction of bleeding recurrence. So, using only conservative prophylactic methods in a period of up to 3 years of observation, complication recur in 60.7% of patients with post-hemorrhagic mortality indicator - 46.4%, while their implementation reduces these values to 18.0%, respectively.

Modern opportunities of endoscopic technologies have significantly improved the results of treatment and prevention of varicose bleeding or the threat of its recurrence. In this landmark of commitment tactics, with a combination of traditional and minimally invasive decompressive surgery, allowed to increase the survival rates of patients from 80% to 88% - up to 1 year and 42% to 64% - to 3 years of follow-up.

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Competing interests

The authors declare that they have no competing interests.

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