

Clinical implementation of partial splenic artery embolization for the prevention of recurrent bleeding from esophageal varices in portal hypertension

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ABSTRACT

Aim: To evaluate the effectiveness of PSAE for secondary prevention of VB episodes in patients with chronic liver disease (CLD) and CSPH.

Materials and Methods: One hundred twenty patients (from 2008 to 2020) were submitted of PSAE as secondary prevention treatment. The results of the treatment of 27 patients between 2008 and 2012 (first period) were compared with those of 93 patients treated with PSAE since 2013 (second period), as procedure and management protocol were modified. VB recurrence rate and mortality (related and non-related to bleeding episodes) were defined as study end-points in both groups at 12-months follow-up.

Results: At 12-months follow-up, 11 (40,7 %) and 54 (58,1 %) patients in groups 1 and 2, respectively, were free from VBs ($p=0,129$). Overall mortality rate was significantly higher in group 1, as compared to group 2: 10 (37,0 %) versus 6 (6,4 %) patients, respectively ($p<0,001$), – due to higher frequency of fatal VB events (7 (26,0 %) vs. 3 (3,2 %) patients, respectively; $p=0,001$).

Conclusions: PSAE is an effective treatment for secondary prevention of VB in patients with CLD and CSPH. The management protocol modification resulted in the decrease in overall mortality rate and mortality related to recurrent VB episodes.

KEY WORDS: partial splenic artery embolization, chronic liver disease, liver cirrhosis, variceal bleeding, portal hypertension

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INTRODUCTION

Portal hypertension leads to a number of complications, including the development of portosystemic shunts and esophageal varices. Such complications can lead to bleeding from varicose veins in the esophagus and patient death. Currently, the leading role of visceral hemodynamics disturbances in the development of the portal hypertension syndrome has been proven [1].

To correct portal hypertension and prevent recurrences of esophageal bleeding in patients who have undergone an initial episode of variceal bleeding, non-selective beta-blockers are prescribed [2]. However, the effectiveness of pharmacological methods for preventing variceal bleeding is limited.

Another direction for the prevention of variceal bleeding in portal hypertension is surgical. This includes the creation of portosystemic shunts, including the minimally invasive version of this operation – the transjugular intrahepatic portosystemic shunt (TIPS). Such surgeries lead to a re-

duction in pressure in the portal system, a decrease in the frequency of bleeding recurrences, but result in a number of complications, among which is encephalopathy. Consequently, the use of such operations in clinical practice is limited [3].

Liver transplantation is considered the «gold standard» for the treatment of complicated portal hypertension. This surgery is one of the most complex and expensive in the field, which limits its application [3].

Under such circumstances, partial splenic artery embolization (PSAE) may become the treatment of choice for patients. At the same time, despite the long history of the method (since 1979), there is currently no universally recognized surgical technique or patient management protocol in the world [3].

From the literature, there are known cases of PSAE complications, including fever, abdominal pain, ascites, pleural effusion, splenic abscess, and peritonitis. Late period observations include cases of recanalization of the

Table 1. Clinical evaluation of result of PSAE application

Code	Result evaluation	Description
1	«Good»	No VB episodes during follow up 12 months
2	«Stable»	No more than 1 non-fatal VB episode
3	«Unstable»	Two or more non-fatal VB episodes
4	«Fatal», related to VB	Lethal result due to fatal VB episode
5	«Fatal», non related to VB	Lethal result not related to VB episode

Table 2. Baseline demographic, anthropometric and clinical characteristics of the enrolled patients from the studied groups

Parameters	PASE, n=120		p
	Group 1 (N=27)	Group 2 (N=93)	
Age, years	47,8±11,00	50,2±10,30	0,296
Gender, n (%)	Males	18 (66,7)	0,379
	Females	9 (33,3)	
BMI, kg/m ²	24,3±4,73	25,6±4,30	0,179
Esophageal varices grade, n (%)	2	18 (66,7)	0,819
	3	9 (33,3)	
MELD score	9,0±2,81	8,8±3,30	0,775

Notes: BMI – body mass index.

splenic artery [4–6], necessitating the optimization of the surgical technique and patient management protocol. This optimization aims to enhance the efficacy of partial splenic artery embolization and minimize the surgical risk.

AIM

The aim of the study was to optimize the technique for preventing variceal bleeding (VB) from the esophageal and gastric veins using PSAE, and to provide clinical justification for the effectiveness of the proposed method.

MATERIALS AND METHODS

From 2007 to 2020 one hundred twenty patients aged 27 to 72 years (mean [M] ± standard deviation [SD]: 49,5±10,46) years, who had previously experienced one or more episodes of bleeding from gastroesophageal varices GOV-1 and GOV-2 types, underwent PSAE to prevent subsequent VB episodes at Bogomolets National Medical University clinic. The severity of chronic liver disease was assessed by the Model for End-Stage Liver Disease (MELD) score. The grade of esophageal varices development was assessed using the NIEC classification (North Italian Endoscopic Club).

In all cases, the intervention involved combined PSAE with the injection of polyvinyl embolus into the splenic artery lumen, followed by the placement of spiral coils (Gianturco type). The effectiveness and safety of PSAE were evaluated in all 120 patients over a 12-month observation period (Table 1).

The study unfolded in two phases: the first was the initial stage of clinical implementation, which involved 27 patients between 2008 and 2012, referred to as group 1. The second phase was dedicated to applying the refined embolization method, enrolling 93 patients from 2013 to 2020, known as group 2.

During the second stage, a modified protocol was implemented, which included the usage of hydrophilic catheters and introducers of a smaller diameter, hydrophilic wires, innovative methods of embolization using short flexible coils with tight filling of the vessel lumen along the central axis, a smaller volume of contrast media, and a hydraulic method of pushing coils.

Nonselective beta-blockers were administered at a dose of 40-60 mg per day in all cases, in accordance with the AASLD/Baveno recommendations [2]. The effectiveness of PSAE was evaluated by closely monitoring the presence and number of recurrent variceal bleeding episodes during a 12-month follow-up period.

The patients gave their informed consent for the studies conducted in compliance with ethical principles of medical research involving human participation. These ethical principles include the Declaration of Helsinki (2008), the basic provisions of Good Medical Practice, and the Council of Europe Convention on Human Rights and Biomedicine (1997). The clinical study was carried out after obtaining a favorable opinion from the ethics commission and permission to conduct the study in accordance with current legislation in Ukraine and modern ethical norms and principles for conducting clinical studies.

Table 3. The results of clinical implementation of PSAE as secondary prevention option

Result coding	Result evaluation	PASE, n=120		p
		Group 1 (N=27)	Group 2 (N=93)	
[1+2]	«Satisfactory», n (%)	15 (55,5)	78 (83,9)	0,004
1	«Good», n (%)	11 (40,7)	54 (58,1)	0,129
2	«Stable», n (%)	4 (14,8)	24 (25,8)	0,306
[3+4+5]	«Unsatisfactory», n (%)	12 (44,5)	15 (16,1)	0,004
3	«Unstable», n (%)	2 (7,4)	9 (9,7)	1,000
4	«Fatal», related to VB, n (%)	7 (26,0)	3 (3,2)	0,001
5	«Fatal», non related to VB, n (%)	3 (11,1)	3 (3,2)	0,127

The data were analyzed by the use of EZR statistics software package [7]. Quantitative variables were presented as $M \pm SD$, and qualitative – as absolute and relative (%) frequency. To compare the independent groups, we applied the Student's T-test (for quantitative variables) and Fisher's exact test (for qualitative data). The clinical effect size was assessed by odds ratio (with 95 % confidence interval [CI]). A 2-tailed p-value $<0,05$ was considered as statistically significant.

RESULTS

The enrolled patients from the studied groups were comparable by the certain baseline demographic, anthropometric and clinical characteristics (Table 2).

Before undergoing PSAE, 120 patients had a history of 391 episodes of varicose bleeding, with an average of 3,26 episodes per patient. However, during the 12 months of follow-up, only 43 episodes of VB in 49 patients were recorded, with an average of 0,36 episodes per patient. Of the 120 patients, 93 (77,5 %) showed satisfactory results (absence or no more than 1 episode), while 27 (22,5 %) had unsatisfactory outcomes, among them 16 (13,3 %), who died during the observation period. The satisfactory/unsatisfactory ratio was 3,44.

The results of clinical implementation of PSAE in patients from the studied groups are presented in Table 3.

In group 1, satisfactory results were achieved in 15 patients (55,5 %), and in group 2 – in 78 (83,9 %). The result of 11 (9,2 %) patients of both groups, who survived two or more bleeding episodes during follow-up, was evaluated as «unstable». Among the «unsatisfactory» cases, 16 patients died. Seven patients in group 1 and three in group 2 died due to fatal bleeding episodes, while three patients in both groups died from acute liver failure.

Besides achieving a greater number of satisfactory outcomes, the mortality rate from fatal episodes in group 2 was markedly lower than in group 1 (3.2 % compared to 26.0 %, respectively). Furthermore, the likelihood of an unsatisfactory outcome in the second group was reduced by over four times (OR = 0,24 [95 % CI 0,09-0,61]).

The overall mortality rate was significantly higher in the first phase of PSAE clinical implementation, with 10 out of 27 patients (37,0 %) compared to group 2, where it was 6 out of 93 patients (6,4 %) ($p < 0,001$). Thus, the mortality risk in group 2 was reduced by 8,33 times (OR = 0,12 [95 % CI 0,04-0,37]).

Severe post-procedure (within 30 days) complications, not related to recurrent bleeding episodes, were observed in 12 patients, including one case of total splenic abscess complicated by fatal fulminant sepsis. Other complications, such as acute pancreatitis, total portal vein thrombosis, left-sided pleural effusion, hematoma of the approach site (2 cases), and acute renal failure (3 cases), were successfully managed with appropriate therapy. Post-embolization syndrome was not considered as a severe post-procedural complication, as its manifestations were easily mitigated with drug treatment.

The total mortality rate was at 13,3 % (16 out of 120 patients), which was less than the rates observed with other secondary prevention methods such as endoscopic sclerotherapy and the use of non-selective beta-blockers, at 37,1 % and 28,4 %, respectively [8]. In our study this rate dropped to 6,4 % following enhancements in embolization technology

DISCUSSION

The main goal of our study was to determine perspective approaches to the prevention of recurrent bleeding from phlebectasies of the esophagus and stomach. According to the literature sources, endoscopic and pharmacological methods are associated with a mortality rate ranging from 28 % to 32 % [9-11]. Among the existing methods, mini-invasive approaches are currently attracting special attention, the effectiveness of which is explained by the direct effect on the vessels of the splanchnic bed, where the main hemodynamic pathological changes that take part in the formation of portal hypertension occur [12].

We managed to prove the effectiveness of the use of PSAE as a method of secondary prevention of varicose bleeding against the background of diffuse liver diseases. In addi-

tion, the measures proposed by us for the comprehensive management of such patients contributed to an increase in the quality of life of patients and in long-term observation reliably demonstrated an increase in the life expectancy of patients and a decrease in the number of episodes of recurrent bleeding.

Literature data and our experience indicate that PSAE is an effective and safe procedure [3, 6, 13]. One of the effects of PSAE, which is corroborated by both our data and literature, is the correction of thrombocytopenia. This effect additionally contributes to the minimization of the risk of bleeding, including during long-term follow-up [14-15], which we have also observed in our study.

During the first stage of our work, PSAE was performed as an emergency intervention within the first 5-7 days following a bleeding episode. The short preparation period did not allow for a comprehensive examination, nor the preoperative correction of the patient's clinical condition, which worsened the conditions for performing PSAE. The reasons for the unsuccessful outcomes were: the severity of the patient's condition, insufficient examination and assessment of operational risks, lack of clear criteria for patient selection, and management of the postoperative period. The first stage of clinical implementation was accompanied by numerous technical complications due to technological shortcomings and the available means of embolization.

During the second stage, preoperative preparation was optimized, and the endovascular surgery was scheduled no earlier than 2-3 weeks after a bleeding episode to stabilize the patient's condition. A comprehensive evaluation of

portal hemodynamics was performed using ultrasound flowmetry, and CT-angiography of the abdominal organ vessels was carried out. The analysis of CT-angiography data facilitated the planning of the endovascular surgery, revealing individual anatomical features and anomalies of the abdominal organ vessels (splenic artery aneurysms, arteriovenous malformations, etc.).

Summarizing our experience and literature data, we can conclude that negative outcomes after technically successful PSAE may be associated with non-compliance on the part of the patient: refusal to take non-selective beta-blockers, alcohol consumption, ignoring recommendations on restrictions of physical activity in the first months after the intervention [16-18]. Our data indicate that serious complications after PSAE are rare and depend on the patient management tactics and adherence to them by the patient [19-21].

CONCLUSIONS

PSAE, employed as a secondary preventive measure, is recognized as safe and effective for managing clinically significant portal hypertension that is complicated by episodes of VB.

The results obtained at this stage allow for its recommendation in broad clinical practice beyond specialized centers. The refined protocol for the application of PSAE, by addressing technological shortcomings, has allowed unlocking the potential of this preventive method and improving treatment outcomes for patients with chronic liver disease and clinically significant portal hypertension.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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