

Original Article

Possibilities of Endovascular Hemostasis in Treatment of Pancreatic Bleeding

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Abstract

Pancreatic hemorrhage is one of the most severe complications of various pancreatic diseases that are difficult to treat even in multidisciplinary hospitals. Mortality from pancreatic hemorrhage can reach up to 80%. This study aimed to evaluate the possibility of maintaining endovascular homeostasis in the treatment of patients with pancreatic hemorrhage. This retrospective multicenter study included 45 patients (33 men and 12 women) in the age range of 27-84 years. More than 50% (n=23) of the patients were diagnosed with chronic pancreatitis. Malignant pancreatic lesions were observed in 22 patients; of whom 11 patients had acute necrotizing pancreatitis. Acute bleeding was observed in 39 (86.6%) patients, and 6 (13.3%) patients showed chronic symptoms. Single-shot and recurrent bleeding was recorded in 22(48.9%) and 23 (51.1%) patients. In total, 57 patients underwent endovascular surgery. Moreover, 45 patients underwent primary surgery and another 12 (2.2%) underwent reoperation due to recurrent bleeding. Intraoperative complications occurred in 1 (2.2%) patient, and postoperative complications occurred in another. Out of all 45 patients, seven patients had 15 episodes of recurrent bleeding, of whom four patients showed recurrent bleeding at the in-hospital period, and the other three were under local supervision after the previous endovascular intervention. Out of the 45 patients, 35 (77.7%) survived and another 10 (22.2%) died due to multiple organ failure (n=8) and recurrent bleeding and hemorrhagic shock (n=2). Out of 10 patients who died, 4, 3, and 3 patients showed malignant pancreatic lesions after surgery, acute pancreatitis, and chronic pancreatitis, respectively. Endovascular hemostatic interventions can significantly increase the survival rate in severe groups of patients with pancreatic bleeding. Endovascular hemostasis is a safe procedure and may be called the “method of choice” in the treatment of pancreatic bleeding, especially in combination with percutaneous draining, aspiration, and injection of liquid embolic agents into leakage of pancreatic juice.

Keywords: Acute necrotizing pancreatitis, chronic pancreatitis, Embolization coils, Liquid embolic agents, Malignancy of pancreas, pancreatic bleeding, Stent grafts

1. Introduction

According to statistics, bleeding is one of the five most common reasons to visit a gastroenterologist (1) and is often associated with the pancreas pathology.

Pancreatic bleeding (PB) is of particular interest in the scientific and practical field of abdominal surgery, considering the constant increase in the incidence of various forms of pancreatitis, as well as an increase in

detection and surgical correction of malignant pancreatic lesions (1). Pancreatic bleeding is also one of the most severe complications of pancreas diseases (2). Such bleeding is a complicated form of acute and chronic pancreatitis and leakage of pancreatic secretions after interventions on the pancreas (3).

AP is an inflammatory disease of the pancreas that is one of the leading causes of hospital admission due to gastrointestinal disease in the United States and other parts of the world (4). The incidence varies from country to country, depending on the cause (5). Acute pancreatitis (AP) is an acute inflammation of the pancreas due to the activation of enzymes and the destruction of pancreatic tissue (6). Clinically, nausea and vomiting are characterized by acute abdominal pain with or without diffusion to the back and are often diagnosed with elevated serum amylase (7). It is worth mentioning that most (80%) of nausea and vomiting cases are due to gallstones or persistent alcohol abuse (8). About 30%-60% and 15%-30% of AP occur due to gallstones and alcohol consumption, respectively. This incidence is rising in the United States, with an estimated 70 hospitalizations per 100,000 people a year, and more than 200,000 new cases of AP diagnosed per year (9).

AP is a disease of the gastrointestinal tract that causes 280,000 cases of death per year during hospital stays in the United States. The length of hospital stay of these patients in 2010 was estimated to be 5 days, costing an estimated \$ 2.9 million a year (10). The mortality rate in these patients varied from 3% in patients with edematous pancreatitis to 15% in advanced pancreatitis and necrosis (11). Based on the evidence, hospital admissions have been increasing day by day due to AP (12).

It should be noted that AP affects people of all ages; however, its mortality rate increases with age (13). In addition, the pattern of complications and problems of the disease changes with age. The overall mortality rate in patients with AP is 10%-20% and occurs due to shock, anoxia, hypotension, or fluid and electrolyte

imbalance (14). This mortality rate is related to 10%-30% of patients with the severe acute disease diagnosed with necrosis of the pancreas and the surrounding areas (15).

Among patients with AP, the incidence of primary bleeding is up to 6.5%, while with surgical correction of purulent-septic complications, the risk of bleeding increases up to 77.8% (16), particularly in the group of patients with disease duration less than 4 weeks due to "partial removal of necrosis at the cost of severe bleeding and excessive removal of the normal pancreatic parenchyma" (17). Mortality in hemorrhagic complications of AP can range from 40% to 78%.

Bleeding in chronic pancreatitis (CP) occurs in 1-5% of patients. The disease is caused by erosion of blood vessels and the formation of pseudoaneurysms as a result of the high proteolytic activity of the enzyme in postpartum pseudocysts. Mortality in bleeding from pseudoaneurysms in patients with postnecrotic cysts and chronic pancreatitis varies from 60 to 80% (3).

The risk of postoperative bleeding during resection operations on the pancreas is 5%-10%. As with pancreatitis, bleeding after resection of the pancreas is life-threatening and has a mortality rate of 30%-58.5%, according to meta-analyses and several studies (18).

Patients with pancreatic bleeding are among the most difficult cases to treat, due to such factors as the volume of blood loss, septic conditions, multiple organ failure, purulent-septic complications, the volume of surgical trauma, and concomitant pathology. They are also considered among the most interesting cases from a scientific and practical point of view since the issue of tactics in stopping such bleeding remains controversial due to the different possibilities considered by medical institutions (19). Endovascular hemostasis techniques for pancreatic bleeding have become widespread due to the development of angiographic instrumentation as well as publication activity (16). This study aimed to evaluate the possibility of maintaining endovascular homeostasis in the treatment of patients with pancreatic hemorrhage using a retrospective multicenter study.

2. Materials and Methods

2.1. Patients

The current study included 45 patients (33 males and 12 females) in the age range of 27-84 years (mean±SD age: 52±2.02 years). More than 50% (n=23) of patients were diagnosed with chronic pancreatitis. Moreover, 11 patients were suffering from acute necrotizing pancreatitis, and the other 11 had malignant lesions of the pancreas.

About 25% of patients were admitted to the hospital, and the existence of such factors as haematemesis or melena, weakness, and pallor of the skin indicated chronic pancreatitis bleeding. Patients underwent different examinations, such as computed tomography with contrast enhancement, ultrasonic diagnosis, esophagogastrosopy, and digital angiography based on their clinical status and the severity of blood loss. In case of severe blood loss and unstable vital status, patients were directly moved to Cath-Lab for digital angiography and subsequent intervention. In total, 19 (42%) patients underwent angiography and further endovascular hemostasis at the first 24 h of in-hospital stay.

Bleeding in the group of patients with malignant lesions of the pancreas occurred in the postoperative period (resections of the pancreas). It is worth mentioning that, bleeding in the AP group often occurred not less than 7 days after hospitalization.

3. Results and Discussion

Based on the recorded data, patients had different kinds of bleeding, sometimes in combination with intraluminal, intra-organic, and abdominal cavity bleedings.

Bleeding was acute in majority of cases (n=39, 86.6%) and chronic in 6 (13.3%) patients. Single-shot and recurrent bleedings occurred in 22 (48.9%) and 23 (51.1%) patients, respectively. The source of bleeding was often splenic artery (n=18, 40%) and gastroduodenal artery (n=11, 24.4%), followed by branches of hepatic artery (n=8; 17.7%), pancreatoduodenal artery (n=5,

11%), superior mesenteric artery (n=4, 8.8%), gastroepiploic artery/jejunal artery (n=2, 4.4%), celiac artery/left gastric artery/inferior mesenteric artery/gastroduodenal artery+ pancreatoduodenal artery/splenic artery+ gastroepiploic artery/splenic artery+ left gastric artery/splenic artery+ hepatic artery+ artery (n=1, 2.2%).

Mean±SD time from admission to Cath-Lab was 6.8±2.27, 8.4±3.05, and 20.2±4.54 days in chronic pancreatitis group, post-resection patients, and in the group of patients with AP. Mean±SD time from operation to bleeding in the group with malignant diseases was 34±13.01 days, considering two patients who had been operated on the previous hospitalization.

Patients' hemoglobin on admission to Cath-Lab varied from 2.8 to 14 gr/dl (mean±SD: 7.73±0.33 gr/dl), and patients' condition was mostly (73%) severe or life-threatening.

Out of 34 patients with acute or chronic pancreatitis, 25 (73.5%) patients underwent sanation/draining operation during hospitalization.

Patients underwent 57 endovascular operations, including 45 primary operations and 12 reoperations due to recurrent bleeding.

Most often vascular access was patients' femoral artery (80.3%), followed by brachial artery (13.3%) and both femoral and brachial artery (6.3%). Operation duration varied from 20 to 280 min (mean time: 80.8±7 min). Mean±SD volume of contrast-agent injection was 284.73±25.45 ml.

The following procedures were performed for endovascular hemostatic intervention:

- Embolization with liquid embolic agents
- Embolization with a combination of coils and liquid embolic agents – 11 (Figure 1)
- Embolization with coils – 8 (Figure 2)
- Embolization with embols (size not less than 500-710 nm) – 7 (Figure 3)
- Embolization with a combination of coils and embols - 3
- Implantation of stent-graft – 7 (Figure 4)
- Implantation of vascular plug – 1



Figure 1. Angiography: **A.** Splenic artery with extravasation (arrow); **B.** After embolization with coils and liquid embolic agent (arrow)

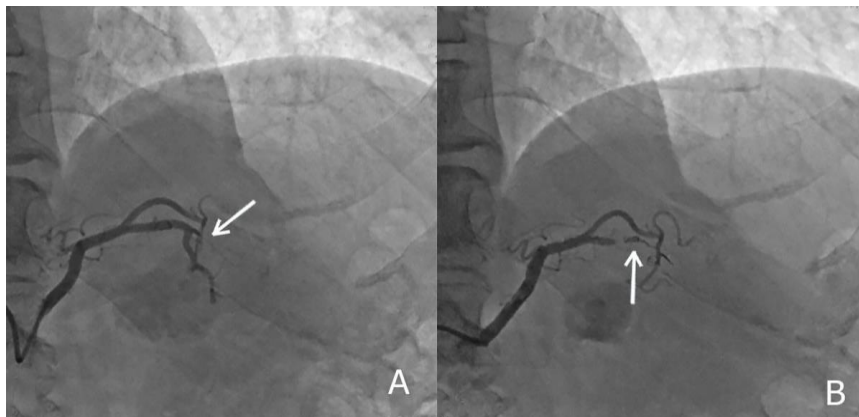


Figure 2. Angiography: **A.** Left gastric artery with extravasation (arrow); **B.** After embolization with coils and “front-to-backdoor” technique (arrow)



Figure 3. Angiography: **A.** Gastroduodenal artery with extravasation (arrows); **B.** After “distal” embolization with embols (arrows)

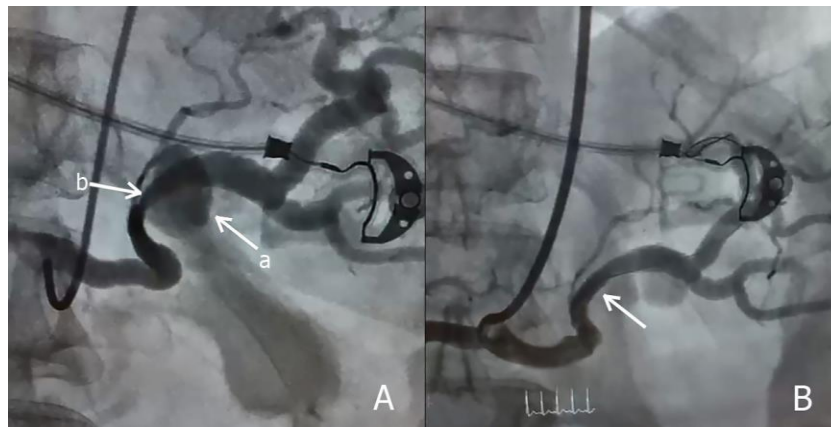


Figure 4. Angiography: **A.** Splenic artery with extravasation (arrow “a”) and vasospasm (arrow “b”); **B.** After stent-graft (arrow) implantation

Intraoperative complications occurred in 1 (2.2%) patient due to distal migration of coils. Postoperative complication occurred in 1 (2.2%) patient due to migration of coils threw arterio digestive fistula from hepatic artery to bowel.

Out of all 45 patients, 7 patients had 15 episodes of recurrent bleeding, of whom 4 patients had recurrent bleeding at the in-hospital period, and the other three were under local supervision 30, 210, and 360 days after the previous endovascular intervention.

Recurrence of bleeding occurred in:

- Embolization with coils – 3
- Embolization with embolic agents – 2
- Embolization with both coils and liquid embolic agents – 2
- Embolization with liquid embolic agents – 1
- Implantation of stent-graft – 1

Furthermore, one of the seven patients with recurrent bleeding underwent an open surgical operation after second-shot bleeding and one did not undergo an operation to stop bleeding.

Estimated reasons for recurrent bleeding revealed that:

1. Recurrence of bleeding in coil embolization (3 episodes in a single patient) occurred due to adverse anatomy and wrong tactics (coiling of false aneurysm). This case has been described in detail in another study (20).

2. None of the patients with recurrent bleeding underwent previous or further puncture/draining of local volume of pancreatic juice leakage.

Out of 45 patients in this study, 35 (77.7%) patients survived and the other 10 (22.2%) patients died (8 patients due to multiple organ failure and 2 patients due to recurrent bleeding and hemorrhagic shock). The cases of death occurred after resection operations due to malignant lesion of the pancreas (n=4); AP (n=3), and chronic pancreatitis (n=3).

Mean statistics of deceased patients included:

Mean age: 60.4 ± 5.42 years.

Mean Hb before operation: 7.78 ± 1.01 gr/dl.

Mean volume of injected contrast agent: 250 ± 39.44 ml.

Mean operation duration: 78 ± 18.26 min.

According to the higher survival rate (77.7%) obtained in this study, compared to that (20-60%) obtained by methods in the group without endovascular hemostasis (based on the existing literature), it could be said, that endovascular hemostatic intervention can be called “method of choice” or “gold standard”. However, some authors noticed that “endovascular hemostatic interventions did not take into consideration pathophysiological mechanisms (influence of pancreatic juice)” in pancreatic bleeding management (3). Therefore, the main finding of this study is that eliminating the influence of pancreatic juice on surrounding tissues is the best prophylaxis for

pancreatic bleeding. An additional advantage of this method was that none of the patients with recurrent bleeding underwent any kind of pancreatic leakage drainage. In all the above mentioned statements, the method adopted by Tarkhanov A (20).

Analysis of complications, such as recurrent bleeding and mortality did not reveal strong predictors of major adverse events.

The results of the current study included the following:

1. Endovascular hemostatic interventions can significantly increase the survival rate in a group of patients with severe pancreatic bleeding.
2. Endovascular hemostasis is a safe procedure and may be called a “method of choice” in the treatment of patients with pancreatic bleeding.
3. A combination of endovascular hemostatic methods with consequent percutaneous draining, aspiration of pancreatic juice, and percutaneous injection of liquid embolization agent can improve treatment strategy in patients with pancreatic bleedings. Such a method might have better outcomes in decreasing the rate of bleeding reoccurrence; however, it must be deeply investigated.
4. Pancreatic bleeding is a severe complication in the group of patients with pathology of the pancreas with high mortality.
5. Source of bleeding is often the splenic artery.
6. Endovascular hemostasis in pancreatic bleeding is safe and effective, and the survival rate in the group of endovascular hemostatic interventions is high (77.7%).

Authors' Contribution

Study concept and design: M. S. K.

Acquisition of data: A. D. K.

Analysis and interpretation of data: S. L. B.

Drafting of the manuscript: S. S. L.

Critical revision of the manuscript for important intellectual content: K. G. M. and I. B. K.

Statistical analysis: A. L. I.

Administrative, technical, and material support: M. S. K. and E. A.

Ethics

The study protocol was approved by the local Ethics Committee of Belgorod State University, Russia and the requirement for obtaining informed consent was waived.

Conflict of Interest

The authors declare that they have no conflict of interest.

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