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CASE SERIES

The use of Arista AH as a local haemostatic agent in distal splenopancreatectomy: report of two cases

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Abstract

Bleeding is still one of the most feared intraoperative and postoperative complications that can lead to an increase in morbidity, mortality, length of hospital stay and costs. Nowadays, in addition to accurate surgical techniques, several local haemostatic agents are available and can be used in case of oozing bleeding. Herein, we report our experience with a ready-to-use polysaccharide powder in two patients undergoing distal splenopancreatectomy. Bleeding control was achieved in both cases. No patient showed postoperative bleeding, and no other complications were reported.

Keywords: case report, haemostasis, pancreatectomy, postoperative haemorrhage.

Citation

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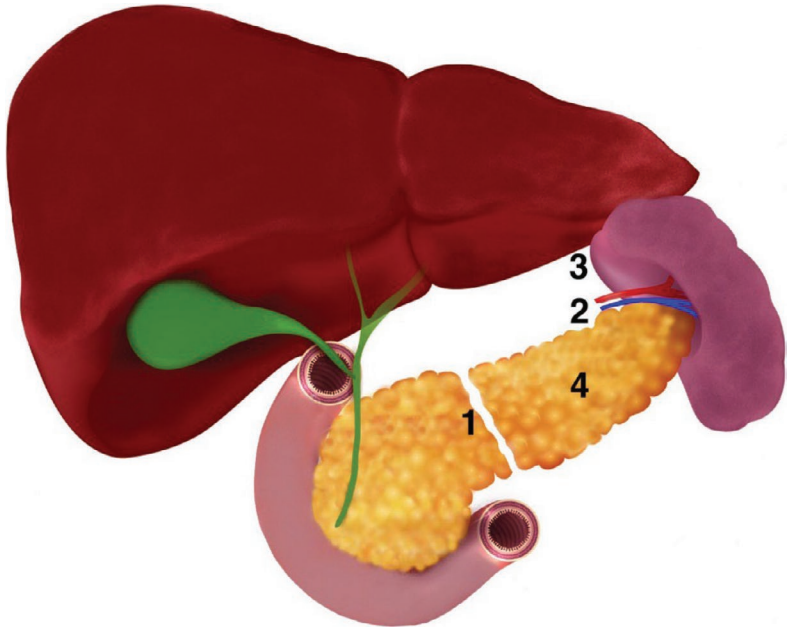
Introduction

Insufficient haemostasis and excessive bleeding at a surgical site are associated with the need for blood transfusion during and following complex surgical procedures and may lead to an increase in morbidity and overall costs of healthcare and, in extreme cases, to mortality.[1] Although perioperative mortality of pancreatic surgery has declined in the last two decades, postpancreatectomy haemorrhage (PPH) is one of the most dreaded and potentially lethal complications that require prompt diagnosis and treatment.[2,3] According to the International Study Group of Pancreatic Surgery (ISGPS) definition, PPH is classified as A, B or C grade based on time of onset, location (Figure 1), cause and severity.[3] Whilst early PPH, which occurs in the first 24 h after surgery, is often caused by inadequate haemostasis or underlying coagulopathy, late PPH is usually due to a multifactorial pathophysiological mechanism, including an association with postpancreatectomy complications. For example, in the case of postoperative pancreatic fistula, the loss of liquid rich in activated amylase can lead to the erosion of peripancreatic vessels with consequent bleeding.[4] A systematic review and meta-analysis performed by Lyu et al. including 1952 patients showed an incidence of PPH of 4.2%.[5] Moreover, the incidence of PPH was 2.95% (29/984) in the laparoscopic distal pancreatectomy group and 5.48% (53/968) in the open distal pancreatectomy group. Intraoperative control of bleeding depends on several aspects such as scrupulous surgical technique, use of classical haemostasis procedures (i.e. vessel suturing or ligation and use of electrocauterization or other energy-based devices), antifibrinolytic agents and topical haemostats.

Whilst the use of topical haemostats is an old concept, advances in biotechnology over the last three decades have resulted in the development of several agents at the surgeon's disposal.[6] Although there is a degree of overlap between these agents, they are divided into three main categories: (1) topical haemostats providing a surface enhancing blood clotting; (2) sealants preventing blood and lymphatic leakage from tissues; and (3) adhesives used to bond tissues.[7] Arista (the drug is a registered trademark of C.R. Bard, Inc., MA, USA) is a newly developed topical absorbable haemostatic agent with broad potential application in several surgical fields, intended to assist when control of capillary, venous, and arteriolar bleeding is ineffective or impractical by conventional procedures, especially in heparinized patients. It is composed of a

Figure 1. Potential bleeding sites in a distal splenopancreatectomy.



(1) Pancreatic stump; (2) main tributary vessels of the splenic artery; (3) short gastric arteries; and (4) remaining area after resection.

microporous polysaccharide haemosphere (MPH) powder of dry, hydrophilic, flowable particles synthesized by crosslinking purified plant-based polysaccharide, typically absorbed within 24–48 h postapplication. MPH powder works by concentrating platelets, red blood cells and blood proteins on the particle surface, creating a gelled matrix that acts as a scaffold, concentrating clotting factors and creating stable haemostatic plugs.[8,9]

To the best of our knowledge, the application of MPH powder as a local haemostatic agent in pancreatic surgery has not been reported to date. Herein, we report two clinical cases of distal splenopancreatectomy (one laparoscopic and one laparotomic, respectively) performed for neoplastic disease in which MPH powder (Arista; registered trademark of C.R. Bard, Inc. Woburn, MA, USA) was used.

Methods

No information is reported that could enable any patient to be identified; therefore, no patient consent was required to report these cases. This manuscript was prepared according to CARE guidelines.

MPH powder is a haemostatic agent derived from purified potato starch incorporating a sophisticated, plant-based polymer crosslinking that creates ultrahydrophilic, biocompatible particles. MPH powder aids the coagulation process by absorbing the liquid portion of the blood, and increasing the concentration of the platelets and coagulation factors.[9]

Case series

Case 1

Case 1 involved a 51-year-old woman with a body mass index (BMI) of 29 kg/m^2, no relevant medical history or allergies, non-smoker, and non-drinker. She had a negative family history for oncological pancreatic disease or coagulopathies. Her father was diagnosed with diabetes at the age of 30 years, and her mother was diagnosed with breast cancer at the age of 60 years.

The patient was referred to our unit after an incidental finding of a pancreatic lesion at ultrasonography, which was further investigated with a CT scan and echoendoscopy. The lesion was a 50 × 60 mm cystic formation of the pancreatic body with exophytic growth without communication with the main pancreatic duct or vascular involvement. No enlarged regional lymph nodes were detected at echoendoscopy. The findings were compatible with mucinous cystic pancreatic neoplasm. The patient was in good clinical status and reported no complaints. After discussion within the pancreatic oncological board, a laparoscopic distal splenopancreatectomy was planned.

The patient was positioned in a modified lithotomic position with both arms abducted, and four trocars

were placed. Dissection was conducted using a harmonic ultrasound laparoscopic scalpel, starting with the incision of the gastrocolic ligament and the short gastric vessels, exposing the anterior surface of the pancreas. The inferior border of the pancreas was then separated from the mesocolon and the retroperitoneal sheath. The splenic artery was identified and ligated near its origin. The pancreas was then transected with a linear endo-stapler device (reinforced reload, fit for thick tissues). Detachment of the pancreatic body from the retroperitoneal sheath was conducted from medial to lateral, exposing the left kidney and left adrenal gland. Despite adequate exposure, the dissection of this plane resulted in oozing bleeding from the fatty tissue covering these organs, in which lymphatic vessels are commonly found. Dissection of the short gastric vessels was completed, and the spleen was freed. The surgical specimen was then extracted via a Pfannenstiel incision, and the specimen resection margin was sent for extemporaneous histological examination (negative for malignancy). Laparoscopic lavage was performed to identify potential sources of bleeding. MPH powder was applied through a laparoscopic applicator to achieve appropriate haemostasis (Figure 2), thus avoiding the use of electrocautery on the pancreatic dissection plane. Drainage was placed close to the pancreatic section margin and another one in the splenic lodge. Port sites were sutured. The operating time was 217 minutes.

After the operation, oral intake was progressively reintroduced (liquids until day 2 and solid food from day 3). The aspect of the drainage fluid was always serous, testifying no evidence of bleeding, and the amylase count from both drainages progressively diminished. The splenic drainage was removed on the third day postsurgery, and the pancreatic drainage was removed on the fifth day. The patient was discharged on day 6 in good clinical condition. Table 1 shows in detail the drainage output and blood test results during the hospital stay. At 1 week from discharge, the patient was in good clinical condition. At the 1-month follow-up, the patient reported no physical complaints but had some difficulties in keeping glucose levels in the appropriate range and was therefore referred to a diabetologist for consultation. The histopathological examination revealed a solid pseudopapillary tumour stage pT3N0 according to the TNM classification, eighth ed. The case was discussed again by the tumour board, and due to the favourable prognosis of this specific tumour histotype, no further treatment was required. The patient was advised to perform an annual follow-up with an abdominal MRI.

Figure 2. Use of Arista AH during laparoscopic distal pancreatectomy.

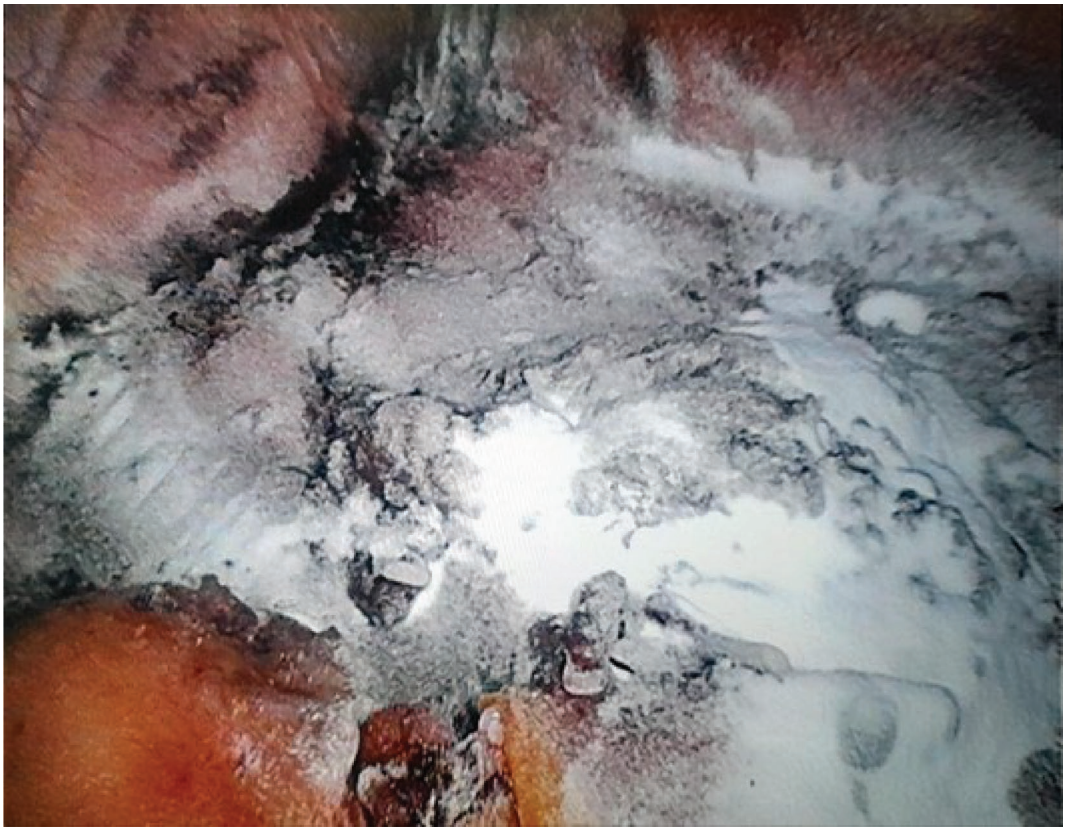


Table 1. Case 1 drainage output and blood test results during hospital stay.

Case 1		POD 1	POD 2	POD 3	POD 4	POD 5	POD 6
Drainage output (mL/day)	Pancreatic	25	150	200	25	25 (removed)	–
	Splenic	30	25	50 (removed)	–	–	–
Amylase count in drain fluid (U/L)	Pancreatic	3370	–	364	375	254	–
	Splenic	521	–	75	–	–	–
Haemoglobin levels (g/dL)		–	–	10.9	10.9	11	11.5
Haematocrit (%)		–	–	32	32.5	32.2	33.8

POD, postoperative day.

Case 2

Case 2 involved a 79-year-old man, with a BMI of 23.45kg/m^2, type 2 diabetes under treatment with metformin and chronic pancreatitis, with allergies to penicillin and salicylate.

His past medical history included a left hemicolectomy for colon carcinoma and a right hip replacement. The patient was a previous smoker (stopped 20 years before diagnosis) and an occasional alcohol consumer. The family history is negative for oncological pancreatic disease; an uncle was diagnosed with gastric carcinoma, and his mother died from an unspecified tumour.

The patient was referred to our unit after the detection of a pancreatic lesion during regular follow-up for chronic pancreatitis. Blood testing only showed an increase in glucose levels. The CT scan and MRI confirmed chronic pancreatitis and the presence of a 27 mm lesion at the pancreatic tail, causing dilation of the main pancreatic duct and microscopic intraductal papillary mucinous neoplasm-like cysts at the tail. The lesion was confirmed and biopsied at echoendoscopy, with malignant findings. The pancreatic board discussed the case, and the patient was a candidate for exploratory laparoscopy to rule out metastatic disease, assess resectability and eventual open distal pancreatectomy.

Prolonged lysis of adhesions due to the previous colectomy and the dissection was carried out with electrocautery. The pancreas, which showed an intense chronic inflammatory reaction, was cautiously isolated, and the splenic artery was identified and ligated at its origin. The pancreas was dissected with a surgical scalpel at the isthmus. Ligation of the splenic vein was performed. Dissection of the pancreatic body and tail from the posterior plane with partial removal of the Gerota sheath beneath the lesion resulted in exposure of the adrenal gland, and oozing bleeding of the perirenal adipose tissue. Splenic dissection was completed, and the splenopancreatic specimen was removed. The Wirsung duct on the pancreatic stump was sutured with two prolene 5.0 stitches. Because classic haemostatic procedures were not satisfactory, haemostasis was controlled with the application of MPH powder on the pancreatic stump and perirenal fat (Figure 3). Two drains were positioned, one close to the pancreatic resection margin and one in the splenic lodge. The abdominal wall was then sutured. The operating time was 248 minutes.

After the operation, oral intake was progressively resumed (liquid diet until day 3 and solid food starting from day 4). The aspect of the drainage fluid was at first serosanguineous and, on the third day, turned completely serous with no evidence of bleeding. The amylase count progressively diminished until the removal of the two drainages (on the third postoperative day for the splenic drainage and on the fifth postoperative day for the pancreatic drainage). On day 6, the patient was discharged in good clinical condition. Table 2 shows in detail the drainage output and blood test results during the hospital stay. At 1 week after discharge, the patient was in good clinical condition. At 1-month follow-up, the patient reported no physical complaints. The histopathological examination revealed, in the context of an intraductal papillary mucinous neoplasm, a double ductal adenocarcinoma grade 2 staged as pT2(m)N2R1 (due to the posterior margin being infiltrated at less than 1 mm, and involvement of 7/23 lymph nodes) according to the latest eighth edition of the TNM classification.

The tumour board discussed the case, and the patient was advised to undergo adjuvant chemotherapy.

Discussion

Postoperative haemorrhage remains one of the most feared complications after pancreatectomy because it is associated with high mortality.[2] Wellner et al. analyzed data from more than 1000 patients who

Figure 3. Use of Arista AH during open distal pancreatectomy.

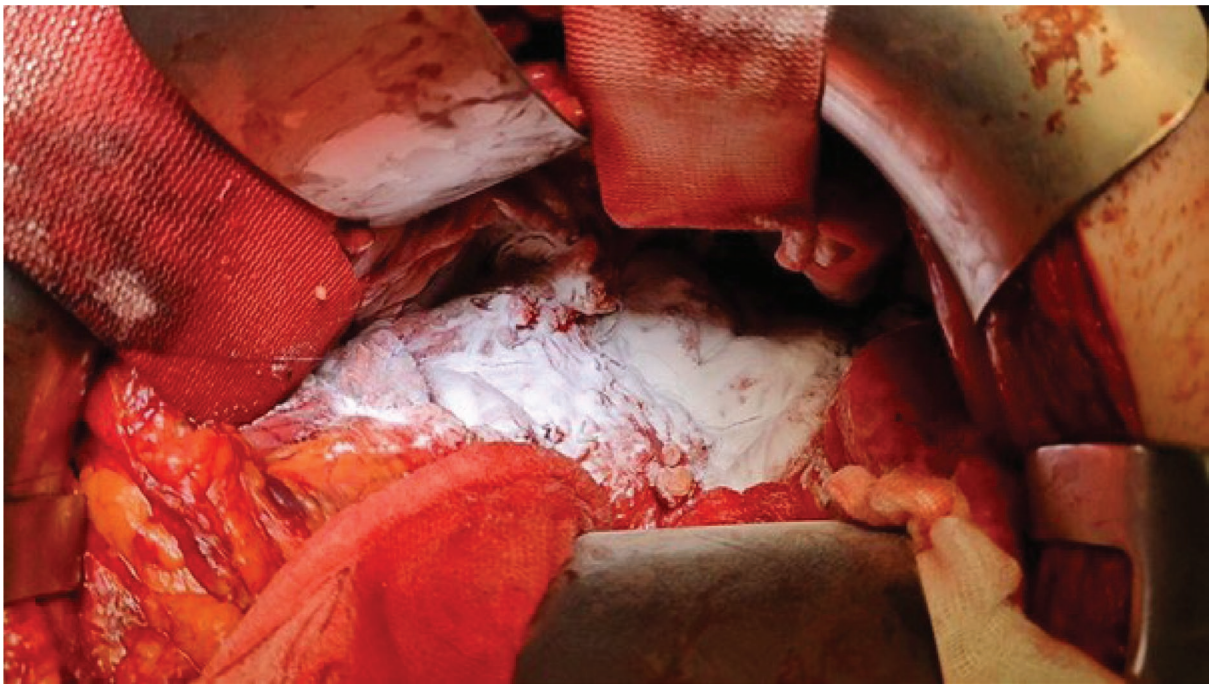


Table 2. Case 2 drainage output and blood test results during hospital stay.

Case 2		POD 1	POD 2	POD 3	POD 4	POD 5	POD 6
Drainage output (mL/day)	Pancreatic	100	200	100	100	50 (removed)	–
	Splenic	100	100	100 (removed)	–	–	–
Amylase count in drain fluid (U/L)	Pancreatic	2105	–	976	213	80	–
	Splenic	204	–	88	–	–	–
Haemoglobin levels (g/dL)		14.1	–	12.8	12.3	12.9	12.4
Haematocrit (%)		42.1	–	37.6	36.6	37.7	36.7

POD, postoperative day.

had major pancreatic resections at their institution, describing characteristics and management of PPH, defined according to ISGPS criteria.[10] In their cohort, 188 patients underwent distal pancreatic resection, of whom eight (4.3%) had PPH, (three (1.6%) patients had grade A or B PPH (not severe) and five (2.7%) patients had grade C PPH). In the latter group, two patients died (1.1% of the total distal pancreatic resection, 25% of total PPH of any grade and 40% of PPH grade C). They confirmed that PPH is an independent predictor of mortality, underlying the importance of correct intraoperative haemostasis. According to the meta-analysis by Peng et al., intraoperative blood loss in distal pancreatectomy was significantly associated with the development of postoperative pancreatic fistula (odd ratio 2.25; $p<0.0001$), suggesting that adequate control of haemostasis can also prevent this fearsome complication.[11] The availability and use of topical haemostatic agents in daily practice have significantly increased in recent years and have become part of the surgeon's armamentarium. Although no convincing results were achieved in the attempt to prevent other postoperative complications (i.e. postoperative pancreatic fistula[12,13]), promising goals for correct intraoperative haemostasis have been achieved, especially in cases of oozing bleeding. If a major vessel bleeding occurs, haemostasis is performed mechanically or with different energy-based devices. On the contrary, in the case of minor vessel haemorrhage (such as the ones at the level of the Gerota space or on the surface of friable organs, pancreas or adrenal gland), bleeding is usually in the form of oozing and its control

with the classical surgical methods may be ineffective or even dangerous. Thus, topical haemostats can be used to stop blood loss.

Haemostatic powders, such as MPH powder, are a subgroup of topical haemostats; the advantages in clinical practice consist in the broad surface area that may be covered and in their ease of use, even in laparoscopy. Moreover, they can be efficiently distributed and can easily adhere even on irregular surfaces. For these reasons, they can be useful in a variety of surgical sites, including solid organs and cavities, such as in digestive surgery, where a significant risk of oozing may occur due to the large surface areas involved or on rough surfaces after organ resection or removal[7] (such as after distal splenopancreatectomy).

In the two cases reported, MPH powder was used as a local haemostat on the pancreatic stump, on the Gerota sheath and on the prerenal area after distal splenopancreatectomy. Indeed, in case 2, MPH powder was also used on the retroperitoneal plane up to the exposed left adrenal gland after the removal of the Gerota fascia. The patients mentioned in this article had excellent control of intraoperative haemostasis and did not develop any postoperative complications. The clinical course was favourable, and both were fit for discharge on the fifth postoperative day and discharged the day after. At the first outpatient consultation 1 week after discharge, both patients reported good clinical conditions.

Conclusions

MPH powder is a local haemostatic proven to provide intraoperative haemostasis during distal splenopancreatectomy, both in laparoscopic and open surgery. It can be applied in case of oozing bleeding, which is difficult to control with classic haemostasis methods, even on large and irregular surfaces. Our findings support the use of MPH powder as a safe and feasible local haemostat in surgical practice. Further studies are needed to establish its effectiveness in intraoperative bleeding control and early PPH in large cohorts.

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References

1. Stokes ME, Ye X, Shah M, et al. Impact of bleeding-related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. *BMC Health Serv Res*. 2011;11:135. https://doi.org/10.1186/1472-6963-11-135
2. Floortje van Oosten A, Smits FJ, van den Heuvel DAF, et al. Diagnosis and management of postpancreatectomy hemorrhage: a systematic review and meta-analysis. *HPB*. 2019;21(8):953–961. https://doi.org/10.1016/j.hpb.2019.02.011
3. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery*. 2007;142(1):20–25. https://doi.org/10.1016/j.surg.2007.02.001
4. Ansari D, Tingstedt B, Lindell G, et al. Hemorrhage after major pancreatic resection: incidence, risk factors, management, and outcome. *Scand J Surg*. 2017;106(1):47–53. https://doi.org/10.1177/1457496916631854
5. Lyu Y, Cheng Y, Wang B, et al. Assessment of laparoscopic versus open distal pancreatectomy: a systematic review and meta-analysis. *Minim Invasive Ther Allied Technol*. 2020;31(3):350–358. https://doi.org/10.1080/13645706.2020.1812664
6. Pereira BM, Bortoto JB, Fraga GP. Topical hemostatic agents in surgery: review and prospects. Agentes hemostáticos tópicos em cirurgia: revisão e perspectivas. *Rev Col Bras Cir*. 2018;45(5):e1900. https://doi.org/10.1590/0100-6991e-20181900
7. Eden C, Buonomo OC, Busch J, et al. An international multidisciplinary peer-driven consensus on the optimal use of hemostatic powders in surgical practice. *Updates Surg*. 2021;73(4):1267–1273. https://doi.org/10.1007/s13304-021-01136-x
8. Bruckner BA, Blau LN, Rodriguez L, et al. Microporous polysaccharide hemosphere absorbable hemostat use in cardiothoracic surgical procedures. *J Cardiothorac Surg*. 2014;9:134. https://doi.org/10.1186/s13019-014-0134-4
9. Humphreys MR, Castle EP, Andrews PE, Gettman MT, Ereth MH. Microporous polysaccharide hemospheres for management of laparoscopic trocar injury to the spleen. *Am J Surg*. 2008;195(1):99–103. https://doi.org/10.1016/j.amjsurg.2007.03.006
10. Wellner UF, Kulemann B, Lapshyn H, et al. Postpancreatectomy hemorrhage – incidence, treatment, and risk factors in over 1,000 pancreatic resections. *J Gastrointest Surg*. 2014;18(3):464–475. https://doi.org/10.1007/s11605-013-2437-5
11. Peng YP, Zhu XL, Yin LD, et al. Risk factors of postoperative pancreatic fistula in patients after distal pancreatectomy: a systematic review and meta-analysis. *Sci Rep*. 2017;7(1):185. https://doi.org/10.1038/s41598-017-00311-8
12. Montorsi M, Zerbi A, Bassi C, et al. Efficacy of an absorbable fibrin sealant patch (TachoSil) after distal pancreatectomy: a multicenter, randomized, controlled trial. *Ann Surg*. 2012;256(5):853–859; discussion 859–860. https://doi.org/10.1097/SLA.0b013e318272dec0
13. Hüttner FJ, Mihaljevic AL, Hackert T, et al. Effectiveness of Tachosil® in the prevention of postoperative pancreatic fistula after distal pancreatectomy: a systematic review and meta-analysis. *Langenbecks Arch Surg*. 2016;401(2):151–159. https://doi.org/10.1007/s00423-016-1382-7