



# Postoperative hemorrhage complications after the Whipple procedure

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## ABSTRACT

**Introduction:** The Whipple operation is an essential surgical technique; however, its high morbidity (30% to 60%) and mortality (5%) rates are problems that should be addressed. The incidence of postoperative hemorrhage is 5% to 16% in the literature. In this study, the data and results in our clinic regarding postoperative hemorrhage complications were evaluated.

**Material and Methods:** The files of 185 patients who underwent the Whipple operation in our hospital in the last five years were evaluated retrospectively, and we attempted to determine the causes of hemorrhage. It was found that 13 (7%) patients experienced hemorrhage, and six of them were found to have died. In six of these cases, hemorrhage occurred due to fistulas from the portal vein, gastroduodenal artery, and pancreatic arteries at variable periods. Two cases were found to have developed disseminated intravascular coagulation as a result of sepsis. Early intervention was performed in two cases who bled from the meso veins and in one case who bled from the portal vein. Laparotomy and hemostasis were performed on a patient who bled from the gastric anastomosis line. In a patient who had been taking low molecular weight heparin, bleeding from the drains and nasogastric tube stopped following cessation of the drug.

**Discussion:** Preventive procedures such as connection of the vascular structures, use of vascular sealants, omental patching during surgery, and reducing the risk of complications by using somatostatin analogs were performed to prevent hemorrhages after Whipple surgeries.

**Results:** In addition to known methods, angiography and embolization are emerging as effective methods in the diagnosis and treatment of hemorrhages. Furthermore, the determination and elimination of independent risk factors, such as jaundice, that affect fistula formation and bleeding in the perioperative period is important for prevention

**Keywords:** Complication, hemorrhage, pancreas, treatment, Whipple operation

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## INTRODUCTION

The Whipple operation is an essential surgical technique for periampullary tumors; however, its high morbidity (30% to 60%) and mortality (5%) rates are problems that should be addressed (1-3). Pancreatic fistulas (2% to 62%) are among the most common complications after the Whipple procedure (1, 4). The incidence of postoperative hemorrhage is 5% to 20.2% in the literature. Mortality due to hemorrhage is reported as 15% to 58% (1, 5-7). Hemorrhages may arise from the suture lines in the early period; here, we evaluate the data and results from our clinic regarding postoperative hemorrhage problems in cases who developed infections and fistula in the days following surgery.

## MATERIAL AND METHODS

The files of 185 patients who underwent the Whipple operation in our hospital in the last five years (2011 to 2015) were evaluated retrospectively; we also attempted to determine the causes of hemorrhage. As a routine procedure, all patients signed consent forms containing information about the routine procedures and complications. Cases who had hemorrhoids, anal fissure, etc. were excluded from the study. Our patients were classified as A, B, or C (Table 1) on the basis of the postoperative pancreatic hemorrhage (PPH) consensus classification by the International Study Group of Pancreatic Surgery in 2007 as onset of hemorrhage (early or late), localization (extraluminal or intraluminal), and intensity (mild or severe) (5, 6). Hemorrhages that were seen in the first 24 hours were identified as early hemorrhage. Leaking hemorrhages that originated from drains or nasogastric tubes in the early postoperative period, those that stopped spontaneously, and those that did not alter the patient's hemodynamic stability were not taken into consideration. Mild hemorrhage was identified as the condition where the patient was hemodynamically stabilized or where no need for any interventional or surgical procedures was identified during follow-up of the patient. Severe hemorrhage was identified as hemorrhage with a high flow rate, originating from the drains or lumens, that altered the hemodynamic stability of the patient. The deaths that were seen in the postoperative 30 days were accepted as postoperative death. In our hospital, low molecular weight heparin (LMWH) is administered routinely 12 hours after surgery and

Table 1. Patient characteristics

Patient no	Age/ Sex	Indication for Whipple/PD	Etiology	Bleeding site	ISPG group	Onset of bleeding	Procedure	Outcome
1.	58/M	Bile duct tumor	PO arrest-CPR-sepsis	DIC	C	Day 5	ICU	Died
2.	65/M	Pancreatic carcinoma	PJ hematoma	Pancreatic artery?	B	Day 4	Primary suture	Died
3.	66/M	Pancreatic carcinoma	Fistula	GDA	B	Day 35	Laparotomy+primary suture+angiography+embolization	Survived
4.	60/M	Ampullary cancer	LMW heparin	Drain+nasogastric sond	A	Day 14	Cessation of LMW heparin	Survived
5.	69/M	Ampullary cancer	Pancreatic fistula, sepsis	DIC	C	Day 11	ICU	Died
6.	42/F	Pancreatic carcinoma	Inadvertent surgery?	GJ anastomosis	A	Day 1	Laparotomy+gastrostomy+primary suture	Died
7.	65/F	Ampullary cancer	Pancreatic fistula	Portal vein		Day 8	Laparotomy+primary suture	Survived
8.	74/M	Pancreatic carcinoma	Pancreatic fistula	Portal vein	C	Day 27	Angiography+laparotomy+primary suture	Died
9.	67/F	Pancreatic carcinoma	Pancreatic fistula, PJ leakage+GJ leakage	Traumatic portal vein laceration?	C	Day 15	Laparotomy+primary suture	Died
10.	65/M	Bile duct tumor	Pancreatic fistula	GDA	B	Day 7	Angiography+laparotomy+primary suture	Survived
11.	58/M	Pancreatic carcinoma	Inadvertent surgery?	Mesenteric vein branches	B	Day 2	Laparotomy+primary suture	Survived
12.	67/M	Ampullary cancer	Pancreatic fistula	Mesenteric vein	C	Day 7	Laparotomy+primary suture	Died
13.	45/M	Pancreatic carcinoma	Inadvertent surgery?	Mesenteric artery and vein branches	B	Day 1	Laparotomy+primary suture	Survived

ISPG: international study group of pancreatotomy; GDA: gastroduodenal artery; PJ: pancreaticojejunostomy; GJ: gastrojejunostomy; PO: postoperative; DIC: disseminated intravascular coagulation; ICU: intensive care unit; PD: pancreaticoduodenectomy

is stopped if any hemorrhage is suspected. Angiography and embolization can be performed in daytime cases.

## RESULTS

A total of 185 pancreaticoduodenectomy surgeries, including 165 classical Whipple procedures and 20 pylorus-preserving surgeries, were performed in our hospital in the last five years (2011 to 2015) due to periampullary region tumors. Three of the patients were female, and 10 were male. The mean age was 61.6 years (ages 42 to 72).

It was found that in 13 (7%) of the patients who underwent operations, a procedure was performed due to hemorrhage. Among the patients who had follow-ups due to hemorrhages, nine (77%) underwent surgeries and six (46%) died in the early period (Table 1). In our series, pancreatic fistula was detected in 46 (24.8%) patients, and 6 (13%) of these patients had complications of hemorrhage due to fistulas. It was also found that endoscopic retrograde cholangiopancreatography (ERCP) was performed diagnostically in nine patients, a stent was placed to lower bilirubin levels in six patients, and a drain was placed with percutaneous transhepatic cholangiography in two patients.

In seven patients in our series, there was a combination of wide duct (4 to 7 mm) and soft pancreatic texture; the presence of fistula was detected in three of these patients as a cause of hemorrhage. In three of our cases, soft pancreatic texture and the presence of a 2 mm duct were detected. In three of our cases, normal pancreatic tissue was detected; the duct widths ranged from 2 to 5 mm (Table 1). Among our patients with hemorrhage, three of the five patients whose bilirubin

levels were high (direct bilirubin, range: 10.6 to 21.6 mg/dL) died as a result of hemorrhage complications. Another result we found in our patients is that serum protein levels were normal in three patients and below normal in the remaining patients. Platelet count was higher than normal in five of our patients and was normal in the remaining patients. In cases who did not develop fistulas, C-reactive protein (CRP) levels were within normal limits in the preoperative period, increased in the postoperative early period, and decreased progressively. In all the cases who developed fistula and anastomotic leakage, CRP levels continued to increase until clinical recovery was obtained. In general, it was found that in our patients who developed fistulas and had high CRP levels, blood calcium levels decreased and remained below normal.

Of our two cases who developed hemorrhage in the early postoperative period, one underwent surgery due to hemorrhage from the gastric anastomosis (nasogastric tube) and the other underwent surgery due to hemorrhage from the branches of the mesenteric vein (drain); both were discharged with complete healing. Six of our patients were found to bleed from the portal vein (three cases), gastroduodenal artery (two cases), meso veins, and pancreatic artery (one case) due to fistulas at variable periods. Hemorrhage from the portal vein after fistula was seen on the postoperative 8<sup>th</sup>, 15<sup>th</sup>, and 27<sup>th</sup> days; two of these patients died after surgery (Table 1). In one of the cases that was on follow-up due to a fistula and bleeding from the nasogastric tube, an anastomotic leakage was detected by endoscopy. The patient was taken into surgery on the postoperative 15<sup>th</sup> day; however, the patient died from a hemorrhage that was found to be due to erosion from the portal vein. In another patient who had blood coming out of the

drain on the postoperative 7<sup>th</sup> day, the hepaticojejunostomy and pancreaticojejunostomy were found to be opened, and hemorrhage from the pancreatic artery and branches of the mesenteric vein were found. In two cases, laparotomy was performed on the 2<sup>nd</sup> and 4<sup>th</sup> days due to bleeding from the drains; hemorrhages arising from the pancreatic artery and branches of the portal vein were repaired.

Two cases were found to have developed disseminated intravascular coagulation (DIC) as a result of sepsis; these patients died. In a patient who had been taking LMWH, bleeding from the drains and nasogastric tube stopped following cessation of the drug.

## DISCUSSION

Hemorrhage after Whipple surgery is a rare but serious complication that increases mortality. In the early period, hemorrhage may develop from technical problems, bleeding/clotting disorders, and factors related to the patient; in the latter periods, hemorrhage emerges as a serious problem during the course of fistula and anastomosis-related problems (1, 2). The hemorrhage incidence in the postoperative period reported in the literature (5% to 16%) was similar to the results of our series (7%). However, some publications report that the hemorrhage risk is higher (16% to 45%) in cases who develop fistulas (1, 4). Our mortality rate in the Whipple series was 8.5%, whereas that in our patients with hemorrhage was 46%.

First, a medical approach is preferred for the treatment of hemorrhages. In Grade A patients, a conservative approach is more frequently performed in the foreground, whereas in Grade B and C patients, additional processes are required to identify the localization of the hemorrhage. Nasogastric tube (35%), decrease in hemoglobin level (17%), hemodynamic instability (15%), blood coming out of the drains (11%), and the presence of melena (9%) may be helpful to determine the diagnosis and the source of bleeding (8). The source of bleeding can be determined by computerized tomography (CT) angiography in half of these cases (8). In cases where hemodynamic stability is preserved, the first actions are monitoring the patient's hemodynamic levels and drains. Darnis et al. (8) stated that in their case series of 285 cases with hemorrhage, the hemorrhages were stopped with a medical approach in 32% of cases; in 68% of cases, intervention (surgical, endoscopic, or embolization) was needed (9). In our series, CT angiography was performed in seven cases; hemorrhage from the portal vein was found in two cases, from the gastroduodenal artery in one case, and from the pancreatic artery in one case. The hemorrhage was stopped by embolization in one of these patients, and the rest underwent surgery. In a Grade A patient in our series, the hemorrhage stopped after conservative treatment and cessation of LMWH.

Hemorrhages into the lumen are seen in earlier periods. The most common type is hemorrhage arising from pancreaticojejunal anastomosis. In hemorrhages arising from gastrojejunal anastomosis, both diagnostic and therapeutic procedures may be performed by endoscopists. In a series by Eckardt et al. (10), they stated that the source of the bleeding may be detected and treated endoscopically in one third of hemorrhages arising from gastrojejunostomy. Variable approaches are used for this purpose, such as injection, sclerotherapy, and clip application.

It is expressed that the routine use of somatostatin analogs in the postoperative period to both suppress pancreatic secretion and prevent complications due to fistula, particularly bleeding in cases where fistulas developed, reduces morbidity; however, these analogs have no positive effects on mortality (11). However, in some cases, protective effects were reported (3). In our series, we found that the risk of hemorrhage was higher (13%) in patients who developed fistulas. We also use somatostatin analogs routinely in our patients with fistulas. Soft pancreatic texture, thinness of the pancreatic duct, and the presence of fistulas are defined as major risk factors for hemorrhage (8). Tani et al. (12) defined male gender, prolonged surgery, and blood transfusion as independent risk factors. Some studies report that parameters such as prolonged hospital stay, ERCP and stenting, the presence of preoperative jaundice, trauma/resection of the splenic vessels, additional surgical procedures, older age, the presence of intraabdominal infection, and nutritional risk index are factors that increase the risk of hemorrhage (2, 7-9, 12-14). Most of the factors mentioned above are present in our series (Table 1). We believe that even though ERCP and stenting provides an advantage in reducing the bilirubin levels of the patient, it may cause new problems, such as technical difficulties and increasing the risk of infection by reducing the diameters of the ducts. It was detected that the duct was thin and the texture of the pancreas tissue was soft in cases with continued pancreatic secretion from the duct, whereas the duct was wide and the texture of the pancreas tissue was hard in cases in which the duct of Wirsung was invaded by tumor.

Elevated CRP levels in the early postoperative period is an expected condition; however, continued elevation on the postoperative third day may be a precursor of fistulas and additional complications. In our series, the continuation of elevated CRP levels was evaluated as a precursor of fistula rather than hemorrhage. In the clinical study by Ansorge et al. (15), it was stated that elevated CRP levels may be an important precursor of fistula development (16).

In cases with hemorrhage, the first preferred methods for locating the hemorrhage site are contrast-enhanced CT, CT angiography, and interventional angiographic embolization (Figure 1). The hemorrhage site can be localized by contrast-enhanced CT in half of these cases (8). It is shown in studies that the most important causes are hemorrhages arising from the stump of the gastroduodenal artery or pancreatic vessels and rupture or erosion of the pseudoaneurysms of splenic vessels. It is stated that hemorrhages can be stopped in 50% to 80% of cases who underwent embolization (1, 8). Darnis et al. (8) recommend performing routine splenic artery embolization in cases with hemorrhage who underwent pancreaticoenteric anastomosis. Roulin et al. (1) state that angiography and embolization can be performed easily in all vessels except for the hepatic artery and mesenteric artery and that these procedures are at least as effective as surgery. In our series, foci of hemorrhages that arose from the portal vein (three patients), gastroduodenal artery (two patients), pancreatic artery, and mesenteric veins were detected in six of the Grade B and C cases. The hemorrhage from the gastroduodenal artery was successfully stopped by inserting an angiographic coil in only one of these cases. In 3 of 13 patients who underwent angiography, the bleeding site could be localized. However, in two of these patients, interventional coiling was not feasible

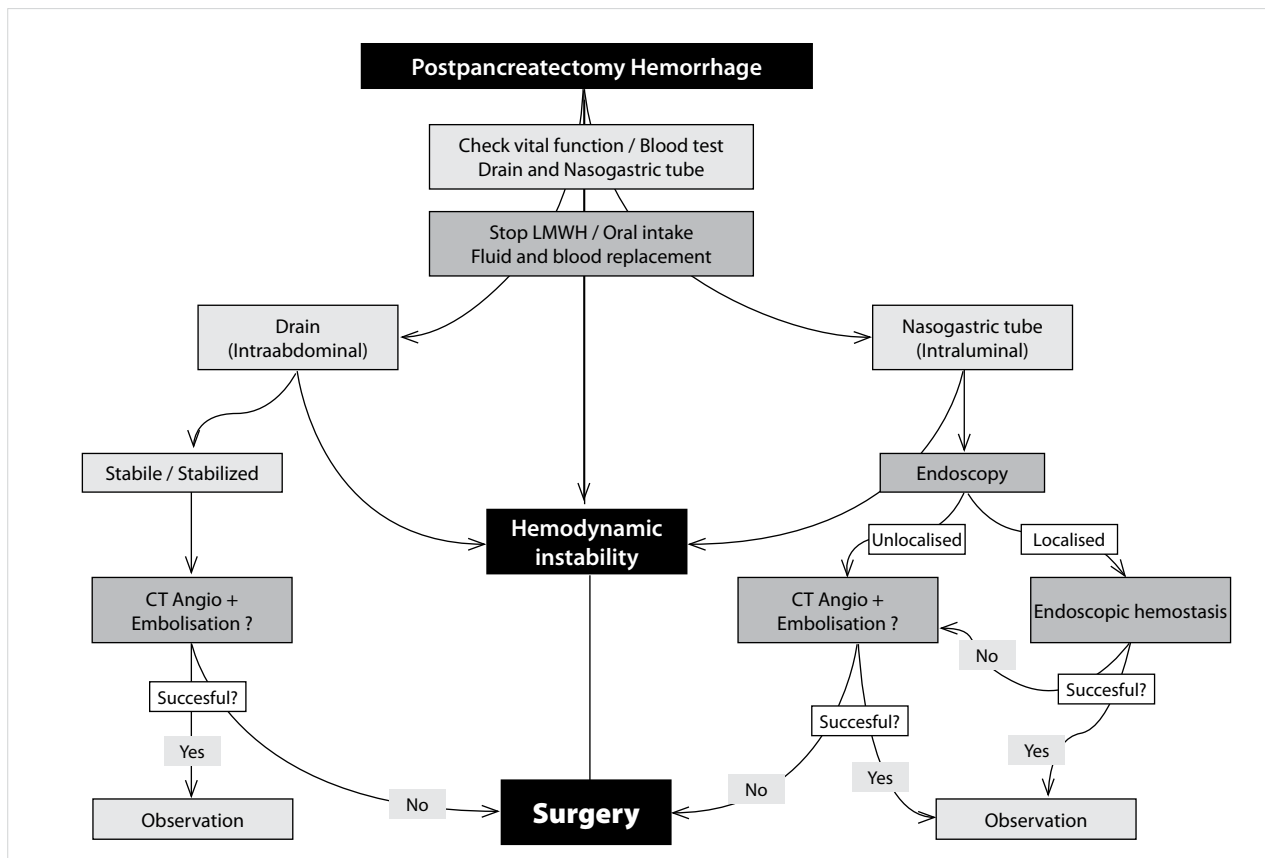


Figure 1. Algorithm for postoperative pancreatic hemorrhage

due to the direct vicinity of the bleeding source to the portal vein. These methods were performed during the day because our hospital does not have 24-hour availability of endoscopists and interventional radiologists.

Some studies suggest covering the mesenteric artery/vein and the stumps of cut splanchnic vessels with omental or falciform flaps to prevent hemorrhage (17-19). In a clinical study performed in Japan, it was stated that the risk of aneurysm development due to erosion is four times higher in patients without omental flap applications and that flaps are effective in preventing the formation of aneurysms (17). However, in the literature, in series with low numbers of cases, the use of omental flap is described as a protective and useful procedure, whereas in meta-analyses and Cochrane studies, the use of omental flap is not described as useful (12, 20, 21).

It is stated that hemorrhages arising from cut pancreatic surfaces are important in etiology (22). Binding the vascular structures in pairs, using vessel sealers, and performing omental patches are suggested methods to prevent hemorrhages arising from pancreatic vessels. Adherence to the rules of surgical technique and hemostasis plays an important role in preventing hemorrhages in the early period (14, 23, 24). Surgery remains the only option in conditions when conservative approaches, radiologic intervention, and endoscopic procedures are insufficient (Figure 1). Surgical treatment is performed in 30% to 49% of hemorrhages seen in patients with pancreaticoduodenectomy (1, 23, 25, 26). In our series, this rate was found to be 77% due to our lack of 24-hour availability of endoscopy and interventional radiology.

## CONCLUSION

In addition to known methods, angiography and embolization are emerging as effective and promising methods in the diagnosis and treatment of hemorrhage. Furthermore, the determination and elimination of independent risk factors, such as jaundice, that affect fistula formation and bleeding in the perioperative period is important for prevention.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - O.N.D.; Design - O.N.D.; Supervision - O.N.D.; Resource - O.Ö., N.C., T.A.; Materials - O.Ö., N.C., T.A.; Data Collection and/or Processing - E.Ö.G., M.H., S.C.Ç.; Analysis and/or Interpretation - O.N.D., E.Ö.G.; Literature Search - M.H., O.N.D.; Writing Manuscript - O.N.D.; Critical Reviews - O.N.D., M.H.

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