

## Delayed Postoperative Hemorrhage after Pancreaticoduodenectomy

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### ABSTRACT

#### **PURPOSE**

To propose an analysis of treatment between RE-Laparotomy (RE-LAP) versus Arterial Embolization (AE) related to Delayed Post-operative Hemorrhage (DPH) management.

#### **MATERIALS AND METHODS**

We have retrospectively evaluated PUBMED articles to analyze what is the best method for Delayed Post-operative Hemorrhage (DPH) management.

#### **CONCLUSION**

Not significant advantages or disadvantages were found comparing RE-LAP *versus* AE.

#### **KEYWORDS**

Delayed postoperative hemorrhage; Pancreatoduodenectomy; Arterial embolization

#### **INTRODUCTION**

Duodenopancreatectomy (DPC) is the gold standard surgery for the treatment of malignant tumors of the duodenum, periampullary tumours and tumours of the head of the pancreas. It is burdened by a high morbidity and mortality, which, in recent decades, have seen their reduction thanks to a greater selection of patients, an improvement in surgical techniques, a dedicated anesthetic management and the establishment of high-volume centers. However, morbidity and post-operative mortality still remain high [1].

The complications of DPC are varied and are divided into early and delayed. By early, we mean the complications that occur within 24 hours of resection and late those after 24 hours or after several days. Among the early complications, certainly, the greatest incidence is bleeding that often requires, re-laparotomy. Among the late complications, we highlighted anastomotic leakages, especially pancreatic-jejunosomy leaks, Delayed Gastric Emptying (DGE), pancreatic ascites and Delayed Post-operative Hemorrhage (DPH).

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Postoperative bleeding represents a life-threatening complication after pancreatic surgery [2,3]. The International Study Group of Pancreatic Surgery (ISGPS) has defined post pancreatectomy hemorrhage by schematizing it as follows: time of onset of the hemorrhage, cause, location of the hemorrhage and, finally, severity of the hemorrhage [4]. The ISGPS suggests a cut-off of 24 hours, while many studies used cut-offs of 5 days - 7 days post-surgery to define 'late' bleeding [5-8]. Delayed bleeding is not easy to diagnose and to treat. Treatment involves embolization angiography or re-laparotomy [9-11]. The use of arterial embolization as a minimally invasive technique has offered new alternatives to the treatment of this serious complication, giving an alternative treatment as well as surgery in these high-risk patients [12]. In the literature, in general, it is reported incidence rates range from 1% to 12% but it seems to attest the incidence was 3.9 per cent and it seems that one third of patients died when it happened [13,14].

## **METHODS**

We have retrospectively evaluated PUBMED articles. Studies was evaluated from 1990 to 2020. Only very few studies analyzed a "Delayed Postoperative Hemorrhage after Pancreaticoduodenectomy". Two independent research DC and SL performed the review. The search terms were identified with medical subject heading (MeSH). Research inclusion criteria were "pancreatoduodenectomy delayed post-operative hemorrhage (DPH), arterial embolization". The object of this retrospective study is to analyze treatment between Arterial Embolization (AE) *versus* Re-Laparotomy (RE-LAP) in Delayed Postoperative Hemorrhage After Pancreaticoduodenectomy. The point estimate of the odds ratio was considered to be statistically significant at the level of  $P < 0.5$ . The outcomes were complete hemostasis, morbidity, and mortality.

## ***Current Status of Knowledge***

Schäfer et al. [1] performed a retrospective analysis of 18 patients who had DPH. The authors noted that in 78% of cases there was a leak of the pancreatic-jejunal anastomosis resulting in the formation of pseudoaneurysms. Of these patients 10 were referred for arterial embolization (AE) and achieved arrest of bleeding, 2 died for massive re-bleeding, while 5 out of six of them who underwent a RE-LAP died. The study further highlights the fact that immediate CT scan with contrast is the gold standard, that pseudoaneurysm is often the cause of bleeding, and that use of RA is often t is currently the most life-saving approach. Tien et al. [6] on 402 patients, stated a p value of 0.005 when pancreatic fistulas or biliary leak were present. This combination provided the highest estimate of massive bleeding. In their study, Choi et al. [7] on 1008 DPC had 14 DPH. On 14, ten had pancreatic fistulas. 71.4% had sentinel bleeding. The therapeutic modalities included interventional therapy (n = 8) and surgery (n = 5), 1 died before treatment. According to the therapeutic modalities, the re-bleeding rate, morbidity and final mortality of two groups were 50.0% vs 40.0% ( $P = 0.83$ ), 75.0% vs. 60.0% ( $P = 0.96$ ) and 50.0% vs 80.0% ( $P = 0.62$ ) respectively. Sato et al. [14] published a retrospective analysis of 10 patients who underwent a DPH, of which 8 underwent A.E. and 5 of these had a total stop of bleeding with a success rate of more than 60%. However, the authors underline that a 40% mortality due to complications of A.E. Brodsky et colleagues [15] focused their attention on the early recognition of bleeding in DCP with pancreatic fistula and showed that out of 5 patients with sentinel bleeding, 3 of these performed A.E. with complete arrest of bleeding. For these reasons, the study highlights the fact that the recognition of a fistula associated with one or more episodes of sentinel bleeding, can help in an early treatment of the patient and can contribute to change the prognosis.

Yoshida et al. [16] treated 6 patients with delayed massive bleeding between 14 days and 38 days later. One patient with bleeding from the left gastric artery stump was treated with RE-LAP. Two patients with hemorrhage from the gastroduodenal artery stump were successfully treated with selective embolization of the common hepatic artery. The remaining two patients died of re-bleeding or hepatic failure following hemostasis. Okuno et al. [17] observed 6 bleeds of pseudoaneurysms after duodenopancreatectomy and two after hepatopancreaticoduodenectomy in the postoperative time of 910 hepatobiliopancreatic procedures. They observed an onset of rupture of a pseudoaneurysm mean of 35.4 days (range 12-76). In all of them pancreatic leak and abscess were present. Hemostasis was obtained in near 85% of patients with A.E. The study concluded that "Early detection and immediate embolization might bring about a favorable outcome in patients with hepatobiliary pancreatic diseases". Ota et al. [18] also stressed the importance of early recognition of bleeding and the efficacy of angiography on 5 patients treated for DPH after pancreas surgery. Santoro et al. analyzed two patients on 84 DPC about 2.3% with DPH, between the 8th and the 30th post-operative days. Unlike the other studies, they reported a surgical treatment with suture ligation of the stump of the gastroduodenal artery or completion pancreatectomy or a new pancreaticojejunostomy. The mortality was 50%. Yoon et al. [19] found a percentage of DPH about of 4% noticing a DPH occurred in 21 patients on 456 DPC. Of them, five patients had early bleeding and they were treated by RE-LAP and 16/21 cases had DPH after about 5 days, of which 12 patients (75%) had pancreatic leaks and 8 pseudoaneurysms of major arteries. "Sentinel bleeding" was evident in 8/16 cases. Angiographic embolization was performed in 8 cases, 7/8 of which were successful. Reoperation was tried in 7 cases with complete hemostasis being achieved only in 2.

The mortality rate was 28.6% (6/21). Balachandran et al. [20] conducted a retrospective study on 218 cases of DPC. Forty-four on 218 had bleeding. Makowiec et al. [21] noted only 14 DPH after 336 patients performed DPC in a time between 7 and 72 days. All 14 patients had intra-abdominal septic complications. AE was successfully in 85.7% of cases as the first-line diagnostic and treatment choice. Koukoutsis et al. [22] had highlighted 32 on 362 patients has DPH in the first 30 days after DPC. They found pancreatic leak, sepsis and sentinel bleed as risk factors for post-PD haemorrhage ( $p < 0.05$ ). Boggi et al. [23] found the same results of literature in their retrospective study of 818 patients.

### **CONCLUSION**

The etiology of DPH appears to be multifactorial. Often Post-Operative Pancreatic Fistula (POPF) or pancreatic and biliary fistula due to anastomotic leaks, the formation of infected abscesses and sepsis, associated with the manipulation and skeletonization of the vessels due to lymphadenectomy, seem to be the major causes of bleeding predispositions that may destroy vascular structures and sutures [13,24-26]. Some studies have shown that bleeding is due to these reasons for 66 percent of cases and, of these, as many as 30% to 90% percent are due to pseudoaneurysms of the superior mesenteric artery (SMA) or branches of the coeliac trunk [2,27-29]. Pancreatic-jejunosotomy leakage seems to be the most frequent cause of a pseudoaneurysm in more than 75% of patients. For this reason, the prevention of pancreatic fistula becomes important because the leak predisposes to pseudoaneurysms and the latter to delayed and massive bleeding. Patients with known pancreatic fistulas, therefore, must be followed closely to diagnose and prevent DPH in time [1]. Bleeding into the gastrointestinal tract generally becomes clinically than peritoneal bleeding. Extraluminal Bleeding, in more than 30 percent, is preceded by a sentinel bleeding event from the drainage.

This sentinel event requires immediate aggressive treatment by the surgeon [6,15,30,31]. DPH may require invasive treatment such as RE-Laparotomy or non-invasive treatment such as arterial embolization angiography. Sometimes the two treatments can be combined. From the study of the literature, comparing the two treatments confirming as a goal the arrest of bleeding, morbidity and post-operative mortality, we did not show a p value <0.5. So, we can deduce that the two treatments show no big difference in results. Keep in mind, however, that for RE-LAP it has the enormous advantage of carrying out haemostasis, by linking the affected arterial or venous vessels, allowing to identify the cause of bleeding, to resolve the cause by eliminating the pancreatic anastomosis and any abscess. However, however, the RE-LAP, if we look at the numbers, has a morbidity of 70% and a mortality of 40%. On the other hand, embolization has the advantage of being less invasive with h reported success rates ranging from 80% to 100% of stopping bleeding [12,13,15,17,21,26,29], a morbidity of 30% and a mortality of 20% but, however, it does not resolve the underlying cause of the bleeding [17,18,32,33-35]. Embolization should be as selective as possible to minimize organ ischaemia. If A.E. is not selective, it can cause cholangitis, abscess, hepatic failure. Other disadvantage is the fact that it cannot resolve venous bleeding [27]. We believe that the treatment of choice is very much based on the patient's condition. If the patient is hemodynamically stable, we can perform an embolization. If the patient is hemodynamically unstable or the cause of the hemorrhage cannot be resolved with angiography, RE-LAP is required. DPH after DPC surgery must be attributed to a hemorrhagic pseudoaneurysm of a major visceral artery until proven otherwise. For these reason, repeated episodes of minor bleeding may be the pathognomonic sign preceding massive bleeding and should therefore require immediate diagnostic workout to avoid the occurrence of hemorrhagic shock [1,36,37,38].

### ***What is Known about this Topic***

- Morbidity and post-operative Mortality of DCP still remain high.
- Delayed Post-operative Hemorrhage(DPH). Delayed bleeding is not easy to treat. Treatment involves embolization angiography or re-lapartomy.
- Repeated episodes of minor bleeding may be the pathognomonic sign preceding massive bleeding and should therefore require immediate diagnostic workout to avoid the occurrence of hemorrhagic shock.

### ***What this Study Adds***

- If the patient is hemodynamically stable, we can perform an embolization. If the patient is hemodynamically unstable or the cause of the hemorrhage cannot be resolved with angiography, RE-LAP is required.
- The RE-LAP, if we look at the numbers, has a morbidity of 70% and a mortality of 40%. It has the enormous advantage of carrying out hemostasis, by linking the affected arterial or venous vessels, allowing to identify the cause of bleeding, to resolve the cause by eliminating the pancreatic anastomosis and any abscess.
- A.E. has the advantage of being less invasive with the same percentage of stopping bleeding, a morbidity of 30% and a mortality of 20% but, however, it does not resolve the underlying cause of the bleeding. It can cause cholangitis, abscess, hepatic failure. other disadvantage is the fact that it cannot resolve venous bleeding.

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### **HUMAN RIGHTS STATEMENT**

All procedures and experiments met the ethical standards.

### **COMPETING INTERESTS**

The authors declare no competing interests.

### **AUTHORS' CONTRIBUTIONS**

All the authors have read and agreed to the final manuscript.

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