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# Acute and Chronic Pancreatitis — Complications

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Additional information is available at the end of the chapter

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## 1. Introduction

Over the course of pancreatitis, the first two to four days of symptoms are the most important because this is the period during which 15% to 25% of patients evolve to its severe form. According to clinical and experimental data, this period is characterized by an initial state of hypovolemia.

It is known that the morbidity of severe acute pancreatitis appears in two stages. The first two weeks are characterized by a systemic inflammatory response syndrome (SIRS), which results from release of inflammatory mediators.

Organ failure is common and often occurs even in the absence of infection. The early mortality rate is 42 to 60%.

The second stage begins around two weeks after the start of symptoms and is characterized by sepsis-related complications that result from the infection of pancreatic necrosis. Thus, there is an association with systemic complications, like pulmonary insufficiency, kidney failure and cardiovascular insufficiency, known as multiple organ failure syndrome (MOFS).

The inflammatory mediators are primarily released from the area of the viscera and they rise to the systemic compartment mainly through the lymphatic circulation and the circulation of the portal and suprahepatic veins. The lungs are the first organ to be reached by blood and lymph that are rich in activated polymorphonuclear cells, cytokines and other active biological compounds. Failure of the gastrointestinal barrier that enables translocation of bacteria and endotoxins is considered to be one of the major factors responsible for the development of local infection and multiple organ failure that is seen in severe acute pancreatitis, which is responsible for the majority of the deaths.

Independent of the etiology of the acute pancreatitis, once the inflammatory events of the acinar cells have started, this will lead to progression to SIRS. Among the commonest complications, those of the lungs occur most frequently and are potentially the most serious. The spectrum of these complications goes from hypoxemia to acute respiratory distress syndrome (ARDS). [1]

## 2. Hypoxemia without radiological alterations

Tachypnea, moderate respiratory alkalosis and hypoxemia are observed in around two thirds of the patients with acute pancreatitis, over the first 48 hours. This hypoxemia does not match the severity of alterations indicated by examinations. Radiological alterations are only present in 11% of the cases.

However, a study by Lankish *et al.* (1996) [2] showed that around 30% of the patients present PaO2 values lower than 60 mmHg and 63% lower than 70 mmHg.

Respiratory failure develops in around:

- 10% of the cases of mild acute pancreatitis;

- 47% of the cases of sterile pancreatic necrosis;

- 74% of the cases of infected necrosis.

The main cause of hypoxemia is disorders of ventilation/perfusion, which may give rise to an intrapulmonary shunt in around 30% of the cardiac output. The incidence of respiratory failure is unrelated to etiological factors, patients' ages, amylase values, calcium levels or use of fluid therapy. In several studies, a correlation has been found between the degree of hypoxemia and mortality, reaching rates of 14% when PO2 is lower than 60 mmHg.

Some authors have considered that not recognizing hypoxemia and hypovolemia immediately is the most important factor in occurrences of multiple organ failure triggered during the first week. [1]

## 3. Hypoxemia with radiological alterations

In one third of the patients with acute pancreatitis, respiratory complications are detected radiologically. Pulmonary infiltrates or atelectasis are found in 15%, pleural effusion in 4% to 17% and pulmonary edema in 8% to 50%. The morbidity and mortality rates are significantly higher than those in cases of hypoxemia without radiological alterations.

**Pleural effusion** is today considered to be a sign of poor prognosis, with associated mortality of 20% to 30%. It is usually of small proportions and occasionally hemorrhagic, and is characterized by high amylase levels (up to 30 times higher than in serum) and high protein and lactate dehydrogenase levels. Most cases of pleural effusion occur on the left side (68%), while

22% are bilateral and 10% are on the right side. The two main causes are transdiaphragmatic lymphatic blockage and pancreatic-pleural fistulas due to rupture of the pancreatic canal or a pseudocyst. (Fig. 1)
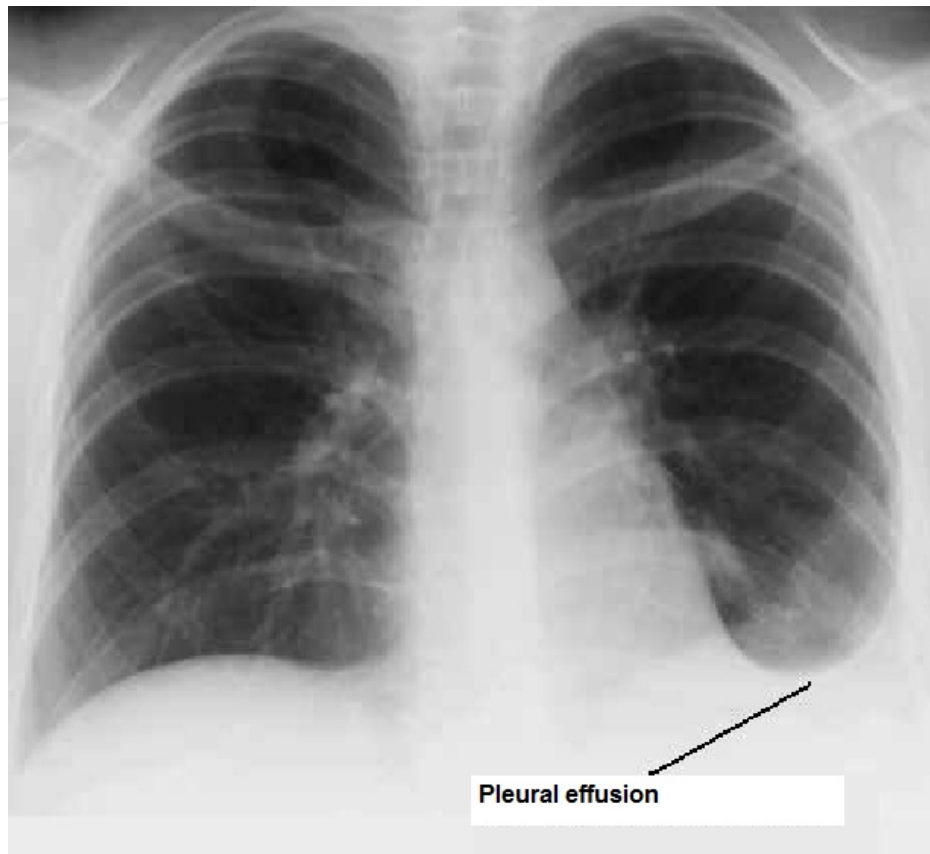


**Figure 1.** Chest x-ray showing left-side pleural effusion

The treatment for pleural effusion is often initially conservative. However, large pleural effusions frequently become symptomatic are require thoracocentesis and endotracheal intubation. When the abdominal pathological condition has been resolved, the pleural effusions are often also resolved. Chronic pleural effusions often necessitate an abdominal approach: drainage of the pseudocyst or abscess and, possibly, resection of the path of the fistula, so as to completely resolve the condition.

**Atelectasis** occurs due to diminution of the quantity of surfactant and is a frequent complication. Because the primary lesion is at the alveolar-interstitial level, this decreases the pulmonary compliance and increases the ventilatory effort, thus leading more quickly to diaphragm fatigue. As previously mentioned, pro-inflammatory cytokines have a preponderant role in the systemic complications of acute pancreatitis. Some experimental studies have shown that TNF-$\alpha$ and IL-1 have a negative inotropic synergic effect on the contractility of the diaphragm, i.e. showing that cytokines also contribute towards atelectasis through diminishing ventilation. [1, 3] (Fig. 2)

**Figure 2.** Chest x-ray showing left-side pulmonary atelectasis

## 4. Acute Respiratory Distress Syndrome (ARDS)

ARDS is the most severe pulmonary complication. It occurs in 15% to 20% of the patients with acute pancreatitis and its mortality rate is 56%. It is responsible for 50% to 90% of all deaths due to pancreatitis. Despite being more frequent in cases of severe acute pancreatitis, it may occur in cases of mild forms, in around 10% of these cases.

ARDS usually manifests between the second and seventh day after the start of acute pancreatitis, but it may have faster evolution. Clinically, it presents with severe dyspnea and extreme hypoxemia that is refractory to supplementation with high concentrations of oxygen. Multilobular pulmonary infiltrates are also observed.

The physiopathology of ARDS remains unclear, but the action of the pancreatic enzymes and inflammatory mediators released by the pancreatic lesion seems to have a key role. ARDS has been described as increased pulmonary vascularization with protein transudation to the alveolar space and decreased pulmonary compliance, manifested clinically by refractory hypoxemia and radiologically by diffuse pulmonary infiltrates. Experimental studies have suggested that acute pancreatitis and its respiratory complications should be treated by combating the pro-inflammatory response, thereby necessitating better comprehension of the physiopathology and the drugs that potentially inhibit this response. [1]

## 5. Kidney failure

Kidney failure is present in around 15% of the cases of mild acute pancreatitis and in 35% to 43% of the cases of severe pancreatitis.

The evolution to kidney failure is influenced by the severity of the episode of acute pancreatitis. The presence of kidney failure notably worsens the prognosis for cases of acute pancreatitis, given that the mortality rate is much higher than in cases without kidney failure. Higher urea levels are one of the items in Ranson's criteria, thus corroborating the relationship between renal alterations and the severity of the episode. The kidney failure that accompanies acute pancreatitis is of pre-renal origin in most cases. It is worth emphasizing that episodes of acute pancreatitis should not be ruled out as a cause of kidney failure even in the absence of hyperamylasemia. There should be strong diagnostic suspicion, given that normal amylase levels are found in around 19% to 32% of the patients with acute pancreatitis. [1]

## 6. Pseudocysts

Pancreatic pseudocysts can be defined as organized accumulations that are rich in pancreatic enzymes, which arise as a consequence of and remain after an episode of acute pancreatitis or after exacerbation of chronic pancreatitis. Their content is variable but is predominantly fluid. They may or may not present necrotic material and debris, and they are rich in amylase and lipase. Biochemical studies on their content have demonstrated that the carcinoembryonic antigen (CEA) levels are low but that the CA 19.9 levels may be high. These pseudocysts have low viscosity and cytological evaluations show that inflammatory cells predominate.

These are the commonest cystic lesions associated with pancreatic diseases. They are a relatively common complication in adult patients with a diagnosis of pancreatitis, occurring in 16%-50% of the cases of acute pancreatitis and in 20%-40% of the cases of chronic pancreatitis.

Pseudocysts are initially connected to the pancreatic duct system, either directly or indirectly via the pancreatic parenchyma. Two thirds of the patients with pseudocysts have demonstrable connections between the pseudocyst and the pancreatic duct, when the duct is ruptured on the posterior face. In one third of the cases, there is a very significant inflammatory reaction that seals the connection such that it is not demonstrable. [4]

### 6.1. Etiology

Alcoholic pancreatitis seems to be the biggest cause of pseudocysts in countries in which alcohol consumption is high, and this accounts for 59% to 78% of all the cases. Biliary pancreatitis is most commonly in second place among the causes. Patients with chronic pancreatitis who develop acute exacerbations seem to have greater incidence of pseudocysts than do patients with acute pancreatitis. Patients with biliary acute pancreatitis present it with a lower incidence. [4]

## 6.2. Classification

Pancreatic cystic lesions were classified by D'Egidio and Schein, in 1992, as follows:

- Type I: post-necrotic, arising after episodes of acute pancreatitis, without identifiable abnormalities in the pancreatic ducts; rarely, they are in communication with a pancreatic canal;

- Type II: occurring in cases of chronic pancreatitis that become acute; recognized through alterations in the pancreatic ducts, with which the pseudocysts are often in communication;

- Type III: retention pseudocysts from calcifying chronic pancreatitis, proven by characteristic ductal alterations or the presence of intracanalicular calculi (calcifications).

In 2002, Nealon and Walser proposed another classification system that was more detailed, composed of seven different types that were based on the ductal anatomy and its relationships with the pseudocyst. [5]

## 6.3. Differential diagnosis between pseudocysts and cystic tumors

The main differential diagnosis for pancreatic pseudocysts is made in relation to cystic neoplasia of the pancreas. The main categories are summarized in Box 1, along with their essential characteristics. (Table 1)

|  | SCA | MCN | IMPN | SCPN | Pseudocyst |
|---|---|---|---|---|---|
| **Age** | Middle age | Middle age | Elderly | Young | Variable |
| **Gender** | Female | Female | Male | Female | Male |
| **Presentation** | Mass/pain | Mass/pain | Pancreatitis | Mass/pain | Pain |
| **Location** | Entire pancreas | Tail and body | Head | Entire pancreas | Entire pancreas |
| **Malignant potential** | Very low | Moderate to high | Variable | Low | None |

**SCA**-serous cystadenoma; **MCN**-mucinous cystic neoplasm; **IMPN**-intraductal mucinous papillary neoplasm; **SCPN** – solid-cystic pseudopapillary neoplasm

**Table 1.** Differential diagnosis of cystic lesions of the pancreas

The examinations most used for making the differential diagnosis and for making therapeutic decisions are multichannel computed tomography (CT) scans, magnetic resonance imaging (MRI) with pancreatic resonance, endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (US). (Fig. 3)

The sensitivity varies. If on the one hand, ERCP should be weighted carefully because of its complications, on the other hand it provides a dynamic and anatomical view of the pancreatic duct.

**Figure 3.** Abdominal CT scan showing pancreatic pseudocyst

Pancreatic resonance does not present the complications of ERCP, but it does not provide the same standard of imaging and information about the pancreatic duct. CT is more widely used, but it does not define the anatomy of the pancreatic duct so well. Endoscopic US has the advantage of also supplying punctured material from inside the accumulation for biochemical and other analyses, but it is not yet universally available. Recent studies have proven the relevance of such information for making the differential diagnosis of pseudocysts, as shown (Table 2). [6]

|  | SCA | MCN | MCA | Pseudocyst |
|---|---|---|---|---|
| **CEA** | low | high | high | low |
| **CA 125** | variable | variable | high | low |
| **CA 19-5** | variable | variable-high | variable-high | variable |
| **Amylase** | low-high | low-high | low-high | high |
| **Lipase** | low | low | low | high |

**SCA**-serous cystadenoma; **MCN**-mucinous cystic neoplasm; **MCA**-mucinous cystadenoma

**Table 2.** Differential diagnosis of cystic lesions of the pancreas

### 6.4. Box 2

Before dealing with any peripancreatic accumulation, the differential diagnosis between pseudocysts and cystic neoplasms of the pancreas needs to be established. In this process, a variety of factors need to be comprehended, reviewed and investigated, such as the history of the disease and previous imaging examinations (when available). In some cases, biochemical and cytological analyses should be performed on the peripancreatic fluid.

If a peripancreatic fluid accumulation becomes established due to an episode of acute pancreatitis and then persists for several weeks, the diagnosis of pseudocyst is confirmed. This direct relationship between episodes of pancreatitis and appearance of pseudocysts may be particularly more difficult to establish in cases of chronic pancreatitis. On the other hand, cystic neoplasms may give rise to a moderately inflammatory process in the pancreas that, in turn, may mimic chronic pancreatitis. This situation is particularly more frequent in cases of intraductal mucinous papillary tumors. [7]

It is important to review all the radiological examinations on the patient that are available. An abdominal CT scan may define the presence or absence of cystic lesions over time. When this possibility does not exist, MRI and endoscopic US examinations may aid in making the differential diagnosis. Both of these may reveal septal divisions, solid components inside the cyst or communication between the cyst and the main pancreatic duct. [8]

It is worth emphasizing that communication between the main pancreatic duct and the cyst may occur both in cases of chronic pancreatitis with an association pseudocyst and in cases of mucinous papillary neoplasia of the main duct. In the first case, other signs are generally seen to be associated with the chronic pancreatitis, such as calcifications and multiple ductal stenosis. In the second case, the cystic lesion is associated with dilatation of the main pancreatic duct. If the diagnosis nonetheless still remains undefined, aspiration should be performed on the cyst, for histological analysis and biochemical tests. [9]

## 6.5. Clinical picture

The clinical presentation of pancreatic pseudocysts may vary from asymptomatic to major abdominal repercussions caused by the possible complications. The acute complications include bleeding (generally from pseudoaneurysms of the splenic or hepatic artery), infection and rupture. The chronic complications include obstruction of the pylorus, biliary obstruction and thrombosis of the splenic or portal vein with development of gastric varices.

## 6.6. Treatment

For acute fluid accumulations, no intervention is necessary, since most of these tend to resolve spontaneously. If pseudocysts develop, the current knowledge suggests that, depending on their characteristics and location, they can be treated expectantly unless they present related symptoms or complications: abdominal pain, early satiety, weight loss and persistent fever [9]

## 6.7. Surgical treatment

The classical surgical options are cystogastrostomy, cystoduodenostomy and Roux-en-Y cystojejunostomy, depending on the location of the cyst. Laparoscopic approaches have progressively become more used over the last decade. Even so, and despite the growth of less invasive techniques such as endoscopic, percutaneous and ultrasound-guided drainage, controversy still exists in the literature regarding the best form of therapeutic approach for pancreatic pseudocysts. [11]

### 6.8. Percutaneous drainage

A recent cohort study showed that percutaneous drainage is associated with high mortality, prolonged hospital stay and greater incidence of complication than seen with surgical drainage. Although percutaneous drainage seems to be convenient for both physicians and patients, it should only be performed in patients with acute pseudocysts that are radiologically associated with normal ductal anatomy, or in cases in which the associated comorbidities make surgery a high-risk procedure. The main predictors for failure of this method are sudden ductal obstruction (cutoff), communication between the cyst and the pancreatic duct and an association with chronic pancreatitis. [11, 12]

### 6.9. Endoscopic drainage

ERCP is better than magnetic resonance cholangiopancreatography (MRCP) for characterizing the pancreatic duct. In cases of chronic pancreatic pseudocyst, endoscopic treatment is currently used as an initial option, except in patients with chronic pain, biliary obstruction or pseudocysts involving the pancreatic tail. Two different types of approach are used: (1) transmural endoscopic drainage (transgastric or transduodenal); and (2) transpapillary drainage.

The transpapillary approach requires that the pseudocyst is in communication with the main pancreatic duct and that there is no significant septum formation that would impede complete drainage. Any ductal stenosis that might be identified can be dilated using a balloon, and then an endoprosthesis is placed inside the pancreatic duct.

For transmural drainage to be performed safely, certain inclusion criteria need to be observed: six weeks of clinical treatment without regression; size greater than or equal to 4 cm; distance between the gastroduodenal wall and the pseudocyst wall less than or equal to 1 cm; absence of associated neoplastic processes; and evident bulging of the gastroduodenal wall. [13]

### 6.10. Technique

- Endoscopic retrograde pancreatography is performed in order to study the duct and classify the cyst;

- The area of the gastroduodenal segment with the greatest bulging, as seen on tomography and endoscopy, is identified;

- The area selected is punctured using an endoscopic sclerosis needle (10 x 4 mm), in order to confirm its proximity to the cyst;

- A fistula is constructed from the gastrointestinal tract (duodenum or stomach) to the pseudocyst, by means of a semi-open polypectomy loop connected to an electrocauterization device, using only the coagulation function, in monopolar mode, at an intensity of 30 watts;

- The cyst is immediately cannulated using a cholangiography catheter and nonionic iodinated contrast is injected to document and certify the cyst, with placement of one or two
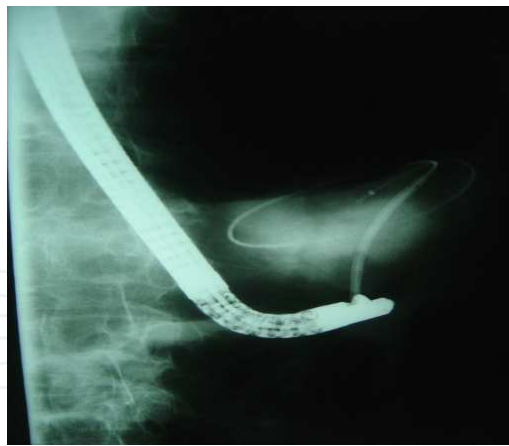
pigtail biliary stents of caliber 10 Fr, which should be short (maximum of 6 cm) Once the fluid has drained through the stent, the procedure can be terminated. (Figs. 4-8).
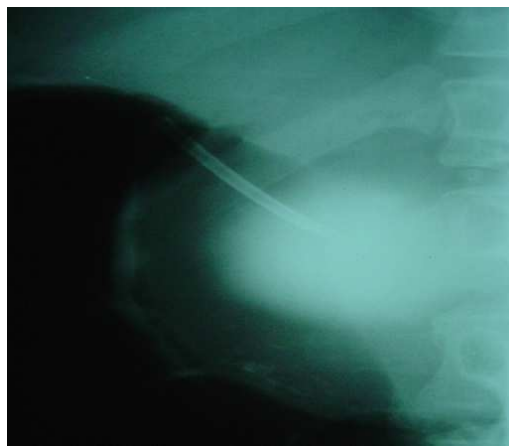


**Figure 4.** Pancreatography showing absence of communication between the Wirsung duct and the pseudocyst



**Figure 5.** ERCP showing guidewire inside the pancreatic pseudocyst

**Figure 6.** ERCP showing location of the endoprosthesis through the anterior wall of the stomach



**Figure 7.** Final appearance showing stent providing communication between the pseudocyst and the gastrointestinal tract



**Figure 8.** Abdominal CT on the 14th day after drainage, showing stent (arrow) providing communication between the pseudocyst and the stomach

We have had the opportunity to treat and follow up 14 patients initially, with five years of follow-up, and we concluded that transmural endoscopic drainage could be used as the first choice, provided that the inclusion criteria were rigorously respected. [13]

### 6.11. Infected pseudocyst

For a long time, infected pseudocysts were considered to be a contraindication against construction of a cystenterostomy. Endoscopic approaches have come to simplify this procedure and expand its indications. Today, cystenterostomy is considered to be the first choice in these cases. The limit for not performing the procedure, when infection coexists, is the patient's clinical state and the presence of sepsis and associated hemodynamic instability. In these cases, it is more prudent to use a conservative approach with external drainage. However, it is emphasized in the literature that the endoscopic approach is particularly attractive under these circumstances, since it achieves the therapeutic objectives with less surgical trauma and without creation of an external fistula that is difficult to manage. In addition to infected pseudocysts, other complex situations such as infected pancreatic necrosis have been successfully managed by means of endoscopy in selected cases.

The debate between the various techniques is far from being exhausted. Comprehension of the physiopathology and natural history has helped in choosing the best form of treatment. The important point is that the therapeutic principles can be attained through careful assessment and actions by professionals with experienced of the various types of treatment available. [14, 15]

# 7. Vascular complications

Although pseudoaneurysms and obstruction or thrombosis of the splenic vein, with consequent segmental, selective or left-side portal hypertension, are rare, they follow a course with high morbidity and mortality, especially if not identified and treated effectively. Recent studies have shown that vascular complications of chronic pancreatitis occur more frequently than had been supposed in the past. It is therefore necessary for physicians to be alert in relation to the clinical situations from which these complications may arise, and for them to know the options available for making the diagnosis and implementing effective treatment. These complications have high morbidity and mortality, such that the mortality rate may reach levels close to or even exceeding 50%.

Among the causes of digestive hemorrhage in situations of chronic pancreatic disease, not only the commonest causes like peptic ulcer disease and acute lesions of the gastroduodenal mucosa should be considered, but also the vascular complications of chronic pancreatitis. [16]

### 7.1. Arterial complications

When the vascular involvement is arterial, it can evolve in two distinct manners: free hemorrhage in the abdominal cavity or formation of a vascular cystic mass called a pseudoaneurysm.

The splenic artery is the one most commonly involved, followed by the gastro-duodenal, pancreatico-duodenal and hepatic arteries. [16, 17]

### 7.1.1. Pseudoaneurysm of the splenic artery

Pseudoaneurysm of the splenic artery generally results from the action of proteolytic enzymes that are released during the pancreatic inflammatory process. These enzymes cause arterial erosion that may result in free hemorrhage into the gastrointestinal tract or directly into the peritoneal cavity (thereby leading to hemoperitoneum), or may result in formation of pseudoaneurysm. (Diagram 1.)

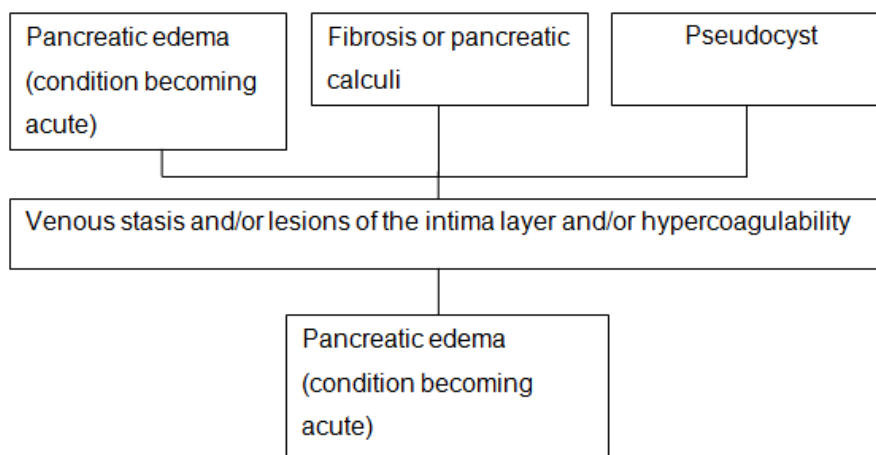Pathogenesis of obstruction of thrombosis of the splenic vein

| Pancreatic edema (condition becoming acute) | Fibrosis or pancreatic calculi | Pseudocyst |
|---|---|---|

Venous stasis and/or lesions of the intima layer and/or hypercoagulability

Pancreatic edema (condition becoming acute)

**Diagram 1**

Pseudoaneurysms originate when weakening of the arterial wall leads to aneurysmatic vascular dilation, generally of an artery adjacent to a pancreatic pseudocyst. The latter then tends to involve the aneurysmatic sac. Pseudocysts occur in 10% to 40% of the patients with chronic pancreatitis and up to 10% of these patients present associated pseudoaneurysms. Bleeding occurs in up to 75% of the cases and is often severe. The mortality rate ranges from 18% to 29% among the patients undergoing treatment and may reach 90%-100% among untreated individuals.

### 7.1.1.1. Clinical picture

Clinically, the bleeding that results from pseudoaneurysms can manifest in different forms, from intermittent gastrointestinal bleeding to massive hemorrhage with collapse of the circulation and death. Rupture of the pseudoaneurysm into the pancreatic duct, with subsequent gastrointestinal bleeding, known as *hemosuccus pancreaticus* or Wirsungorrhage, should be considered as a complication in patients with chronic pancreatitis and digestive hemorrhage, and it is potentially fatal. This complication generally presents as intermittent digestive

hemorrhage in association with abdominal pain, hyperamylasemia and/or hyperlipasemia resulting from acute distension of the pancreatic duct due to the hemorrhage. Through the Wirsung duct, the blood crosses the ampulla of Vater and flows into the gastrointestinal tract, which may result in melena, hematemesis or hematochezia. In cases in which the pseudoaneurysm is not in communication with the pancreatic duct, the bleeding originating from its rupture may continue to be held inside the pseudocyst and is manifested in the form of abdominal pain, a rapid increase in pseudocyst volume (identified on physical examination or through image evaluation methods) and a decrease in hematocrit. [19]

### 7.1.1.2. Diagnosis

Some authors have suggested that abdominal ultrasound should be the first examination to be performed. Ultrasound used in association with Doppler is very useful, since it allows the pulsatile arterial flow to be viewed inside cystic masses, thus strengthening the diagnosis of pseudoaneurysm.

Dynamic CT with venous contrast in a bolus seems to be the best noninvasive method for diagnosing arterial complications in patients with chronic pancreatitis, especially in relation to identifying pseudoaneurysms, with sensitivity of around 80% to 100%.

In comparison with CT, MRI presents the advantage of not requiring ionizing radiation. Moreover, it can be performed with intravenous administration of gadolinium, which is a substance equivalent to the iodinated contrast medium of CT, but free from its adverse effects. Thus, this method can be used safely in individuals with a previous history of hypersensitivity to contrast and also in those with kidney disorders. Vascular anatomical studies conducted using MRI (angioresonance) have provided images similar to those obtained through conventional angiography. Thus, during the arterial phase, after intravenous administration of gadolinium in bolus form, it is possible to analyze the vascular anatomy in detail and identify cases of pseudoaneurysm formation.

ERCP has less usefulness in cases of complications vasculares pancreatitis chronic (CVPC) in particular, except that on rare occasions it is able to demonstrate active bleeding originating from the ampulla of Vater.

Out of all the methods available, angiography is still the most trustworthy of them and it continues to be the gold standard for diagnosing the arterial complications of chronic pancreatitis. It makes it possible to diagnose pseudoaneurysms, even if they are small, which is an advantageous characteristic given that up to 20% of these are not large enough to be detected through other imaging methods. Furthermore, if it is performed during the active phase of hemorrhaging, it allows the exact site of bleeding to be located, identified from the extravasation of contrast from a given vessel. It should always be performed before the surgical procedure, of the patient's hemodynamic state allows this, thus ensuring safety and success in the operation. The main reason for this is that identifying the bleeding vessel during surgery may be difficult due to the inflammation, necrosis and friability of adjacent tissues (caused by the pancreatitis), which may result in incorrect ligature of a vessel or even total inability to

control the bleeding. Angiography also offers the advantage that, in selected patients, it also constitutes a therapeutic method, as will be seen below. [18-19].(Fig. 9-10)
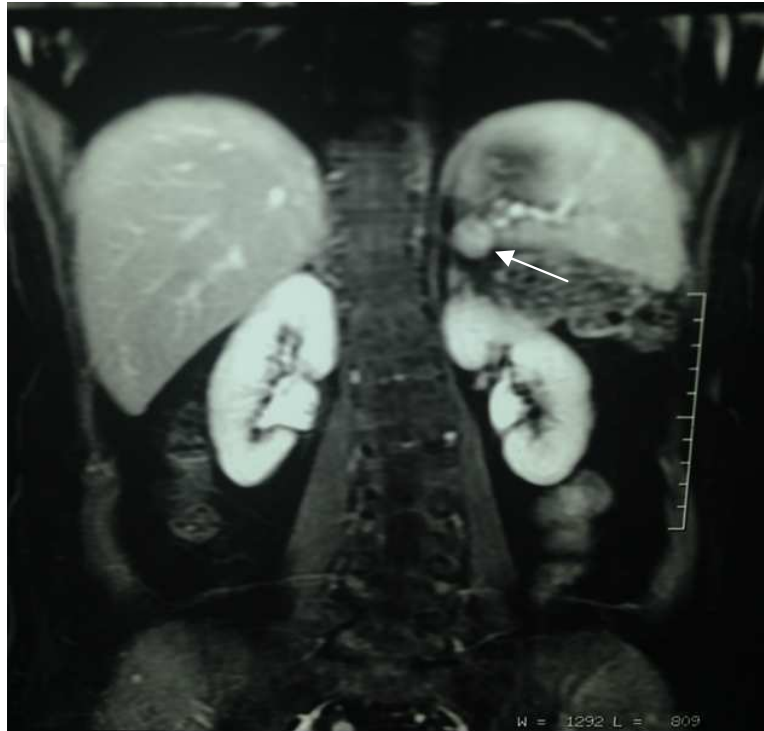


**Figure 9.** RM, arrow showing pseudoaneurysm of splenic artery

### 7.1.1.3. Treatment

After diagnostic confirmation and angiographic identification of the origin of the bleeding, treatment should be instituted as soon as possible. The ideal strategy for pseudoaneurysms is still a matter of debate, but the choices are surgical treatment, therapeutic angiography or a combination of these two. Nonetheless, the choice has to be guided by two main factors: the patient's hemodynamic condition and identification of the exact site from which the bleeding originates.

In patients who are unstable from a hemodynamic point of view, the preferred treatment is surgical, which should be performed immediately. However, there is no consensus among the various authors regarding the ideal surgical procedure to perform. Most authors have recommended surgical resection of the pseudoaneurysm in association with resection of the pancreatic area affected. On the other hand, others have suggested performing proximal and distal ligature of the vessel that has been identified as the source of the bleeding, in association with internal drainage of the pseudocyst, without the need for pancreatic resection.

Locating the exact point of origin of the bleeding is essential for determining the best thera‐ peutic option, given that it has been observed that pseudoaneurysms located in the body or tail of the pancreas are more easily dealt with surgically than are those located in the head of
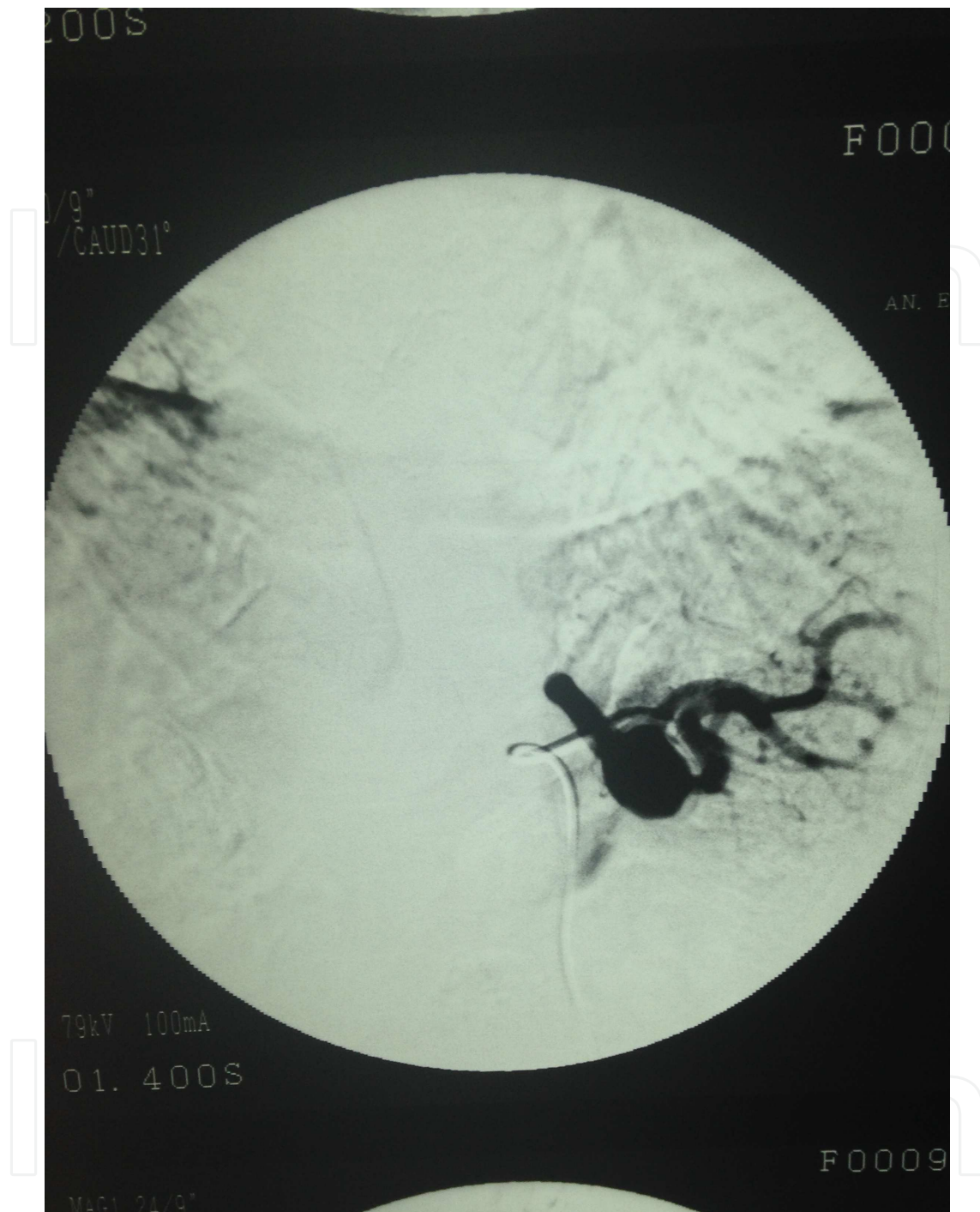
**Figure 10.** Arteriography showing pseudocyst of splenic artery

the organ. The latter generally require the Whipple procedure (duodeno-pancreatectomy), a procedure that leads to much higher surgical mortality. From reviewing the literature, Marshal et al reported that the overall mortality was 16% when pancreatic resection was performed as therapy for pseudoaneurysms located in the body or tail of the pancreas, but when the same procedure was performed to treat pseudoaneurysms located in the head of the pancreas, the mortality rate was much higher, estimated as 43% (Fig. 11)
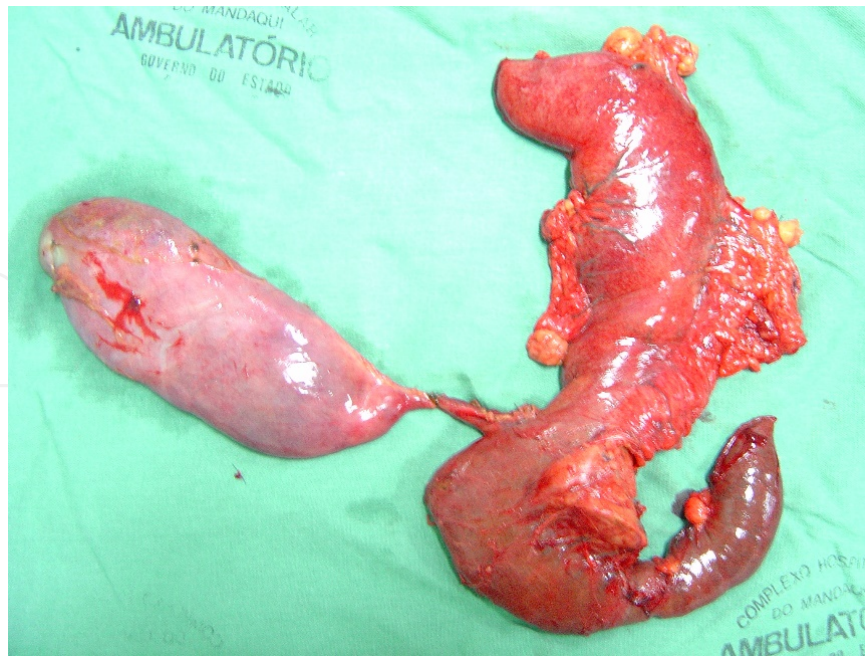
**Figure 11.** Whipple procedure (gastroduodenopancreatectomy)

Although surgical manipulation is frequently necessary for treating the arterial complications of chronic pancreatitis, its use as emergency therapy is becoming progressively lower, as experience with transcutaneous angiographic embolization is being acquired. This method can be used as definitive therapy, or even as temporary therapy. The latter allows bleeding to be controlled so that a surgical procedure can subsequently be performed more safely.

Temporary angiographic embolization consists of selective embolization using gel foam or by means of occlusion using a balloon in the celiac trunk. In both of these procedures, the aim is to reduce the bleeding and bring it under control, to the point at which the patient can be sent for surgery more safely. In some cases, the angiographic procedure may cause not only reduction of the bleeding but also its complete control, thus reducing the need for subsequent surgical treatment. In these cases, angiographic embolization may constitute the definitive therapy. [18, 19]

### 7.1.2. Pseudoaneurysms of the hepatic artery

Pseudoaneurysms of the hepatic artery occur only rarely, but when present, they often rupture (in 56% of the cases). The mortality rate varies, but may reach 40%. The variants that most influence the prognosis for these patients are the individual clinical conditions, the bleeding characteristics of the lesion and the surgical procedure used.

Patients with pseudoaneurysms of the hepatic artery are frequently asymptomatic or present vague pain in the upper quadrant or epigastrium. Symptoms generally appear when complications arise: these are mainly due to extrinsic compression of the biliary tract or rupturing of the pseudoaneurysm. [17]

The natural history of pseudoaneurysms of the hepatic artery is unclear, unlike those of the splenic artery. The first clinical manifestation of pseudoaneurysms of the hepatic artery is a rupture, which occurs in 64-80% of the cases. In 30 to 50% of the cases, these aneurysms are only discovered in autopsies, thus suggesting that a significant number of aneurysms remain asymptomatic throughout life.

Rupturing occurs with almost equal frequency in the biliary tree (41%) (in the common hepatic duct or right hepatic duct) and in the peritoneal cavity (44%). In the latter situation, this is associated with a high mortality rate (greater than 35%). Among the remaining cases, 10% are manifested within the gastrointestinal tract, particularly the duodenum, and 5% in the portal vein, which may lead to portal hypertension. Unlike what is seen in relation to aortic aneurysms, there are no data correlating the size of the pseudoaneurysm with the likelihood of rupture (Diagram 2.).
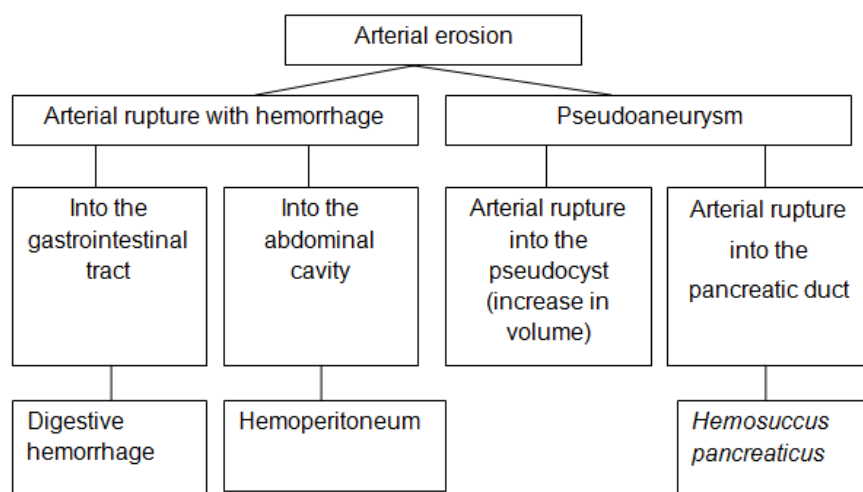
Arterial complications of chronic pancreatitis

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                        ┌─────────────────────┐
                        │   Arterial erosion  │
                        └─────────────────────┘
                ┌──────────────┴──────────────┐
    ┌───────────────────────────┐   ┌─────────────────────┐
    │ Arterial rupture with     │   │   Pseudoaneurysm    │
    │ hemorrhage                │   │                     │
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│ Into the ││ Into the │ │ Arterial     ││ Arterial     │
│gastro-   ││ abdominal│ │ rupture      ││ rupture      │
│intestinal││ cavity   │ │ into the     ││ into the     │
│tract     ││          │ │ pseudocyst   ││ pancreatic   │
│          ││          │ │ (increase in ││ duct         │
│          ││          │ │ volume)      ││              │
└──────────┘└──────────┘ └──────────────┘└──────────────┘
┌──────────┐┌──────────────┐              ┌──────────────┐
│ Digestive││ Hemoperitoneum│             │ Hemosuccus   │
│ hemorrhage││              │             │ pancreaticus │
└──────────┘└──────────────┘              └──────────────┘
```

**Diagram 2**

Obstructive jaundice may result from hemorrhaging within the biliary tree and secondary obstruction due to coagulum or from extrinsic compression of the duct by a pseudoaneurysm that has not yet ruptured, and this is found in 51% of the patients. The pain presented may be a consequence of coagulum inside the biliary tree or of compression of this, and it is typical of biliary colic.

It is generally difficult to make this diagnosis before the operation and it depends on whether there is a high degree of suspicion. The diagnosis may particularly be suspected in cases of upper digestive hemorrhage in which endoscopy fails to reveal its origin. Regarding diagnostic means, the propaedeutics are the same as cited above for aneurysms of the splenic artery.

Currently, the preferred treatment is embolization by means of angiography. In patients who are hemodynamically unstable, the management indicated is emergency surgery. Some
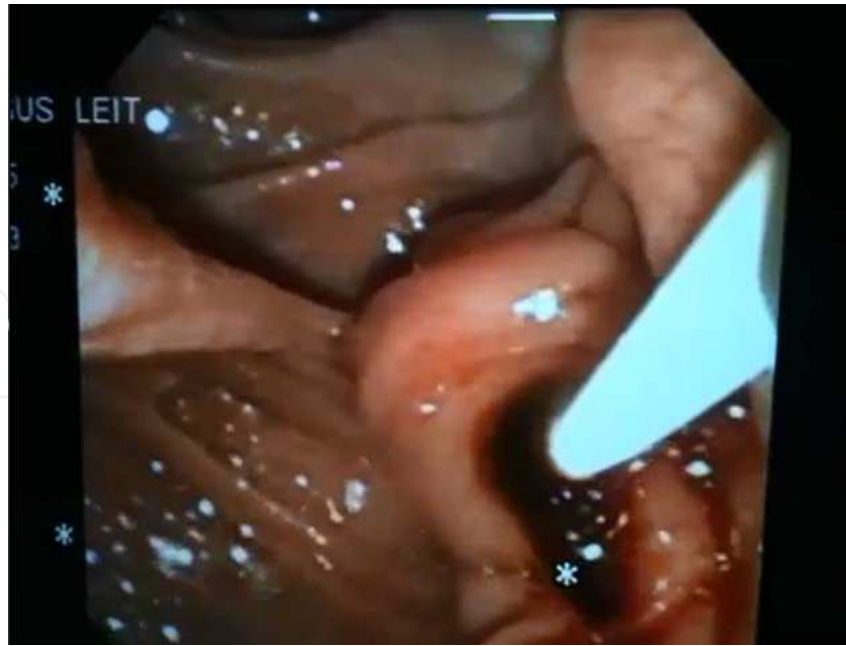
**Figure 12.** ERCP showing hemobilia

exceptional cases without immediate risk of rupture and without progressive increase in size or hemodynamic instability can be managed using conservative therapy, through serial imaging examinations and appropriate treatment of the associated infections. [18, 19-20]

## 7.2. Venous complications

### 7.2.1. Extrahepatic portal hypertension

The main cause of hypertension of the portal vein system is cirrhosis, while pancreatitis is an uncommon etiology. It may be limited to the superior mesenteric vein (which is a branch of the splenic vein) or it may involve the entire splenic-mesenteric-portal system. The portal hypertension caused by pancreatitis usually results from extrinsic venous compression due to a pseudocyst or pseudotumor, which are the most frequent complications of chronic pancreatitis. It can be classified into two forms: occlusive and non-occlusive. [21]

Its pathogenesis involves various factors. It is believed that the inflammatory process causes the initial damage, with degeneration of the vascular wall, venous spasms, stasis and thrombosis. The anatomical location and contiguity processes have the effect that the splenic vein is more vulnerable to this process, because of its location close to the posterosuperior border of the pancreas. It has been observed that simple dilation of the pancreas is sufficient to produce an obstruction of the splenic vein.

Venous drainage of the spleen usually takes place not only through the splenic vein but also through the short gastric veins and from these to the right and left gastric veins. Thus, if the splenic vein is obstructed, dilation of the venous system of the submucosa of the stomach may occur, with formation of gastric varices, separately or in association with esophageal varices.

Although it has been observed that gastric varices alone are highly suggestive of obstruction of the splenic vein, with consequent left segmental hypertension, an association with esophageal varices is not uncommon. [22, 23]

Another drainage route for the spleen is through the gastroepiploic veins, which drain to the superior mesenteric vein and then to the portal vein. In the presence of left segmental hypertension, the left gastroepiploic vein may also drain through tributaries of the inferior mesenteric vein, thus resulting in formation of colonic varices. [22]

### 7.2.1.1. Clinical picture

The presence of gastric varices in association with splenomegaly, with preserved hepatic function, should suggest a diagnosis of left segmental hypertension with consequent O/TVS (obstruction / thrombosis of the splenic vein), although not all patients present this complete trio. Clinically, the evolution may be either asymptomatic or symptomatic. [22]

### 7.2.1.2. Diagnosis

By performing upper digestive endoscopy, gastric and/or gastroesophageal varices and their characteristics, including signs or current or recent bleeding, can be viewed. The diagnosis can be complemented with abdominal US with color Doppler, MRI (angioresonance), angiography and, more recently, endoscopic US. [23]

### 7.2.1.3. Treatment

Among symptomatic patients, splenectomy is the most effective surgical procedure for permanently controlling the gastrointestinal bleeding in patients with O/TVS and left segmental hypertension. Among asymptomatic patients, even if they present varices in the gastric fundus but without evidence of bleeding, there is controversy regarding the case management. It has been proposed that these patients should be treated expectantly, considering that only a small percentage will possibly present bleeding and that these patients would only require a surgical procedure at that time. For patients for whom surgery is impossible, endoscopic treatment comprising sclerotherapy can be attempted. [24]

## 8. Cavity effusion

Cavity effusion in cases of chronic pancreatitis can be explained by two theories: they may arise through the outflow of pancreatic juices anteriorly to the peritoneum (pancreatic ascites) or posteriorly through the diaphragm to the pleura (pleural effusion), through rupturing of the main pancreatic duct or one of its branches. Pleural effusion may also be caused by the passage of blood and lymph that are rich in pancreatic enzymes, close to the pleura, thus causing reactional pleurisy with small-scale effusion. [25]

Both of these are rare complications, but they are significant in cases of chronic pancreatitis and have a mortality rate of 20% if they are not adequately treated.

Both the volume of ascites and the abdominal pain vary in intensity. Most patients present painless voluminous ascites and almost always believe that they have alcoholic cirrhosis with ascites. Recent histories of acute pancreatitis are rarely present.

Pleural effusion is more common on the left side and it consists of an exudate rich in amylase and lipase. When the patients are symptomatic, they most commonly present thoracic pain, dyspnea and weight loss. [25, 26]

The diagnosis depends on there being great clinical suspicion and can be confirmed through imaging examinations and analysis of pleural and ascitic fluid in which high amylase and protein content is demonstrated.

In up to 25% of the patients, simultaneous presence of pancreatic ascites and pancreatic pleural effusion can be seen.

Imaging examinations with CT and MRI are useful because, in calcifications of the pancreatic parenchyma, they show dilatation and stenosis of the Wirsung duct and the presence of pseudocysts and fistulas. ERCP is indicated in all cases of internal pancreatic fistulas with ascites and pleural effusion, to search for ductal pathological conditions and to locate the paths of fistulas. [27, 28]

Non-surgical treatment is indicated for patients with pancreatic ascites and pleural effusion of pancreatic origin. The rationale of the treatment consists of diminishing the exocrine pancreatic secretion, thereby stimulating closure of the pancreatic duct at the rupture site. The treatment includes suspension of the oral diet, use if a diet administered via an enteral probe and use of paracentesis or thoracocentesis, as appropriate. For patients who are not treated using clinical means, surgical treatment is indicated after delineating the anatomy of the pancreatic duct, by means of ERCP. Most patients with pancreatic ascites or pleural effusion present extravasation from an incompletely formed or ruptured pseudocyst, whereas a minority present direct extravasation through the duct. Use of endoscopic treatment with sphincterotomy or insertion of a prosthesis into the pancreatic duct to aid in evaluating a small number of patients has been reported, and occlusion of the ductal extravasation can be attempted. [28]

The surgical treatment is based on the findings from pancreatography. Rupture of the pancreatic duct or extravasation from a pseudocyst into the body or tail of the pancreas can be treated by means of distal pancreatectomy or Roux-en-Y pancreatojejunostomy at the extravasation site. Extravasation from the pancreatic duct in the more proximal parts of the gland are treated by means of Roux-en-Y pancreatojejunostomy at the rupture site. [29]

## 9. Obstruction of the bile ducts and gastrointestinal tract

Obstruction of the bile ducts and gastrointestinal tract occurs more in chronic pancreatitis cases because of the repeated upsurges. Over time, these cause replacement of the pancreatic parenchyma by fibrous tissue that, in turn, causes extrinsic compression of the pancreatic duct,

end of the bile duct and the second portion of the duodenum and may also cause mechanical obstruction of these structures. [30]

## 9.1. Biliary obstruction

The incidence of biliary obstruction in patients with chronic pancreatitis ranges from 4% to 30%. In 80% to 85% of all individuals, the distal bile duct is completely surrounded by the pancreas, and in the remaining 15% to 20%, it is closely related to the posterior wall of the head of the pancreas. The extent of the bile duct stenosis caused by pancreatic fibrosis depends on the length of the intra-pancreatic portion of the bile duct, which ranges from 1.5 to 6.0 cm. The compression of the bile duct may be of definitive nature, when produced by pancreatic fibrosis in advanced cases, or of transitory nature, as occurs in the majority of the initial forms of the disease. It is caused by edema during acute inflammatory upsurges. The obstruction occurs in such a way that it does not cause total obstruction of the biliary flow, unlike in malignant processes. [30, 31]

### 9.1.1. Clinical manifestations of biliary obstruction

Biliary obstruction is characterized by episodes of exacerbation and remission. In some patients, it may be totally asymptomatic and an incidental finding. Jaundice occurs in 30% to 50% of the patients and may be transitory, recurrent or persistent. Fever, hot and cold flushes and abdominal pain may also occur. Other symptoms include weight loss, weakness, nausea and vomiting.

### 9.1.2. Laboratory tests

Elevation of alkaline phosphatase levels is the most reliable early sign of biliary obstruction, even in the absence of hyperbilirubinemia. Persistently high levels (twice the normal values) are indicative of bile duct obstruction in patients with chronic pancreatitis. Nonetheless, elevated alkaline phosphatase levels are unrelated to the severity of the condition. Transitory increases in alkaline phosphatase and plasma bilirubin levels, which occur frequently during upsurges with acute transformation of chronic pancreatitis, result from pancreatic edema and are only rarely associated with bile duct stenosis. Because of low sensitivity, bilirubin should only serve for providing diagnostic suspicion when there is persistent hyperbilirubinemia.

### 9.1.3. Radiological examinations

US and CT are the methods for investigating obstruction of the biliary tree. CT enables greater diagnostic precision, since it more clearly identifies the nature of the lesion. It also allows evaluations of the pancreatic anatomy and alterations, such as the presence of calcifications, which are indicative of chronic pancreatitis. CT is the main examination for the initial investigation of patients with obstructive jaundice. (Fig. 13)
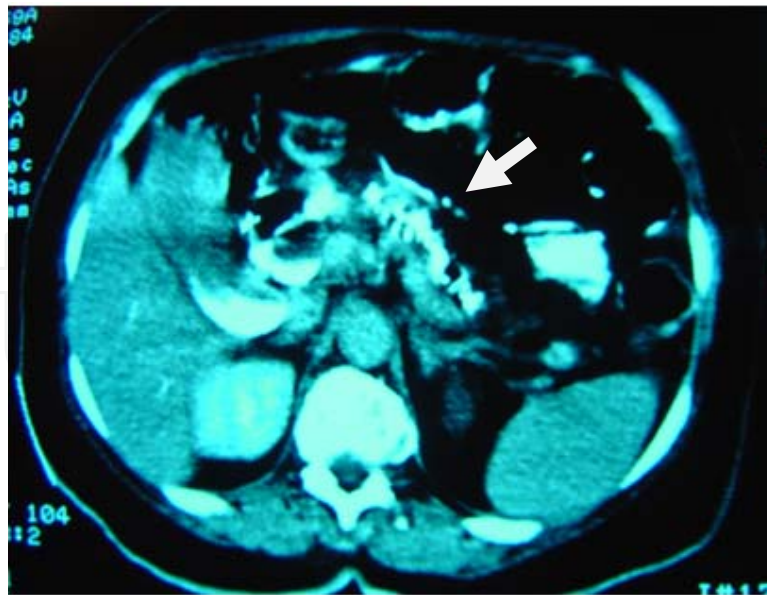
**Figure 13.** Abdominal CT showing pancreatic calcifications

The definitive proof of biliary obstruction comes from cholangiography via ERCP or transhepatic puncture. Another means of obtaining confirmatory images is through using MRI, which enables evaluation of the bile duct without administration of contrast.

The differential diagnosis between cholestasis caused by chronic pancreatitis and by pancreatic adenocarcinoma may be difficult, particularly among patients with preexisting chronic pancreatitis. The parameters that are most useful for this differentiation are age (lower among patients with chronic pancreatitis) and bilirubin levels (higher among patients with adenocarcinoma). The cholangiographic appearance of the progressive compression of the bile duct in chronic pancreatitis cases may be useful for distinguishing it from adenocarcinoma. [25]

*9.1.4. Treatment*

The decision on the management to be used in treating biliary obstruction in patients with chronic pancreatitis should be based on the form of clinical presentation and on an assessment of the risks involved in expectant management. The clinical and laboratory data that favor interventionist management include the presence of jaundice and elevated bilirubin and alkaline phosphatase levels for a period of more than one month, presence of associated cholangitis and/or choledocolithiasis, biliary cirrhosis diagnosed by means of liver biopsy and suspected presence of cancer. Another indication for biliary drainage in patients with chronic pancreatitis is a finding of compression of the bile duct in patients with an indication for surgical treatment of their chronic pancreatitis in order to control pain. (Fig.14)

**9.2. Duodenal obstruction**

Duodenal obstruction in patients with chronic pancreatitis occurs much less frequently than biliary obstruction. The precise mechanism for the duodenal obstruction caused by chronic

**Figure 14.** During the operation: dilation of the Wirsung duct and bile ducts

pancreatitis is unknown. It can present in two forms: transitory obstruction (more frequent) caused by the edema that is characteristic of periods when the disease becomes acute; and, more rarely, obstruction that is more prolonged or even permanent, caused by fibrosis located in the cephalic portion of the pancreas. The factors responsible for transformation of the edema in the fibrosis that causes the obstructive process are not fully known, but several studies have shown that pancreatic-duodenal ischemia (which is known to occur in experimental and clinical chronic pancreatitis) has a role. [25]

### 9.2.1. Clinical manifestations

The main symptoms of duodenal obstruction are persistent nausea and vomiting of increasing intensity, without accompanying pain. This diagnosis should be suspected when the symptoms persist for more than two weeks after the start of the clinical treatment. Vomiting generally occurs soon after meals and brings back the recently ingested food. It may be bilious if the obstruction is distal to the duodenal papilla.

### 9.2.2. Radiological and endoscopic diagnosis

Duodenal obstruction caused by chronic pancreatitis can be demonstrated through upper digestive endoscopy or contrasted radiological examination of the stomach and duodenum. The appearance is nonspecific, but the contrasted examination generally shows long uniform compression in the second portion of the duodenum, while the endoscopic examination demonstrates a fixed extrinsic concentric obstruction in the post-bulbar portion [26-28]. (fig 15)
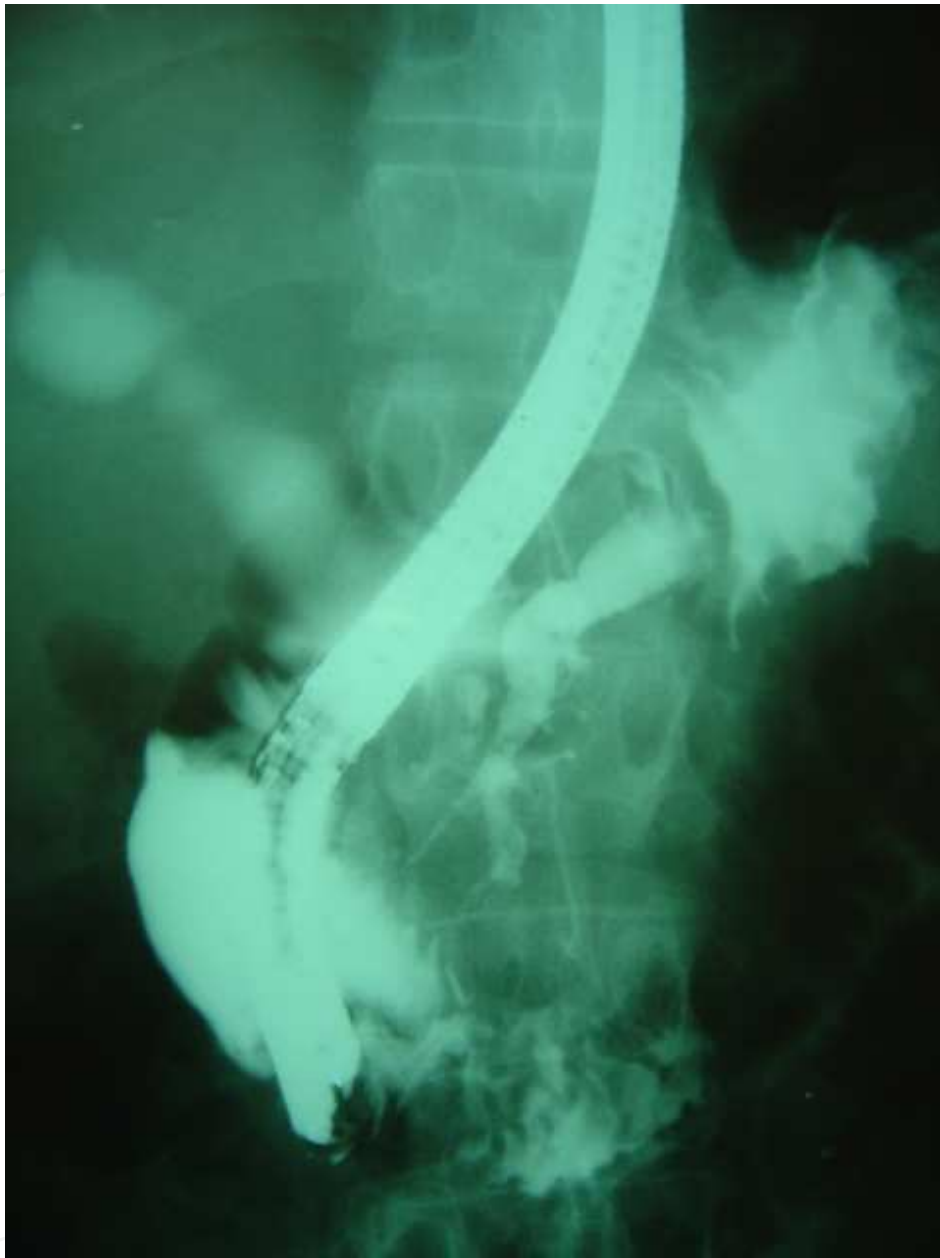
**Figure 15.** ERCP showing dilation of Wirsung duct and bile duct

### 9.2.3. Treatment

In most cases, the duodenal obstruction caused by pancreatic edema during crises of acute transformation of chronic pancreatitis responds favorably to clinical treatment consisting of fasting and parenteral nutrition. Persistence of the obstructive condition for more than four weeks of conservative treatment is very rare, but constitutes an indication for a surgical bypass. Patients with previous episodes of intermittent obstruction of the upper digestive tract probably have obstructions caused by fibrosis of the pancreas and are also candidates for surgical treatment. [29-32]

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