

Pancreatic Resection and PostOperative Pancreatic Fistula: Review on Predictions and Risk Factors of POPF

Lica Mircea^{1*}, Negoii Ionut², Lica Ion^{1,2}, Paun Sorin^{1,2}

¹Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; ²Clinical Emergency Hospital of Bucharest, Romania

ABSTRACT

Postoperative pancreatic fistula is the major cause for survival after pancreatic resection, as it is being life threatening complication than pancreatic cancer. This study aims on the detail concept of pancreatic cancer, whipple procedure and major complication postoperative pancreatic fistula, risk factors and its predictive methods.

Keywords: Whipple procedure; Postoperative pancreatic fistula; Pancreatic cancer; Risk Factors; Complications

INTRODUCTION

Pancreatic cancer is a leading cause of cancer death as they are no detection procedures to diagnose the cancer disease in the early stages. Going in details of pancreatic cancer, where the cells of the pancreas which is present behind the stomach begins the process of metastasis to form a mass. The most common cancer among the pancreatic cancer is pancreatic adenocarcinoma, which starts with in the portion of pancreas and may spread to the surrounding parts of pancreas [1].

In the united states About 28,000 new cases were diagnosed yearly are of pancreatic cancer. As per the American cancer society, estimated pancreatic cancer in United states is: [1]

- about 57,600 people were diagnosed with pancreatic cancer, out of where 30,400 are men and 27,200 are women.
- About 47,000 people dead due to pancreatic cancer, out of where 24,640 are men and 22,410 are women.
- Pancreatic cancer is more common in the men than in women.

Survival rate for cancer of about past 5 years i.e., from 2014–2019 is 6.5% for males and 8.1% are of females, which has a great fall from 24.8% of males survival rate in a year and 26.2% of females survival rate in an year.

In 2015 4,11,600 deaths were seen globally due to pancreatic cancer of all types[1].

In United Kingdom pancreatic cancer is the fifth most common disease-causing death and in United states pancreatic cancer is the third, causing death.

There are many treatment procedures for the pancreatic cancer as chemotherapy, radiotherapy and laparoscopic surgery. The procedures appears to be successful but the cancerous cells may be remained that are not evident microscopically, that may be reason for reoccurrence of developing and spread of cancer.

For the effectiveness of pancreatic cancer whipple procedure introduced in 1818 by an Italian surgeon [6]. They are complications involved after the pancreatic resection, there are delayed gastric emptying, bile leak, and pancreatic leak. The pancreatic leak also called as pancreatic fistula. This study, discuss about the whipple procedures, method and major involved complication of postoperative pancreatic fistula in detail.

PRESUGRICAL ADMINISTRATION

Pancreatic surgery depends on the size and tumor location. Pancreatic cancer might also be reported in the patients with non-specific abdominal symptoms which includes abdominal pain, vomiting nausea along with weight loss [3].

Pancreatic tumours anatomical location are suggested as potential determinations of survival-

- 65% pancreatic cancers occur in the head of the pancreas,
- 15% occurs in the body and tail of the pancreas,
- The remaining lesions diffusely involve the gland.

The tumours locations predict the survival of the patients due to pancreatic cancer. 18,666(56%) had pancreatic tumour located on head portion and 5982(18%) pancreatic tumours are located in the body and tail, 9104(26%) patients have tumours on pancreatic

Correspondence to: Lica Mircea, Carol Davila University of Medicine and Pharmacy, Bucharest, 37 Dionisie Lupu Street, 1st district, 020022; Tel: +40 724 962 797; E-mail: mircealica@yahoo.com

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duct, islets of Langerhans and unspecified locations.

Before the surgical procedure, preoperative work should be done i.e., several diagnostic procedures. The diagnostic procedures that include are CT scan, MRI, Magnetic resonance cholangiopancreatography, x-ray. Clinical staging has to be done to reduce the surgical interventions [4].

OPERATIVE PRINCIPLE

Whipple procedure is the most common attempt of the curative surgical treatment. This major operation involves pancreatic head removal and curve of duodenum called as pancreatoduodenectomy and making a bypass for food from stomach to jejunum called gastrojejunostomy. Resection of tail of pancreas is known as distal pancreatectomy.

Laparoscopic distal pancreatectomy can be done as an optional procedure for benign tumours when oncological management not an issue [2, 6, 9].

PANCREATODUODENECTOMY

Kausch and Whipple et al. developed pancreatoduodenectomy in the beginning of the twentieth century, as a two-step procedure: resection on one day followed by later reconstruction of the intestinal continuity on a different day. The operation was continuously improved till surgeons were able to proceed with a one-step operation. For a long time, the procedure was associated with high morbidity and mortality, not only because the surgical technique is highly demanding, and also owing to the difficult perioperative management where anesthesia involved. Pancreatoduodenectomy is a safe operation for pancreatic cancer that results in low morbidity and mortality. Pancreatoduodenectomy is divided into three steps: exploration; resection; and reconstruction of the intestinal continuity. Careful inspection and palpation of the abdominal cavity should be initiated for the procedure with a particular attention to the liver, the peritoneum, and the pelvis, in order to rule out metastases, which would preclude resection. Any evidence of metastasis, an appropriate decision should be made as whether to bypass is needed and whether this treatment is suitable [1, 8].

Resection

The procedure usually involves performing a cholecystectomy in a fundus.

First, divide the bile duct distally, and clamp its openings to prevent spillage of bile. Attention should be paid to avoiding injury to the hepatic artery. To divide the stomach with the linear stapler, the gastroduodenal artery should be divided near its origin and the duodenum is skeletonized up to two centimeters distal of the pylorus. The stomach is dissected posteriorly attached part, lifted up, and divided. The uncinate and duodenal mesentery is dissected. A tunnel is created between the posterior section of the SMV-portal vein trunk and in the anterior of the pancreatic neck. The pancreatic head is sharply transected from the pancreatic body/tail, followed division of the third part of the duodenum. The jejunum has to be repositioned up into the supramesocolic compartment before the reconstructive phase of the operation. In the abdomen a large incision will be made. The head of the pancreas and the gallbladder, pylorus, and duodenum will be removed [5].

Reconstitution

The digestive organs and remaining pancreas will be reconnected. This will allow the digestive enzymes to flow into the small intestine. the pylorus is not removed In some cases.

For laparoscopic procedures, a small surgical instruments and camera are inserted through the incisions into the abdomen. After the area should be carefully examined, laparoscope will be removed. using stitches or staples the incision will be closed. The incisions will be covered with bandages[5, 9].

COMPLICATIONS INVOLVED

- Infection of the incision area
- Delayed emptying of the stomach,
- Leakage from the pancreas or bile duct connection
- Diabetes, temporary or permanent

The major complication involved is the leakage from the bile duct or pancreas called as pancreatic fistula (postoperative pancreatic fistula) [7,8].

POSTOPERATIVE PANCREATIC FISTUAL

There are many new advancements in the operative management and surgical techniques, despite this postoperative pancreatic fistula is still been considered as the greatest cause for the morbidity and mortality after pancreatic resection(pancreatoduodenectomy). This postoperative fistula still remains as unsolved challenge. The mortality rate is less than 4% over recent decades. In the recent study from japan using national clinical database revealed that 30-day and in hospital the mortality rates were 1.2 and 2.8 % respectively [1].

Pancreatic fistula has still no universally accepted definition. Most of the definition. Most of the definitions pertaining to pancreatic fistula states that “fluid drained after postoperation 3rd day which contains amylase content 3times greater that the normal limit”. This definition which was given by an international working group of 37 pancreatic surgeons in 2005 for the first time.

- A grading system was established-
- Benign clinical course(grade A fistula)
- Moderately unwell patients requiring medical/invasive intervention (grade B fistula)
- Critically ill patients, with sepsis, require massive intervention (grade C fistula)

This definition was revised in 2016 as “association with clinically relevant development/ condition related directly to the postoperative pancreatic fistula”. Where as grade A has been redefined as term “biochemical leak”, grade B and grade C as grade B postoperative fistula and grade C postoperative fistula. This grading system repeatedly validated along with other non POPF complications [4].

PATHOPHYSIOLOGY

The pathophysiology leads to loss of mechanical integrity of the pancreatoenteric anastomosis causing to “leakage” of pancreatic fluid into free peritoneal cavity causing pancreatic ascites.

The disruption of duct takes place posteriorly, the secretions leak through retroperitoneum to media sternum along the aortic or oesophageal hiatus. The secretions in the media sternum may cause pseudocyst or leak through pleura and enter the chest forming pleural effusion [1, 6].

RISK FACTORS AFTER PANCREATIC RESECTION LEADING TO PANCREATIC LEAKAGE

According to Norman oneil Machoda et al. says they are several risk factors included are [2]

- age, gender, jaundice, malnutrition which are categorised as patient related risk factors.
- Pancreatic pathology, pancreatic texture, pancreatic duct size, pancreatic juice output which comes under diseases related risk factors.
- Operative time, resection type, anastomotic technique, intraoperative blood loss comes under procedure related factors.

According to Anubhav Mittal et al., risk factors after pancreatic resection includes non-pancreatic cancer, pancreatic small duct diameter, soft gland texture and high intraoperative blood loss, increased body mass index, increased pancreatic parenchymal remnant volume, male gender, poor preoperative nutrition and obesity.

HOW TO PREDICT POSTOPERATIVE PANCREATIC FISTULA

Early prediction of a pancreatic fistula after pancreatic resection is important for identification at risk patients and equally the implementation of enhanced recovery protocols who are deemed to be at low risk.

According to Anubhav Mittal et al., he mentioned that earlier prediction of POPF was done by axial imaging studies by characterising its enhanced pattern. At same time preoperative imaging of pancreas and its remainants play as an important factor. He further used fistula risk score as a predictive tool considering several factors like gland texture, histological diagnosis, pancreatic duct diameter and intraoperative blood loss score out of 10, which is then used to determine whether the patient is at negligible (score 0), low (score 1-2), moderate (score 3-6), or high (score 7-10) risk of developing a POPF[1].

Baek Hwan Cho et al., used 38 preoperative and intraoperative variables that are associated with POPF such as serum C-reactive protein, amylase, lipase, and carbohydrate antigen and CT scan as an intraoperative variable testing the pancreatic texture and fluid infusion. He used Two ML algorithms i.e., random forest (RF) and neural network (NN) to predict POPF, but using these statistical and analytical methods the area under the curve (AUC) is measured. He says among these neural network is the good predictive tool for POPF [2].

Patryk Kambakamba et al., used preoperative non contrast CT scan as a predictive tool [3].

Beside, Hiroyuki Kato et al., used pancreas visceral fat CT value ratio and serrated pancreatic contours as predictive tools for POPF.

pancreas-visceral fat CT value ratio of ≥ 0.4 or greater and serrated-type contour, says that the patients with soft pancreas should be categorized into POPF high-risk and low-risk groups according to results, so that the risk of POPF can be reduced [4].

Raja Kalayarasan et al., used amylase drain fluid level on the first day after postoperation as a predictive tool. He observed daily drainage output, drain fluid nature, and the levels of serum and drain fluid amylase were measured on post-operative day 1 and 3. The laboratory normal value of amylase is 110u/l the variation of this showed the risk of POPF [5].

Masatsugu Hiraki et al., says prespin biomarker is the early predictive marker for POPF. They considered various factors like age, Gender, age, body mass index, American Society of Anesthesiologists (ASA) physical status score, diameter of the main pancreatic duct, origin of the primary disease, TNM-staging, presence of extended vascular resection, operative time, intra- and post-operative blood transfusion, pancreatic texture, presence of postoperative complications, length until removal of the surgical drainage tube, history of diabetes mellitus, presence of preoperative biliary drainage current smoking habit, prior abdominal operations . these variables were compared used AUC and identified the risk of POPF [6].

Masashi Utsumi et al., used CONUT score as the predictive tool using Data of 97 consecutive cases of PD performed in Iwakuni Clinical Center, from April 2008 to May 2018 were considered . Data includes sex, age, and hypertension, and postoperative complication and this data was collected to analyze pancreatic fistula occurrence [7].

PREVENTION AND MANAGEMENT:

As far the information we came to know that the postoperative pancreatic disorder is the major complication caused after pancreatic resection in the patients with pancreatic cancer and chronic pancreatitis leading to effect on mortality and morbidity of the pancreatic cancer patients. Hence, to decrease this impact different predictive tools are used to identify the POPF affected patients that they range of risk can be predicted and can be treated and prevent form POPF [10-12].

They are several preventive methods like pancreatic anastomosis, pancreatic transection, laparoscopic operations, stump coverage, pancreatic stenting and somatostatin analogues are used [13, 14].

DISSCUSSON:

As far this study was discussed on about the pancreatic cancer its morbity and mortality rates and deaths due to PC, detailed description of whipple procedure, complications after pancreatic resection and major complication postoperative pancreatic fistula, risk factors and its several predictive methods to find the range of risk in the patients along with the preventive methods to manage POPF. This review update of the pancreatic resection process and POPF could guide only to an extent of attempt to try to prevent the patient with risk of POPF after Pancreatic resection and reduce the deaths due to POPF.

CONCLUSION:

Although they are many predictive tools and preventive techniques

are developed to prevent POPF after pancreatic resection, but it has no constant procedure has been established for precautionary measure against POPF. Therefore as the study done it was suggested that further investigation is necessary to develop a reliable strategy for the prevention of POPF to reduce the risk after pancreatic resection as a side effect in the pancreatic cancer individuals.

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