

Principles of Resection for Pancreatic Cancer – Pancreaticogastroanastomosis Experiences

– Study

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1. Summary

Carcinoma of pancreas is also called ductal carcinoma, adenocarcinoma, is the most common type of pancreatic cancer, accounting for more than 90 percent of pancreatic cancer diagnoses. This cancer occurs in the lining of the ducts in the pancreas. It's also possible for adenocarcinoma to develop from the cells that create pancreatic enzymes. If the cancer is detected at an early stage when surgical removal of the tumor is possible, the 5-year relative survival rate is 44%. About 12% of people are diagnosed at this stage. If the cancer has spread to surrounding tissues or organs, the 5-year relative survival rate is 15%.

2. Introduction

Every person is different, with different factors influencing their risk of being diagnosed with this cancer and the chance of recovery after a diagnosis. It is important to talk with your doctor about any questions you have around the general statistics provided below and what they may mean for you individually. In 2023, an estimated 64,050 adults [33,130 men and 30,920 women] in the United States will be diagnosed with pancreatic cancer. The disease accounts for approximately 3% of all cancers. Pancreatic cancer is the eighth most common cancer in women and the tenth most common cancer in men. In both men and women, the number of new cases of pancreatic cancer have gone up by around 1% each year since the late 1990s. Worldwide, an estimated 495,773 people were diagnosed with pancreatic cancer in 2020. It is estimated that 50,550 deaths [26,620 men and 23,930 women] from

this disease will occur in the United States in 2023. It is the fourth leading cause of cancer death in both men and women. Pancreatic cancer accounts for 7% of all cancer deaths. Since the late 1990s, the death rate has very slowly increased by 0.2% per year in men and stayed steady in women. In 2020, an estimated 466,003 people worldwide died from pancreatic cancer. Carcinoma of pancreas is 7th place in mortality in oncologic patients as men and in women it is worldwide dominante in developed countries. despite intensive research is 5-year survival rate in patients approximately 10%. Surgical complete R0 resection means the only surgical treatment with comedy to survival rate up to 23% [1]. In case of localized disease in time of diagnosis 5-year survival rate done $\geq 20\%$ while in advanced diseases is media of survival 6-10 months, but without adjuvant therapy its only 3-5 months.

3. Surgical Therapy of Pancreatic Cancer

Surgical resection is it the only the therapeutic methos with potential of curative effect. The goal of treatment is complete removal of the tumor and dissection of lymph nodes. This treatment is only possible in approximately 11.20% patients. Resection with microscopically positive resection lines or with macroscopic positive resection line doesn't improve prognosis of the patient in comparison with palliative treatment. Respectability of the carcinoma increased over the years, by increasing of the diagnostic methods, better surgical techniques and experience of the surgeon. There has to be noted that survival depends on type of carcinoma, size of tumor. Terminology "small carcinoma tumor" is for tumors smaller

than 2cm and according to different authors 5-years survival interval 33-55%. in tumor up to 4 cm survival rate 12% and in tumors over 5 cm 0% survival rate [2,3].

Invasion of tumor into venous structures is not a contraindication of resection [anomaly distance of arteria hepatica from arteria mesenterica superior, whit was for many years an absolute contraindication until that time]. Po operation mortality decreased and 30 days post operation mortality is less than 2%. Also, in surgical treatment of carcinoma of pancreas the surgeon is the factor of prognosis. More experience surgeon increases the outcome.

4. Lymphonodectomy

Problematics of dissection of lymph nodes as if other organ systems is different among Japanese authors and Europeans. European multicentric prospective randomized studies wasn't that optimistic in comparison with standard and expanded dissection of lymph nodes, surviving of patients didn't depend on range of dissections [4]. To the same conclusion came Yeo in prospective randomized study of 114 patients when according to two-year survival rate the benefit wasn't shown for extensive lymph node dissection [5].

Nakagawa finds three ways of metastasing the pancreatic cancer:

- through ligamentum hepatoduodenalis
- in way to radix of mesenterium and arteria mesenterica superior
- in the way to corpus and cauda pancreatis [6]

In this area the most used resection in Japan is completed by en-bloc dissection of the first and second stage of lymph nodes, that means local and locoregional: subpyloric, retropyloric, coelical, pancreatoduodenal, upper and lower pancreatic, lymph nodes from hepatoduodenal ligament, lymph nodes around arteria mesenterica superior and para-aortal lymph nodes. Dissection uses precise sclerotisation of porta hepatis, truncus coeliacus, arteria mesenterica superior, vena cava inferior and Aorta [7]. From our own experience he advanced D2 lymphonodectomy in present time doesn't increase operative and postoperative morbidity and can only benefit from removing potential malignant infiltrated lymph nodes and at the same time sufficient removal of lymph nodes enables exact histopathologic examination, which leads to precise classification of the disease, type of adjuvat CHT/RT therapy as prognostic factor of survival (Figure 1) (Tables 1 and 2).

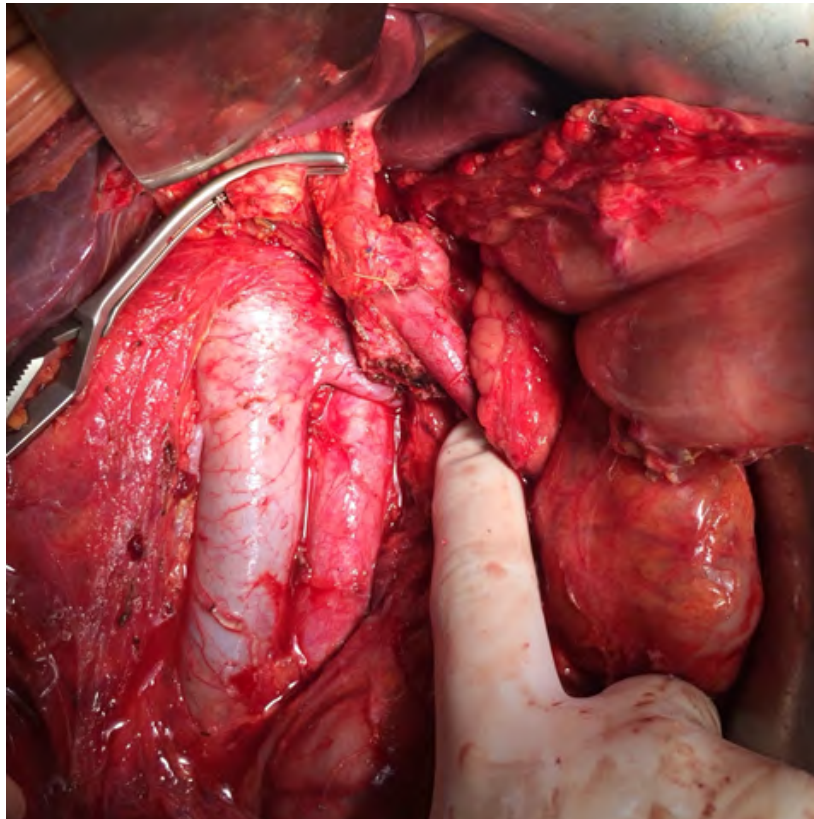


Figure 1: lymphonodectomy

Table 1: History of surgery of pancreatic surgery

Year	Surgeon	Place	Procedure	Notes
1882	Friedrich Trendelenburg	Bonn, Germany	DP and splenectomy	First anatomical solid tumor resection
1898	Alessandro Codivilla	Imola, Italy	One-stage partial PD	First attempted radical PD, unsuccessful
1898	William Halsted	Baltimore, USA	Transduodenal excision	First local periampullary tumor excision
1909	Walther Kausch	Berlin, Germany	Two-stage partial PD	First successful partial PD
1914	Georg Hirschel	Heidelberg, Germany	One-stage partial PD	First successful one-stage partial PD
1929	Roscoe Graham	Toronto, Canada	Enucleation	First neuroendocrine tumor resection
1934	Allen Whipple	New York, USA	Two-stage PD	First anatomical PD (ampullary carcinoma)
1937	Alexander Brunschwig	New York, USA	Two-stage PD	First anatomical PD for PDAC
1940	Allen Whipple	New York, USA	One-stage anatomic PD	First one-stage anatomical PD
1942	Kenneth Watson	Surrey, England	Two-stage PPPD	First PPPD
1944	Priestley			First total duodenopancreatectomy
1946	Waugh and Clagett	USA		Described alternative implantation of rest of pancreas into the gaster
1998	Reding	Europe		First implanted rest of pancreas into the gaster
1978	Traverso & Longmire	Los Angeles, USA	One-stage PPPD	Reintroduction and popularization of PPPD
1994	Gagner & Pomp	Montreal, Canada	Laparoscopic PD	First laparoscopic pancreatic resection
2003	Giulianotti et al.	Grosseto, Italy	Robot-assisted lap PD	First robotic pancreatic resection

Table 2: TNM classification

T category	Tumor criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
	This includes high-grade pancreatic intraepithelial neoplasia, intraductal papillary mucinous neoplasm with high-grade dysplasia, intraductal tubulopapillary neoplasm with high-grade dysplasia, and mucinous cystic neoplasm with high-grade dysplasia
T1	Tumor limited to the pancreas, <2 cm in greatest dimension
T1a	Tumor <0,5cm in greatest dimension
T1b	Tumor <0,5cm and >1cm in greatest dimension
T1c	Tumor 1 to 2 cm in greatest dimension
T2	Tumor > 2cm and < 4cm in greatest dimension
T3	Tumor <4cm in greatest dimension
T4	Tumor involves celiac axis, superior mesenteric artery, and/or common hepatic artery, regardless of size
Regional lymph node (N)	
N category	Lymph node criteria
NX	Lymph node cannot be assessed
N0	no regional node metastases
N1	Metastasis in one to three regional lymph nodes
N2	Metastasis in four or more regional lymph nodes
Distant metastases (M)	
M category	Metastasis criteria
M0	Distant metastases are not present
M1	Distant metastases are present

5. Pancreatico Gastroanastomosis after Whipple Resection

The goal of this article is not to describe all possible surgical technique resection of pancreas [such as technique of arterial or venous resection in case of cancer infiltration] and all the other thematic of pancreatic cancer as genetic mutalities K-RAS, ethiology. And principles of all possible surgical complications in this disease. The subject of this article is to present 37 patients operated in 2015-2020, which were operated in different stages of pancreatic cancer, mostly T2N1M0 and T3N2M0. In all patients were performed cephalic pancreato-duodectomy by Whipple, wish followed-up reconstruction and implantation rest of the pancreas into the gaster (Figure 2-3). First it was described by Waught and Clagett in 1946 and first implant rest of the pancreas into the gaster was performed in 1998 by Reding in Europe. All patients were operated by one surgeon. Dehiscencia of anastomosis wasn't in any patient, peroperatively was inserted 3-way naso-gastric-jejunal probe to ensure to decompression of gaster in postoperative time and fast track enteral nutrition usually 48-72 hours after surgery, when the peristaltics occurred. In one patient by the construction hepatico-jejunoanastomosis we left stent in hepaticus to avoid development of stenosis of anastomosis. Hepaticus was not dilated in early insertion of choledocho-jejunal stent peroperatively. During the surgery we respected all histopathological criteria of resection line and pancreas and choledochus with tumors and resection lines were separately send to ensure histological clear R0 resection (Figure 4). Postoperative morbidity up to 30 days was 0% without need of reoperation. From the latter complications we didn't observe pancreatic fistula, nor intraabdominal abscessus. The only complication was occurring of icterus 2 month later in patient with hepato-jejunal stent, which was dislocated and caused obstruction. This complication was treated by gastroenteroscopic extraction of the stent. 3-year survival rate of this non-homogenous group of patients was 29%.

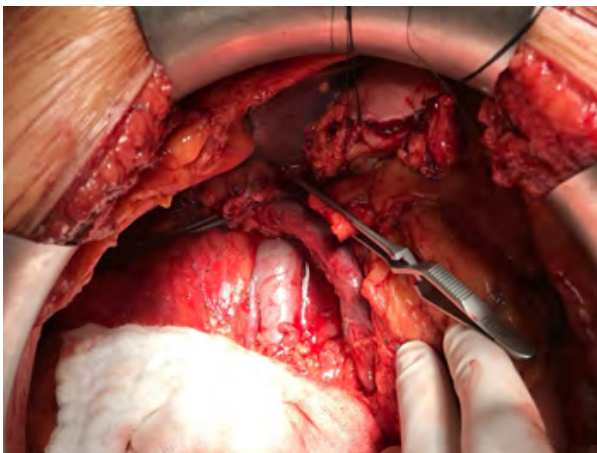


Figure 2: Status post Whipple resection with clamation of rest of pancreas

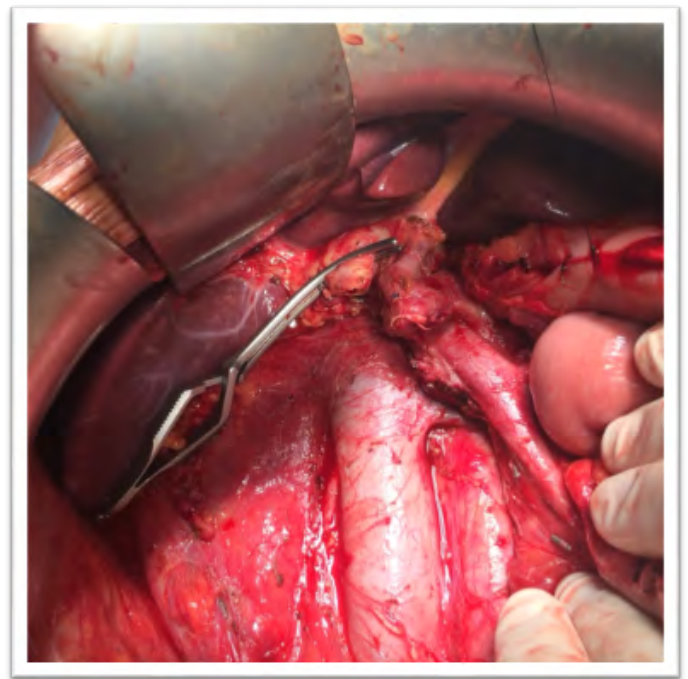


Figure 3: Status post pancreaticogastroanastomosis reconstruction before final complete hepaticojejuno and gastroanastomosis

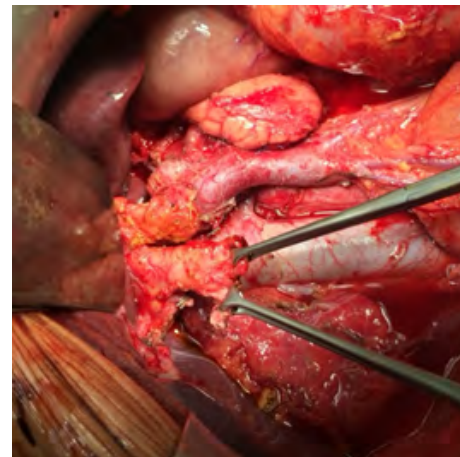


Figure 4: Status post Whipple resection hepatocholedochus before short-age and histopathologic examination of negative resection line

6. Most Common Complications and Discussion

Most early postoperative complications are bleeding, dehiscencia pancreatico-jejuno-anastomosis or hepatico-jejuno anastomosis, thrombosis of vena mesenterica superior or vena portae. Later complications are intraabdominal abscesses and slower motility of gastric movement. Each complication which needs reoperation for patients is potentially fatal. One of the unusual ways of treatment of thrombosis of vena mesenterica superior I described in previous article, using bypass of vena ovarica l.dx after unilateral adnexectomy and it's implantation under the thrombosis of vena mesenterica superior of vena portae. This venous bypass lets release of congestion of bowels and gives a chance to recanalisation using medicamentous treatment. After successful recanalisation

this bypass is not dominant by pressure gradient in venous blood, therefore complications as systemic portal encephalopathy, is lost [8]. Resection of pancreas is according to the status that dehiscencia pancreatic anastomosis is for patients' life the highest complication, which reoperation leads to total pancreatectomy and every other reoperation leads to higher mortality rate. According to our experience we can recommend one of the safest methods in adequate ensuring of the decompression sond, because overpressure of this dehiscence in gaster would lead to dehiscence of this anastomosis. Drainage put in the most risk places as pancreatico-gastro and hepatico-jejuno is important for early detection of dehiscencia and drainage serosanguinolent fluid, which can lead to intraabdominal abscessus. For precise evaluation of the study, we would need to compare the patients with the same TNM classification before and after the surgery, evaluating size of tumor, number of metastatic lymph nodes, therefore the survival rates are different in different countries.

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