

Clinical Pattern and Histological Variation of Different Pancreatic Tumors Treated by Whipple's Operation at Bangabandhu Sheikh Mujib Medical University

Dr. Anharur Rahman^{1*}, Dr. Zulfiqur Rahman Khan², Dr. Md. Saief Uddin³, Dr. Abu Taher⁴

¹Assistant Professor, Department of Surgery, Ad-din Akij Medical College, Khulna, Bangladesh

²Professor & Ex-Chairman, Department of Hepatobiliary & Liver Transplant Unit, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

³Associate Professor, Department of Hepatobiliary & Liver Transplant Unit, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

⁴Professor, Department of Colorectal Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

DOI: [10.36347/sjams.2022.v10i09.035](https://doi.org/10.36347/sjams.2022.v10i09.035)

| Received: 21.07.2022 | Accepted: 28.08.2022 | Published: 30.08.2022

*Corresponding author: Dr. Anharur Rahman

Assistant Professor, Department of Surgery, Ad-din Akij Medical College, Khulna, Bangladesh

Abstract

Original Research Article

Introduction: The Whipple's Operation was first described in the 1930s by Allan Whipple. In the 1960s and 1970's the Mortality rate for the Whipple Operation was very high. Pancreatic tumors are one of the important indications for Whipple's operation. Approximately 85% of patients have a very aggressive type of tumor called adenocarcinoma of the pancreas. About 15% of patients' other tumors in the pancreas are found in the head region which is a less aggressive type of tumor (Benign) which are curable by Whipple's operation. **Aim of the Study:** The aim of the study was to compare preoperative findings, postoperative complications, and prognosis of different benign and malignant pancreatic tumors of patients who underwent Whipple's surgery. **Methods:** This cross-sectional observational study was conducted at the Department of Hepatobiliary and Pancreatic Surgery, Bangabandhu Sheikh Mujib Medical University (B.S.M.M.U), Dhaka, Bangladesh. The study duration was 2 years, from August 2010 to July 2012. During this period, a total of 20 cases were selected through the purposive sampling technique following the inclusion and exclusion criteria for the purpose of this study. **Result:** In our series 80% of tumors were adenocarcinoma and 20% of tumors were benign Tumors. In this series post, operatively 60% of the total patient had developed wound infections, 40% had wound gaps, 15% had a chest infection, and 10% had pancreatic fistula, and gastroparesis, postoperatively, the death rate was 0%. **Conclusion:** Most pancreatic tumors were located in the head of the pancreas which can be treated by Whipple's operation. Adenocarcinoma of the head is the most common indication of surgery and is surgically resectable. Other large benign tumors which are situated in the pancreatic head region are cystic tumors, including mucinous cystadenoma and serous cyst adenoma, solid pseudo papillary tumors, and papillary cystic neoplasms. The most common complications of surgery include wound infections, wound gaps, chest infections, pancreatic fistula, and gastroparesis. It may also be concluded that postoperative complication is less in benign tumors than malignant pancreatic tumors. Most pancreatic tumors are located in the head of the pancreas which can be treated by Whipple's operation. The most common complications of surgery include wound infections, wound gaps, chest infections, pancreatic fistula, and gastroparesis.

Keywords: Tumor, Malignant, Benign, Carcinoma.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Allan Whipple initially explained The Whipple's Operation in the 1930s. The Whipple Operation had an extremely high mortality rate in the 1960s and 1970s. Up to 25% of patients had surgery-related death [1]. Some doctors are still hesitant to suggest the Whipple procedure because of their

memories of the 1970s experience. The duodenum, gallbladder, and part of the bile duct are also removed during Whipple's procedure. On occasion, the stomach may also be partially removed. The residual pancreas, bile duct, and intestine are sutured back into the intestine after these components have been removed in order to redirect the gastrointestinal secretions back into the gut [2]. One of the key indications for a Whipple

Citation: Anharur Rahman, Zulfiqur Rahman Khan, Md. Saief Uddin, Abu Taher. Clinical Pattern and Histological Variation of Different Pancreatic Tumors Treated by Whipple's Operation at Bangabandhu Sheikh Mujib Medical University. Sch J App Med Sci, 2022 Sept 10(9): 1378-1383.

1378

procedure is the presence of pancreatic tumors. Adenocarcinoma of the pancreas, an extremely aggressive kind of malignancy, affects about 85% of patients [3]. About 15% of patients also have additional, less aggressive pancreatic tumors in the head area that can be treated with the Whipple procedure [4]. Determining the best course of action for pancreatic tumors requires an examination at a facility with experience in the treatment of pancreatic cancer. Adenocarcinoma, a tumor that develops from cells in the pancreatic duct, is the most prevalent kind of pancreatic cancer. Each year, some 30,000 new instances of pancreatic adenocarcinoma are identified, and 28,000 people lose their lives to the disease [5]. At the time of diagnosis, only 20 to 40 percent of individuals with pancreatic adenocarcinoma have a tumor that is restricted to the organ [6]. The Whipple procedure is frequently used to treat other benign pancreatic cancers. This group of tumors includes islet cell tumors (also known as neuroendocrine tumors), papillary cystic neoplasms, and lymphomas of the pancreas, acinar cell tumors of the pancreas, and metastatic tumors to the pancreas. Cystic tumors or neoplasms include mucinous cyst adenoma, solid pseudo papillary tumors of the pancreas, and serous cystadenoma [7]. The majority of these tumors are benign or non-malignant, although depending on the kind of tumor, even malignant tumors have five-year survival rates in the range of 40 to 80 percent. Given the positive results, intensive surgical treatment is recommended for these tumors, and the afflicted portion of the pancreas is excised [8]. Pancreatic cancer and pancreatic tumors are becoming rather frequent in Bangladesh. Many cases of pancreatic cancer are discovered early and treated with Whipple's procedure thanks to contemporary facilities. Whipple's procedure is also used to treat some big benign tumors, and the prognosis is favorable. However, no prior research has been done to compare the outcomes of various pancreatic cancers treated with the Whipple procedure.

OBJECTIVE

General Objective

- To compare preoperative findings, postoperative complications, and prognosis of different benign and malignant pancreatic tumors of patients who underwent Whipple's surgery

Specific Objectives

- To find out different modes of clinical presentation.
- To evaluate the different investigations.

METHODS

This cross-sectional observational study was conducted at the Department of Hepatobiliary and Pancreatic Surgery, Bangabandhu Sheikh Mujib Medical University (B.S.M.M.U), Dhaka, Bangladesh. The study duration was 2 years, from August 2010 to July 2012. During this period, a total of 20 cases were selected through the purposive sampling technique following the inclusion and exclusion criteria for the purpose of this study. Patients were then divided into two groups based on whether the pancreatic cancer was malignant or not. Informed written consent was obtained from all participants or their legal guardians, and ethical approval was obtained from the ethical review committee of the study hospital. Necessary data was collected through face-to-face interviews using a data collection sheet, and collected data were recorded and analyzed using SPSS software.

Inclusion Criteria

- Pancreatic tumor cases who had undergone Whipple's operation
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Non-Pancreatic tumor cases.
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

RESULTS

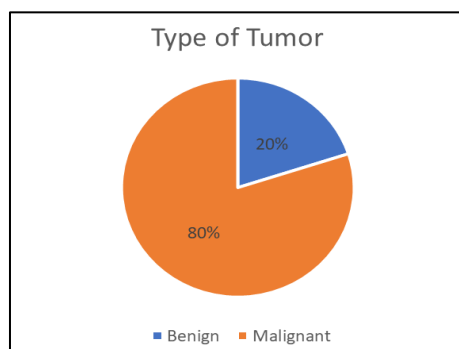


Figure 1: Distribution of patients based on the malignancy of pancreatic tumor [N=20]

Among the total 20 tumor cases, 80% were malignant, and only 20% were benign.

Table 1: Distribution of the participants by presenting characteristics [N=20]

Characteristics	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Age		
<35 Years	4, 100%	0, 0%
35-44 years	0, 0%	4, 25%
45-65 years	0, 0%	12, 75%
Gender		
Male	1, 25%	12, 75%
Female	3, 75%	4, 25%

It was observed that 100% of the benign tumor cases were under 35 years of age, while none of the malignant tumor cases were from that age group. 25% of the malignant tumor cases were from the age group

of 35-44 years, while 75% were from the age group of 45-65 years. 75% of benign tumor cases were female, while 75% of malignant tumor cases were male.

Table 2: Distribution of study participants by chief complaints [N=20]

Chief Complaints	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Yellowish Eye Color	1, 25%	16, 100%
Passing pale stool	1, 25%	16, 100%
Abdominal Pain	4, 100%	2, 12.5%
Itching	0, 0%	14, 87.5%
Vomiting	1, 25%	6, 37.5%
Loss of appetite	0, 0%	16, 100%
Weight Loss	0, 0%	16, 100%
High Color Urine	1, 25%	16, 100%

Among the participants of the benign tumor group, 100% had abdominal pain, and 25% of patients each complained of yellowish eye color, passing pale stool, vomiting, and high color urine. Among the malignant tumor cases, all 100% of the patients

complained of yellowish eye color, passing pale stool, loss of appetite, weight loss, and high color urine. 12.5% also had abdominal pain, 37.5% had vomiting and 87.5% had itching.

Table 3: Comparative results of study subjects by clinical examination findings [N=20]

Clinical Findings	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Jaundice	1, 25%	16, 100%
Anemia	2, 50%	16, 100%
Palpable Gallbladder	1, 25%	13, 81.25%
Palpable Abdominal Lump	4, 100%	0, 0%

According to clinical examination findings, 100% of the benign tumor group had a palpable abdominal lump, 50% had anemia, 25% had palpable gallbladder and 25% had jaundice. Among the

malignant tumor cases, jaundice and anemia were observed in all 100% of cases, while 81.25% had palpable gallbladder.

Table 4: Comparative results of study subjects by investigations [N=20]

Investigative Findings	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Hb <10 gm/dl	2, 50%	16, 100%
S. Bilirubin >1.2 mg/dl	1, 25%	16, 100%
Prothrombin Time >15 Secs	0, 0%	14, 87.5%
S. Alkaline Phosphatase >126U/L	2, 25%	16, 100%
S. Albumin <3.5 gm	0, 0%	14, 87.5%
CA19.9>40U/ml	0, 0%	16, 100%

Among patient having benign pancreatic tumor, 50% patient had Hb10gm/dl<, 25% had S.bilirubin >1.2gm/dl , S.Alk Phosphatase>126U/L but

0% had S.albumin3.55gm/dl<&CA19.9>40U/ml). But in case of patient having malignant tumor, 100% patient had Hb10gm/dl<, S.bilirubin>1.2gm/dl,

CA19.9>40U/ml, S.Alk Phosphatase>126U/L, while 87.5% had S. albumin 3.55gm/dl < & prothrombin time

>15 secs.

Table 5: Comparative results of study subjects by postoperative complication after Whipple's operation [N=20]

Post-Operative Complication	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Wound Infection	1, 25%	10, 62.5%
Wound Gap	0, 0%	7, 43.75%
Pancreatic Fistula	0, 0%	2, 12.5%
Gastroparesis	0, 0%	2, 12.5%
Chest Infection	0, 0%	4, 25%
Anastomotic Leakage	0, 0%	1, 6.25%
Death	0, 0%	0, 0%

After Whipple's operation for solid pseudo papillary tumor of the pancreas, or benign tumor group, 25% of patients had developed wound infection postoperatively. But in the case of Whipple's operation for adenocarcinoma pancreas, postoperatively 62.25%

of patients developed wound infection & 43.75 % patients developed wound gap, 25% patient developed a chest infection, 12.5% patient developed pancreatic fistula, gastroparesis, and 6.25% patient developed anastomotic leakage.

Table 6: Comparative results of study subject by CT scan findings [N=20]

CT Scan Findings	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Tumor Size >5 cm	4, 100%	0, 0%
Tumor at the Head of the pancreas	4, 100%	16, 100%
Dilated Intra & extrahepatic biliary tree	1, 25%	16, 100%
Enlarged gallbladder	1, 25%	15, 93.75%

On CT scan, 100% of benign pancreatic tumor site was the head region of pancreas, 100% had tumor size >5cm, 25% had Intra & extrahepatic biliary tree dilated & enlarge gallbladder each. But in the case of malignant pancreatic tumors, 100% of tumors were

located at the pancreatic head but 0% had a tumor size of >5cm. 100% had Intra & extrahepatic biliary tree dilated and 93.75% of patients had enlarged gallbladder.

Table 7: Comparative results of study subjects based on follow-up reports of 1 year after Whipple's surgery: [N=20]

1-year follow-up	Benign Tumor (n=4),%	Malignant Tumor (n=16),%
Normal Liver Function Test	4, 100%	12, 75%
Normal levels of Ca 19-9	4, 100%	12, 75%
Normal USG findings of the abdomen	4, 100%	12, 75%
Needs Readmission	0, 0%	4, 25%

At a follow-up after 1 year of Whipple's surgery, none of the benign tumor cases needed readmission, as all 100% had normal liver function tests, normal levels of CA 19-9, and normal USG findings in the abdomen. On the other hand, 25% of the malignant tumor cases had some form of complication and needed readmission.

DISCUSSION

Whipple's operation is indicated for a variety of benign and malignant pancreatic tumors. It is most commonly (85%) performed for adenocarcinoma arising in the head of the pancreas. The procedure is also utilized for less common large benign neoplasms (15%) that arise in the head of the pancreas. These include cystic neoplasms, both serous and mucinous cyst adenomas, mucinous cyst adenocarcinomas, intraductal papillary mucinous neoplasms, benign islet

cell tumors, and solid pseudo papillary neoplasms. In our series among 20 patients, 16 (80%) patients had undergone Whipple's operation for adenocarcinoma of the head of the pancreas. Other 4(20%) patients had done Whipple's operation for solid pseudo papillary tumor of the pancreas, which had arisen from the pancreatic head. The incidence of pancreatic carcinoma was higher in men than women, which was supported by the findings of other studies [6]. The present study observed that all 4 patients with benign tumors were <35 years of age, while none from the malignant tumor cases belonged to this age group. It was also observed that patients in the malignant tumor group had a higher prevalence as age increased. This suggests that benign tumors can metastasize with age, which was supported by findings of other studies [9, 10] Early symptoms of pancreatic adenocarcinoma are often vague and nonspecific and their significance is frequently overlooked. Symptoms are generally related to the mass

effect rather than disruption of exocrine or endocrine activity and exact clinical features will depend on the size and location of the tumor as well as its metastases. More than 70% of people with pancreatic adenocarcinoma eventually experience some abdominal pain as the tumor grows. Pancreatic cancer can cause a dull ache in the upper belly and back pain [7]. More than 75% occur in the head of the pancreas and classically present with painless, progressive obstructive jaundice. The urine is dark because of the high level of conjugated bilirubin and the absence of urobilinogen. The stool is pale because of the lack of stercobilinogen in the bowel. In addition to jaundice, rising bilirubin levels can cause severe itching. 30% of a patient having adenocarcinoma head of the pancreas gives a history of unexplained weight loss and loss of appetite. Weight loss may be caused or exacerbated by anorexia, diarrhea, or early satiety. Obstruction of the pancreatic duct causes steatorrhea, exacerbating weight loss and malnutrition. Patients commonly become cachectic as the disease progresses. As hepatic function becomes compromised, patients experience fatigue, anorexia, and bruising caused by a deficiency of clotting factors. In our series, among patients having a malignant pancreatic tumor, all 16 patients (100%) complained of yellowish eye color, weight loss, loss of appetite, h/o passing pale stool & h/o passing high color urine. Only 2 patients (12.5%) complained of abdominal pain & 14(87.5%) patients complained about itching, while another 6 patients (37.5%) complained about vomiting. On clinical examination, all 16 (100%) patients are jaundiced & anemic, and 12 (80%) patients had palpable gallbladder but no patient had an abdominal lump. Accurate diagnosis of the special type of pancreatic tumor is obviously important. ERCP-guided tissue biopsy & CT-guided Fine-needle aspiration biopsy is needed for definitive diagnosis. Kazuki Ogoshi *et al.*, reported that 98% of their study sample had been detected positive for pancreatic malignancy preoperatively by tissue biopsy ERCP [11]. Fine-needle aspiration may play an important role in preoperative planning by helping distinguish SPTs from other pancreatic lesions with a significantly different prognosis and treatment. The serum levels were also investigated in our study. Obstruction of the bile duct can cause jaundice with proportionately increased levels of conjugated bilirubin and alkaline phosphatase in the blood. Serum bilirubin and alkaline phosphatase levels can point to pancreatic cancer, but they are not diagnostic. The serum tumor marker cancer antigen (CA) 19-9 may help confirm the diagnosis in symptomatic patients. In the case of a solid pseudo papillary tumor, there are usually no abnormalities in clinical laboratory tests (eg, S.bilirubin, S.alkaline phosphatase levels) or pancreatic cancer marker CA19-9. The present study supported this statement, as among patients having a benign solid pseudo papillary tumor, 2 patients (50%) had Hb level less than 10gm/dl, 1 patient (25%) had serum bilirubin level > 1.2mg/dl, and another had S. alkaline phosphatase >126U/L. All other

investigations revealed normal findings. But among patient having malignant pancreatic tumor (adenocarcinoma), all 16 patients (100%) had Hb <10 gm/dl, S. Bilirubin (>1.2mg/dl), CA 19-9 >40 U/ml and 14 patients (87.5%) had Prothrombin Time>15 secs & S. albumin <3.5gm/dl. In our series among patients having benign solid pseudo papillary tumor of the pancreas, all 4 (100%) patients had solid hypoechoic mass >3cm on USG of whole abdomen, 1 patient (25%) has dilated Intra & extrahepatic biliary tree dilated & distended gallbladder. But among patients with malignant pancreatic tumor (adenocarcinoma), all 16 (100%) patients had dilated Intra & extrahepatic biliary tree and distended gallbladder on USG of the whole abdomen. On USG of the whole abdomen, no patient had a Solid hypoechoic mass measured. The CT scan results of our study showed among benign tumor patients, all 4 patients (100%) had tumors from the pancreatic head, size >3cm, well- encapsulated tumor, and the tumor were free from other structures, while 1 patient (25%) had distended gallbladder & dilated CBD and Intrahepatic biliary tree. No patients had ascites & abdominal lymphadenopathy. In the case of adenocarcinoma pancreas, a CT scan of the abdomen showed all 16 Patients (100%) had pancreatic tumors arising from the pancreatic head. No patient had abdominal lymphadenopathy or ascites. But in the case of a solid pseudo papillary tumor, a CT scan showed that 100% of the tumor arose from the pancreatic head, and 100% had a tumor size >3cm. The Whipple's operation is a complex operation with a high chance of developing complications if the surgeon performing the surgical procedure has limited experience in this operation [12]. In the hands of surgeons who are experienced with this surgical operation, the complication rate is usually very low. The problems and complications that may be seen after this operation include: pancreatic fistula, gastroparesis, wound infection, anastomotic leakage, or even death. In our study, only 1 patient in the benign tumor group had post-operative complication after Whipple's surgery, while among the malignant tumor cases, 10 patients (62.5%) had wound infection, 5 patients (31.25%) had wound gap, 2 patients (12.5%) had gastroparesis and pancreatic fistula, 4 patients (25%) patient had chest infection & 1 patient had (6.25%) anastomotic leakage. This was much higher compared to another study conducted in 1997 [7]. This higher rate of complications might be due to the small sample size. The overall survival after Whipple's operation for pancreatic adenocarcinoma is about 20% five years after surgery. Patients without the spread of cancer into their lymph nodes may have up to 40% survival [13]. The operation is usually 100 % curative in patients with benign or low-grade tumors of the pancreas [13]. This was proven by the findings of our study, where all 4 patients from the benign tumor group showed no complications at year follow-up, while 25% of the malignant tumor cases had some form of complications and needed readmission at their 1-year follow-up.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Most of pancreatic tumors were located in the head of the pancreas which can be treated by Whipple's operation. Adenocarcinoma of the head is most common indication of surgery and is surgically resectable. Other large benign tumors which are situated in pancreatic head region are cystic tumors, including mucinous cystadenoma and serous cyst adenoma, solid pseudo papillary tumor, papillary cystic neoplasms. Most common complications of surgery include wound infections, wound gap, chest infection, pancreatic fistula, and gastro paresis. It may also concluded that postoperative complication is less in benign tumor than malignant pancreatic tumors. Most of pancreatic tumors are located in the head of the pancreas which can be treated by Whipple's operation. Most common complications of surgery include wound infections, wound gap, chest infection, pancreatic fistula, and gastro paresis.

FUNDING

No funding sources.

CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

REFERENCES

- Salvia, R., Bassi, C., Festa, L., Falconi, M., Crippa, S., Butturini, G., & Pederzoli, P. (2007). Clinical and biological behavior of pancreatic solid pseudo papillary tumors: report on 31 consecutive patients. *Journal of surgical oncology*, 95(4), 304-310.
- Yeo, C. J., Cameron, J. L., Sohn, T. A., Lillemoe, K. D., Pitt, H. A., & Talamini, M. A. (2005). Guidelines for the management of patients with pancreatic cancer perampullary and ampullary carcinomas. *Gut*, 54(5), v1-16.
- Stojadinovic, A., Brooks, A., Hoos, A., Jaques, D. P., Conlon, K. C., & Brennan, M. F. (2003). An evidence-based approach to the surgical management of resectable pancreatic adenocarcinoma. *Journal of the American College of Surgeons*, 196(6), 954-964.
- Freelove, R., & Walling, A. (2006). Pancreatic cancer: diagnosis and management. *American family physician*, 73(3), 485-492.
- Guthrie, J. A., & Sheridan, M. B. (2008). Investigation of abdominal pain to detect pancreatic cancer. *BMJ*, 336(7652), 1067-1069.
- Yang, G. Y., Wagner, T. D., Fuss, M., & Thomas Jr, C. R. (2005). Multimodality approaches for pancreatic cancer. *CA: a cancer journal for clinicians*, 55(6), 352-367.
- Strasberg, S. M., Drebin, J. A., & Soper, N. J. (1997). Evolution and current status of the Whipple procedure: an update for gastroenterologists. *Gastroenterology*, 113(3), 983-994.
- Mortele, K. J., Lemmerling, M., de Hemptinne, B., De Vos, M., De Bock, G., & Kunnen, M. (2000). Postoperative findings following the Whipple procedure: determination of prevalence and morphologic abdominal CT features. *European radiology*, 10(1), 123-128.
- Chan, C. M., Adler, Z., Reith, J. D., & Gibbs Jr, C. P. (2015). Risk factors for pulmonary metastases from giant cell tumor of bone. *JBJS*, 97(5), 420-428.
- Awonuga, A. O., Shavell, V. I., Imudia, A. N., Rotas, M., Diamond, M. P., & Puscheck, E. E. (2010). Pathogenesis of benign metastasizing leiomyoma: a review. *Obstetrical & gynecological survey*, 65(3), 189-195.
- Ogoshi, K., & Niwa, M. (1977). The diagnostic evaluation of ERCP in pancreatic and biliary carcinoma. *Gastroenterological Japonica*, 12(3), 218-223.
- Tran, K. T., Smeenk, H. G., Van Eijck, C. H., Kazemier, G., Hop, W. C., Greve, J. W. G., ... & Jeekel, H. (2004). Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and perampullary tumors. *Annals of surgery*, 240(5), 738.
- Sultana, A., Tudur Smith, C., Cunningham, D., Starling, N., Neoptolemos, J. P., & Ghaneh, P. (2008). Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer: results of secondary end points analyses. *British journal of cancer*, 99(1), 6-13.