Medical Science

pISSN 2321–7359; eISSN 2321–7367

Postoperative outcome of pancreaticoduodenectomy for pancreatic ductal adenocarcinoma and predictors of 1st year mortality

Sayed Shaker Shaeir[1*], **Fouad Abdelshaheed**[1], **Ahmed Elsebaiy**[1], **Mohamed Emam Sobeih**[2], **Eman Desoky**[3], **Ahmed Shaaban Owis**[4], **Mahitab Ibrahim Eltohamy**[5], **Haitham Fekry Othman**[1]

To Cite:
Shaeir SS, Abdelshaheed F, Elsebaiy A, Sobeih ME, Desoky E, Owis AS, Eltohamy MI, Othman HF. Postoperative outcome of pancreaticoduodenectomy for pancreatic ductal adenocarcinoma and predictors of 1st year mortality. Medical Science, 2022, 26, ms290e2294. doi: https://doi.org/10.54905/disssi/v26i125/ms290e2294

Authors' Affiliation:
[1]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt
[2]Department of Medical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt
[3]Department of Cancer Epidemiology and Biostatistics, National Cancer Institute, 11796, Cairo University, Cairo, Egypt
[4]Department of Radiology, National Cancer Institute, 11796, Cairo University, Cairo, Egypt
[5]Department of Pathology, National Cancer Institute11796, Cairo University, Cairo, Egypt

[*]**Corresponding author**
Department of Surgical Oncology, National Cancer Institute, Cairo University, Fom El Khalig Square, 11796,
Cairo, Egypt
Email: sayed.sheier@nci.cu.edu.eg

Peer-Review History
Received: 18 May 2022
Reviewed & Revised: 20/May/2022 to 14/July/2022
Accepted: 15 July 2022
Published: 20 July 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Background: Due to late detection, a low percentage of resectable malignancies, and resistance to systemic therapy, pancreatic ductal adenocarcinoma (PDAC) has the poorest outcome of all pancreatic cancers. The basis of contemporary multimodal therapies aimed at long-term survival is complete lesion excision. Postoperative complications are common consequences following pancreaticoduodenectomy (PD). *Objective:* To investigate the outcome and factors contributing to the 1st year survival after Whipple's procedure for pancreatic ductal adenocarcinoma. *Patients and Methods:* Between January 2020 and December 2021, all patients identified with pancreatic ductal adenocarcinoma (61 individuals) who had Whipple's surgery in the surgical department at the National Cancer Institute were included in this retrospective cohort analysis. *Results:* Wound infection (49.2%), followed by pancreatic leak (41.7%) were the most prevalent complications among the 61 patients who received PD. The 1styear survival rate was 77% (47/61). In multivariate assessment postoperative pancreatic fistula and adjuvant treatment were independent predictors of 1styear survival. *Conclusion:* In multimodally managed patients following curative PDAC surgery, individuals who acquired a postoperative pancreatic fistula and did not get adjuvant therapy had greater 1st year death rates.

Keywords: Pancreaticoduodenectomy; Pancreatic tumor survival; Ductal adenocarcinoma.

1. INTRODUCTION

Pancreatic cancer (PC) is a deadly illness that is usually discovered when it is too late. Despite breakthroughs in medicinal and surgery management

choices, people with PC typically go undiagnosed in the initial phases, resulting in a small number of instances of early identification (Luu et al., 2019; Chari et al., 2015). Pancreatic ductal adenocarcinoma (PDAC) is the most frequent histological form of PC, represents over 95% of all cases (Soloff et al., 2018; Kamisawa et al., 2016; Alenezi, 2021). The pancreatic head is where PDAC is most usually found (54.7 percent). Unfortunately, only around 20% of people with PC have a tumor that can be removed (Soloff et al., 2018). A third of the patients had locally developed cancer, with the bulk of them having already developed distant metastases (Kardosh et al., 2018).

Whipple's operation is linked to substantial postoperative morbidity rates ranging from 30% to 60% (Jakhmola et al., 2014; Sahora et al., 2015). Pancreatic leaking or fistula, intra-abdominal abscess, bile leak, postoperative bleeding requiring blood transfusion or reopening, postponed emptying of the stomach, and risk factors associated to the surgical site such as infection and wound infection are all major postoperative problems from this operation (Martignoni et al., 2000). Overall, 5-year survival rates for all phases of PC vary from 2.5 percent to 5% (Siegel et al., 2019). A big cancer, a elevated cancer grade, lymph node lesions, a higher concentration of carbohydrate antigen 19-9 (CA19-9) and a positive resection margin are all linked with a bad prognosis (Hidalgo, 2010).

Current diagnostic and treatment procedures need a speedy multidisciplinary work flow, which often starts with the general practitioner. Signs such as painless jaundice, stomach discomfort, or loss of weight should always be considered. In such circumstances, abdominal computed tomography or magnetic resonance imaging should be performed as soon as feasible. Following that, a multidisciplinary review of the case will lead to one of three treatment options: primary surgical resection; neoadjuvant planned chemotherapy in situations of locally developed pancreatic tumor; or primary palliative chemotherapy in cases of metastatic cancer stage. The long-term survival (LTS) in PDAC is typically described as a postoperative survival of at least 5 years (Stark et al., 2016). We investigated the result and variables contributing to the first-year survival of all patients who received PD owing to PDAC of the pancreatic head in this research.

2. MATERIALS AND METHODS

This was a retrospective cohort research having all patients diagnosed with pancreatic head and peri-ampullary adenocarcinoma (61 individuals) who had Whipple's surgery in the surgical department at the National Cancer Institute between January 2020 and December 2021.

The archived Hematoxylin and Eosin slides of the specimens were retrieved from pathology department &were examined for confirmation of the diagnosis, and tumor grade was determined using World Health Organization guidelines (WHO). The pathologic stage was evaluated using the tumor-node-metastasis (TNM) classification system. Lymphovascular and perineural invasion and surgical margins were also reviewed (Giuliano et al., 2017).

Preoperative workup

As part of their preoperative workup for anesthetic fitness, all patients who were candidates for (PD) had a complete blood count, hepatic and renal activity test, thyroid function test, serum electrolytes, coagulation profile, electrocardiography, and CT chest. In terms of tumor staging, all patients were evaluated preoperatively using computed tomography scanning using a pancreatic protocol, as well as endoscopic ultrasonography in certain cases. As a therapeutic biliary drainage strategy for jaundice, preoperative ERCP with biliary stent placement was performed in certain patients. All individuals who had an ERCP also had a biliary stent inserted.

Statistical methods

Statistical Package for Social Sciences (SPSS) ver. 24 was used for data management and statistical analysis. Means and standard deviations, as well as medians and ranges, were employed to summarize numerical data. The proportions were employed to summarize categorical data. The t-test was employed to compare the two groups with regard to normally distributed numeric variables. The Mann-Whitney test was employed to analyze non-normally dispersed numeric data. When applicable, variations in categorical variables were evaluated utilizing the chi square test and Fisher's exact test. The Kaplan and Meier approach was employed to determine overall survival rates, and the Logrank test was performed to compare prognostic factors. Significant variables were then incorporated into the Cox Proportional Hazards Model. Overall survival rates were estimated from the time of detection to the time of mortality from any reason, with surviving patients and those who were lost to follow-up censored on the last known alive date. P-values are always two-sided. P-values <0.05 were deemed substantial.

3. RESULTS

61 individuals received Whipple's surgery between 2018 and 2020. The average age was 57.10 years, with a range of 33 to 75 years. There were 43 male patients and 18 female patients in the study. Jaundice was the most prevalent symptom that prompted patients to seek medical care (81.9 percent), followed by anorexia with weight loss (81.9 percent) (73.7 percent) (Table 1).

Table 1 displaying demographics and symptoms of patients.

Variables	Values
Age	57 ± 10
Sex (%)	
Male	43(70.5)
Female	18 (29.5)
Smoker (%)	30 (49.18)
Symptoms (%)	
Jaundice	81 (81.7)
Anorexia & Weight loss	45 (73.7)
Abdominal pain	35 (57.4)
Obstruction of Gastric Outlet	5 (8)

Preoperative factors

The average preoperative blood bilirubin concentration was 1.3 mg/dl, and 85 percent of patients received ERCP as a temporary method of preoperative biliary decompression.

Intraoperative factors

A solid pancreas was found in 38 of the 61 individuals, whereas a mushy and bulky pancreatic was seen in 23. We did not correctly estimate the pancreatic ducts caliber intraoperatively, but we utilized our operating team's impression as a non-standard metric for measuring pancreatic duct diameter, and we detected dilated ducts in 67.2 percent of patients (Table 2).

Table 2 The preoperative and intraoperative factors.

Variable	Value
Laboratory readings:	Median (range)
Hemoglobin level(gm/dl)	11.2(8.9–13.2)
Total white blood cells count	7400(3500–13100)
Serum Albumin(gm/dl)	3.8(2–4.4)
Total serum bilirubin(mg/dl)	1.3(0.9–28)
Serum creatinine(mg/dl)	0.8(0.7–1.5)
Preoperative ERCP (%)	52 (85.24%)
Intraoperative factors	
Pancreatic texture (%)	
Firm pancreas	38(62.3)
Soft pancreas	23 (37.7)
Pancreatic duct status (%)	
Dilated caliber	41 (67.2)
Normal caliber	20 (33.8)

Histopathological features

T3 tumors were the most common size (89.2%). T1, T2, and T4 cancers were quite uncommon. More than half of patients had N0 stage (63.9%). Lymph vessel invasion and perineural invasion were present in 29.5% of patients. The tumor grade was high in 77 percent of patients, and 82.0 percent had negative resection margins (R0).

Postoperative complications

The average hospitalization length was 13 days, and the total complication rate was 12% (73.8 percent). Wound infections were the most common consequence (49.2%), followed by pancreatic leak (40%) and an estimated 8% re-operation rate (Table 3).

Table 3 The complications and their proportions are shown.

Complications	Rate
Wound infection	30 (49.2)
Pancreatic leak & Fistula	25 (40)
Biliary leakage	7(11.4)
Postoperative Hemorrhage	2(3.2)
Reoperation	8(13)

Postoperative oncologic course and 1st year survival outcome

Neoadjuvant therapy had little impact on the whole cohort (n = 5, 8.2%). Gemcitabine was the standard adjuvant chemotherapeutical agent (50.81 percent, Table 5). Radiation treatment was just a tiny contribution. The overall rate of 1st year survival after PD for PDAC was 77.1% (47/61). Preoperative biliary decompression, postoperative pancreatic fistula and adjuvant treatment were substantially related with better outcome in univariate assessment ($P < 0.05$) (Table 4). In multivariate assessment, postoperative pancreatic fistula and adjuvant treatment were independent predictors of 1st year survival (Table 4 and figure 1, 2).

Table 4 Univariate analysis

factors	n	6 months	1 yr.	3 yrs	p value
All	61	81.5	77.6	64.8	NA
Sex					
Female	18	70.6	64.2	NA	0.233
Male	43	85.9	83.1	66.5	
Age					
<59	30	82.6	74.9	60.5	0.679
≥59	31	80.5	80.5	70.5	
Comorbidity					
No	29	85.9	81.8	60.6	0.885
Yes	32	77.4	73.9	73.9	
DM					
No	39	84.3	78.4	61.5	0.966
Yes	22	76.2	76.2	NA	
HTN					
No	53	82.5	78.0	64.4	0.893
Yes	8	75.0	75.0	NA	
LN					
Negative	39	76.1	72.3	64.3	0.576
Positive	22	90.9	86.1	64.6	
LVI					
Negative	43	80.7	78.0	61.9	0.743
Positive	18	83.3	76.4	76.4	
perineural spread					
Negative	43	85.6	85.6	68.0	0.115
Positive	18	71.8	57.6	57.6	
Margins					
Negative	50	83.6	78.8	64.1	0.759
Positive	11	72.7	72.7	NA	

Vascular Resection					
No	56	83.5	79.1	65.3	0.419
Yes	5	60.0	60.0	NA	
perioperative drain					
No	9	100	100	NA	0.042
Yes	52	78.2	73.6	55.8	
Pancreatic leak					
No	35	91.2	91.2	79.8	0.019
Yes	25	72.0	63.2	47.4	
DGE					
No	53	82.6	78.0	63.0	0.896
Yes	8	75.0	75.0	75.0	
Complications					
No	16	93.8	79.5	NA	0.509
Yes	45	77.0	77.0	62.2	
Mets					
No	52	78.2	76.1	69.7	0.787
Yes	9	100	87.5	NA	
Adjuvant					
No	21	51.9	51.9	NA	<0.001
Yes	40	100	91.8	75.3	
Neo-Adjuvant					
No	56	79.9	75.6	61.1	0.173
Yes	5	100	100	NA	

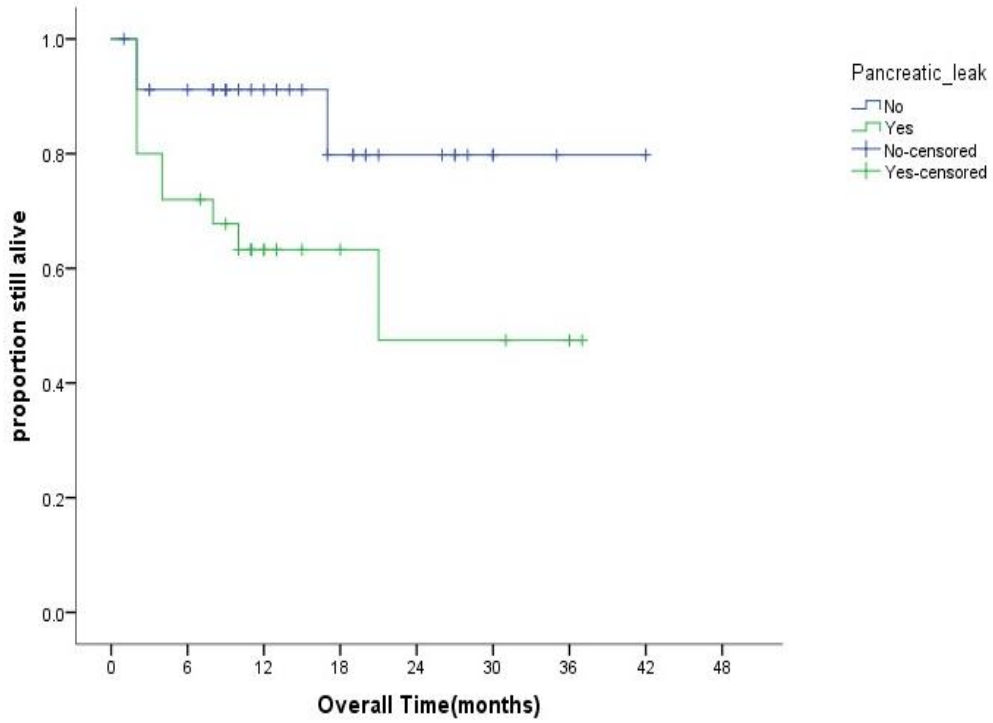

Figure 1 OS & its relation to pancreatic fistula (p value= 0.043)

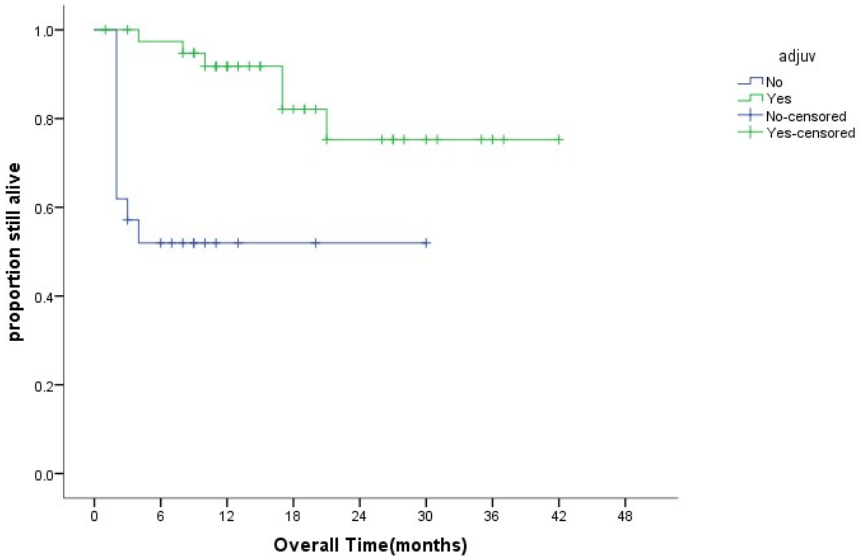

Figure 2 OS & its relation to adjuvant treatment (p value= 0.004)

Table 5 Multivariate analysis

	B	SE	P value	HR	95.0% CI for HR	
					Lower	Upper
Pancreatic leak(yes/no)	1.15	0.57	0.043	3.16	1.03	9.63
Adjuv (no/yes)	1.67	0.58	0.004	5.35	1.72	16.39

B=Regression coefficients, SE=Standard error of the coefficient, HR=hazard Ratio, 95% CI for OR = 95% confidence interval for the hazard Ratio. P-value<0.05 is considered significant

4. DISCUSSION

Pancreaticoduodenectomy is a difficult and time-consuming surgery with a significant complication risk (Nussbaum et al., 2015). Despite morbidity and death have recently increased, and postoperative mortalities have substantially decreased as a result of better critical care treatment and surgical procedures, the occurrence of postoperative complications remains elevated (Conzo et al., 2015). The premise in our district is that this treatment is a sophisticated, demanding, and time-consuming procedure with poor long-term results that requires advanced critical care to be successful. Significant increases in surgical skill, less complications, and favorable short-term results. Patients in this research differed in age from 33 to 75 years old, their mean age of 57 years, which is comparable to earlier studies (Nussbaum et al., 2015; Giorgio et al., 2015; Langan et al., 2016).

Wound infections were the most prevalent complications, with a rate of 49.2 percent, according to the results of this study. This figure is greater than published statistics from other nations, for example, wound infection rates in the United States have been reported as 7–13.3 percent (Leichtle et al., 2013; Padussis et al., 2014), 7.2 percent, according to research in Germany (Padussis et al., 2014). This increased prevalence of wound infections might be explained in part by the 40 percent occurrence of pancreatic fistula. The prevalence of pancreatic leak was 40% in our patients. Although the rate of pancreatic leak varies widely among centers, ranging from 13 to 45 percent, our results are satisfactory. However, this high rate could be explained by the fact that the method for pancreatic duct reconstruction in our institute has not yet been standardized, and various methods were used depending on the surgeon's choice (Cameron and He, 2015; Araujo et al., 2014; Langan et al., 2016). Age, tumor pathology (malignant or benign), malnutrition, pancreatic duct size, soft or firm pancreas, operating time, and surgical procedure are only a few of the variables that might affect pancreatic leak prevalence (Conzo et al., 2015). Several strategies for preventing pancreatic anastomotic leaks have been proposed, but none are ideal (Peng et al., 2002).

The Blumgart pancreaticojejunostomy method reduces the risk of pancreatic leakage (Li et al., 2020). In this research, Blumgart pancreaticojejunostomy was performed on 31 (50.8%) patients, and 11 (35.5%) of them advanced pancreatic fistula, which is lower than the other 30 (49.2%) patients who had pancreaticogastrostomy, and 14 (46.66%) of them established pancreatic fistula, but there was no substantial distinction. Our patients had a 14.8 percent total perioperative death rate, which is greater than the 5% rate

indicated by other facilities (Jakhmola et al., 2014; Nussbaum et al., 2015) The increased prevalence of pancreatic fistula might explain this.

In terms of survival, many investigations have shown that nodal status is a significant prediction of survival in pancreatic lesions (Winter et al., 2012). According to Assifi et al., (2018), tumor regrowth after PD for PDA was unrelated to the formation of a postoperative pancreatic fistula. Nagai et al., (2011), on the other hand, found that pancreatic fistula was a negative predictor of lesions reappearance. It has been discovered that postoperative illness and the start of adjuvant treatment have an inverse association. Node positive illnesses, margin positivity, EBL > 600 ml, extra vascular resections after surgery, and LOS > 10 days were all characteristics that Pugalenthi et al., (2015) found to be predictive of overall survival. In our study, the 1styear survival was 77.6% and patients who developed postoperative pancreatic fistula and didn't receive adjuvant treatment were significantly associated with poor survival outcome during the first year.

5. CONCLUSION

When comparing our results to published data from other facilities, wound infection and postoperative pancreatic fistula were the more prevalent sequelae. In multimodally treated patients following curative PDAC surgery, patients who acquired postoperative pancreatic fistula and did not get adjuvant therapy had greater 1st year death rates.

Conflict of interest

No conflicting interests have been disclosed by the authors.

Authors' Contributions

Fouad Abdelshaheed, Mohamed Emam Sobeih and Ahmed shaaban Owis designed the research study. Sayed Shaker Sheier and Haithm Fekry performed the research. Mahitab Ibrahim Altohamy revised the pathology. Eman Desoky analyzed the data. The manuscript was written by Sayed Shaker Sheier. Editorial modifications in the text were made by all writers. The final text was reviewed and accepted by all writers.

Consent to participate and ethical approval

Approval of the Institutional Review Board (IRB) at the NCI was obtained (IRB approval No. 2106-41004-005). Before participating in the research, all individuals provided their informed permission to be included.

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Alenezi AT. Laboratory prognostic factors correspondence to independent postoperative histo-pathological prognostic factors in pancreatic ductal adenocarcinoma. Medical Science 2021; 25(110):788-805
2. Araujo RL, Karkar AM, Allen PJ, Gönen M, Chou JF, Brennan MF, Blumgart LH, D'Angelica MI, DeMatteo RP, Coit DG, Fong Y, Jarnagin WR. Timing of elective surgery as a perioperative outcome variable: analysis of pancreaticoduodenectomy. HPB: the off j Int Hepato Pancreato Biliary Assoc 2014; 16(3), 250–262. doi: 10.1111 /hpb.12107
3. Assifi MM, Zhang S, Leiby BE, Pequignot EC, Xia B, Rosato E, Lavu H, Kennedy EP, Yeo CJ, Berger AC. Tumor recurrence is independent of pancreatic fistula in patients after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. J Am Coll Surg 2013; 217(4):621-7. doi: 10.1016/j.jamcollsurg.2013.05.014. PMID: 23810574.
4. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg 2015; 220(4):530-6. doi: 10.1016/j.jamcollsurg.2014.12.031. PMID: 25724606.

5. Chari ST, Kelly K, Hollingsworth MA, Thayer SP, Ahlquist DA, Andersen DK, Batra SK, Brentnall TA, Canto M, Cleeter DF, Firpo MA, Gambhir SS, Go VL, Hines OJ, Kenner BJ, Klimstra DS, Lerch MM, Levy MJ, Maitra A, Mulvihill SJ, Petersen GM, Rhim AD, Simeone DM, Srivastava S, Tanaka M, Vinik AI, Wong D. Early detection of sporadic pancreatic cancer: summative review. Pancreas 2015; 44(5):693-712. doi: 10.1097/MPA.0000000000000368. PMID: 25931254; PMCID: PMC4467589.
6. Conzo G, Gambardella C, Tartaglia E, Sciascia V, Mauriello C, Napolitano S, Orditura M, De Vita F, Santini L. Pancreatic fistula following pancreatoduodenectomy. Evaluation of different surgical approaches in the management of pancreatic stump. Literature review. Int J Surg 2015; 21Suppl 1:S4-9. doi: 10.1016/j.ijsu.2015.04.088. PMID: 26118602.
7. Giuliano AE, Connolly JL, Edge SB, Mittendorf EA, Rugo HS, Solin LJ, Weaver DL, Winchester DJ, Hortobagyi GN. Breast Cancer-Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 2017; 67(4):290-303. doi: 10.3322/caac.21393. Erratum in: CA Cancer J Clin 2017; 67(4):345. PMID: 28294295.
8. Hidalgo M. Pancreatic cancer. N Engl J Med 2010; 362(17):1605-17. doi: 10.1056/NEJMra0901557. Erratum in: N Engl J Med 2010; 15; 363(3):298. PMID: 20427809.
9. Jakhmola CK, Kumar A. Whipple's pancreaticoduodenectomy: Outcomes at a tertiary care hospital. Med J Armed Forces India 2014; 70(4):321-326. doi:10.1016/j.mjafi.2014.08.011
10. Kamisawa T, Wood LD, Itoi T, Takaori K. Pancreatic cancer. Lancet 2016; 388(10039):73-85. doi: 10.1016/S0140-6736(16)00141-0. PMID: 26830752.
11. Kardosh A, Lichtensztajn DY, Gubens MA, Kunz PL, Fisher GA, Clarke CA. Long-Term Survivors of Pancreatic Cancer: A California Population-Based Study. Pancreas 2018; 47(8):958-966. doi: 10.1097/MPA.0000000000001133. PMID: 30074526; PMCID: PMC6095724.
12. Langan RC, Huang CC, Mao WR, Harris K, Chapman W, Fehring C, Oza K, Jackson PG, Jha R, Haddad N, Carroll J, Hanna J, Parker A, Al-Refaie WB, Johnson LB. Pancreaticoduodenectomy hospital resource utilization in octogenarians. Am J Surg 2016; 211(1):70-5. doi: 10.1016/j.amjsurg.2015.04.014. PMID: 26122361; PMCID: PMC5224709.
13. Leichtle SW, Kaoutzanis C, Mouawad NJ, Welch KB, Lampman R, Verne L. Hoshal VL, Classic Whipple versus pylorus-preserving pancreaticoduodenectomy in the ACS NSQIP. J Surg Res 2013; 170–176
14. Li Z, Wei A, Xia N, Liangxia Zheng L, Yang D, Ye J, Xiong J, Hu W. Blumgart anastomosis reduces the incidence of pancreatic fistula after pancreaticoduodenectomy: a systematic review and meta-analysis. Sci Rep 2020; 10:17896. doi: 10.1038/s41598-020-74812-4
15. Luu AM, Hoehn P, Vogel SR, Reinacher-Schick A, Munding J, Uhl W, Braumann C. Pathologic Complete Response of Pancreatic Cancer following Neoadjuvant FOLFIRINOX Treatment in Hepatic Metastasized Pancreatic Cancer. Visc Med 2019; 35(6):387-391. doi: 10.1159/000497827. PMID: 31934588; PMCID: PMC6944898.
16. Martignoni ME, Friess H, Sell F, Ricken L, Shrikhande S, Kulli C, Buchler MW. Enteral nutrition proongs delayed gastric emptying in patients after Whipple resection, Am J Surg 2000; 180 18–23.
17. Nagai S, Fujii T, Kodera Y, Kanda M, Sahin TT, Kanzaki A, Hayashi M, Sugimoto H, Nomoto S, Takeda S, Morita S, Nakao ARecurrence pattern and prognosis of pancreatic cancer after pancreatic fistula. Ann Surg Oncol 2011; 18:2329–2337.
18. Nussbaum DP, Penne K, Stinnett SS, Speicher PJ, Cocieru A, Blazer DG 3rd, Zani S, Clary BM, Tyler DS, White RR. A standardized care plan is associated with shorter hospital length of stay in patients undergoing pancreaticoduodenectomy. J Surg Res 2015; 193(1):237-45. doi: 10.1016/j.jss.2014.06.036. PMID: 25062813.
19. Padussis JC, Zani S, Blazer DG, Tyler DS, Pappas TN, Scarborough JE. Feeding jejunostomy during Whipple is associated with increased morbidity. J Surg Res 2014; 187(2):361-6. doi: 10.1016/j.jss.2012.10.010. PMID: 24525057.
20. Peng S, Mou Y, Cai X, Peng C. Binding pancreaticojejunostomy is a new technique to minimize leakage. Am J Surg 2002; 183(3):283-5. doi: 10.1016/s0002-9610(02)00792-4. PMID: 11943127.
21. Pugalenthi A, Protic M, Gonen M, Kingham TP, Angelica MI, Dematteo RP, Fong Y, Jarnagin WR, Allen PJ. Postoperative complications and overall survival after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. J Surg Oncol 2016; 113(2):188-93. doi: 10.1002/jso.24125. PMID: 26678349; PMCID: PMC4830358.
22. Romano G, Agrusa A, Galia M, Di Buono G, Chianetta D, Sorce V, Gulotta L, Brancatelli G, Gulotta G. Whipple's pancreaticoduodenectomy: Surgical technique and perioperative clinical outcomes in a single center. Int J Surg 2015; 21Suppl 1:S68-71. doi: 10.1016/j.ijsu.2015.06.062. PMID: 26122590.
23. Sahora K, Morales-Oyarvide V, Thayer SP, Ferrone CR, Warshaw AL, Lillemoe KD, Fernández-Del Castillo C. The effect of antecolic versus retrocolic reconstruction on delayed gastric emptying after classic non-pylorus-preserving pancreaticoduodenectomy. Am J Surg 2015; 209(6):1028-35. doi: 10.1016/j.amjsurg.2014.04.015. Epub 2014 Jul 1. PMID: 25124295.

24. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019.CA Cancer J Clin 2019; 69(1):7-34. doi: 10.3322/caac.21551. PMID: 30620402.
25. Soloff EV, Zaheer A, Meier J, Zins M, Tamm EP. Staging of pancreatic cancer: resectable, borderline resectable, and unresectable disease. Abdom Radiol (NY) 2018; 43:301-313.
26. Stark AP, Sacks GD, Rochefort MM, Donahue TR, Reber HA, Tomlinson JS, Dawson DW, Eibl G, Hines OJ. Long-term survival in patients with pancreatic ductal adenocarcinoma. Surgery 2016; 159(6):1520-1527. doi: 10.1016/j.surg.2015.12.024. PMID: 26847803; PMCID: PMC4856542.
27. Winter JM, Brennan MF, Tang LH, D'Angelica MI, Dematteo RP, Fong Y, Klimstra DS, Jarnagin WR, Allen PJ. Survival after resection of pancreatic adenocarcinoma: results from a single institution over three decades. Ann Surg Oncol 2012; 19(1):169-75. doi: 10.1245/s10434-011-1900-3. PMID: 21761104.