

MORBIDITY AND MORTALITY OF PANCREATIC TUMORS UNDERGOING SURGICAL TREATMENT

Morbimortalidade do tratamento cirúrgico dos tumores do pâncreas

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HEADINGS - Pancreatic neoplasms.
Postoperative complications.
Duodenopancreatectomy.

ABSTRACT - Background: Pancreatic cancer has a high mortality rate due to late diagnosis and aggressive behavior. The prognosis is poor, with 5-year survival occurring in less than 5% of cases. **Aim:** To analyze demographic characteristics, comorbidities, type of procedure and early postoperative complications of patients with pancreatic cancer submitted to surgical treatment. **Methods:** Cross-sectional study with analysis of 28 medical records of patients with malignant tumors of the pancreas in a 62 month. Data collection was performed from the medical records of the hospital. **Results:** Of the total, 53,6% were male and the mean age was 60.25 years. According to the procedure, 53,6% was submitted to duodenopancreatectomy the remainder to biliodigestive derivation or distal pancreatectomy. The ductal adenocarcinoma occurred in 82,1% and 92,9% of tumors were located in the pancreatic head. Early postoperative complications occurred in 64,3% of cases and the most prevalent was intra-abdominal abscess (32,1%). Among duodenopancreatectomies 77,8% had early postoperative complications. **Conclusion:** Its necessary to encourage early detection of tumors of the pancreas to raise the number operations with curative intent. Refinements in surgical techniques and surgical teams can diminish postoperative complications and, so, operative morbimortality can also decrease over time.

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Financial source: none
Conflicts of interest: none

Received for publication: 25/03/2014
Accepted for publication: 26/06/2014

DESCRIPTOR - Neoplasias pancreáticas.
Complicações pós-operatórias.
Duodenopancreatectomia.

RESUMO - Racional: O câncer de pâncreas apresenta alta taxa de mortalidade por conta do diagnóstico tardio e comportamento agressivo. O prognóstico é reservado com sobrevida de cinco anos em menos de 5% dos casos. **Objetivo:** Analisar as características demográficas, as comorbidades, o tipo de procedimento e as intercorrências pós-operatórias precoces dos pacientes de câncer de pâncreas submetidos ao tratamento cirúrgico. **Métodos:** Estudo transversal, que analisou 28 prontuários de pacientes portadores de tumores malignos do pâncreas, no período de 62 meses. A coleta de dados foi realizada a partir dos prontuários médicos do hospital. **Resultados:** Do total de participantes 53,6% eram do sexo masculino. A média de idade foi de 60,25 anos. Em relação ao procedimento, 53,6% foram submetidos à duodenopancreatectomia e o restante à derivação biliodigestiva ou pancreatectomia corpo-caudal. O adenocarcinoma ductal ocorreu em 82,1% e 92,9% dos tumores estavam localizados na cabeça do pâncreas. As complicações pós-operatórias precoces ocorreram em 64,3%, e a mais prevalente foi abscesso intra-abdominal (32,1%). Entre as duodenopancreatectomias, 77,8% apresentaram complicações pós-operatórias precoces. **Conclusão:** Há necessidade de se incentivar a detecção precoce dos tumores de pâncreas para que se consiga realizar mais operações com intenção curativa. Também, é necessário o aprimoramento das técnicas operatórias e das equipes cirúrgicas para que as complicações pós-operatórias e a morbimortalidade operatória diminuam ao longo do tempo.

INTRODUCTION

The incidence of pancreatic cancer in the United States is 13.6 per 100,000 in men and 10.7 per 100,000 in women¹³. In Brazil, this disease is responsible for about 2% of all diagnosed cancers and 4% of all cancer deaths⁴. The prognosis is poor, with a 5-year survival of less than 5%⁷.

Ductal adenocarcinoma is preferentially localized to the head of the organ (47-65%), followed by the body and tail (15-18%)⁸. The treatment of choice is surgical¹⁴, although not all patients are candidates for this kind of treatment, in which postoperative complications occur in 33.6%, most commonly due to infections (13.8%) followed by pleural effusion (9.8%)¹⁴.

Patients with pancreatic cancer have been studied and observed over a long period of time, and these studies report an increasing incidence of the disease^{30,17}. However, there is also a study reporting a decline²². In any event, the prognosis is bleak¹⁰, but with improved long-term survival^{22,30,6}.

Thus, the objective of this study was to analyze the demographic characteristics, comorbidities, type of surgical procedure, and early postoperative complications in patients with pancreatic cancer undergoing surgery.

METHODS

This cross-sectional study was performed at the General Surgery Service of the Hospital Governador Celso Ramos, Florianópolis, SC, Brazil and approved by the Committee for Ethics in Research at the hospital.

The medical records of 28 patients, who underwent surgical treatment for pancreatic tumors between January, 2008 and February, 2013, were analyzed. The patient charts were obtained from the Medical Archive Service as well as hospital electronic records. The data were recorded on a data collection instrument built exclusively for this study, containing biological and clinical variables pertaining to tumor and postoperative characteristics. All charts of patients suffering from pancreatic cancer and subjected to surgical treatment of any kind were included in the study, and those who received surgical treatment for peritoneal carcinomatosis or those with insufficient chart data were excluded.

Results were entered into the Microsoft Excel Program (OU Epi-DATA) and exported to SPSS 16 (Statistical Package for the Social Sciences 16). Data were analyzed and described as absolute and relative frequencies. The Chi-square test or Fisher's exact test was utilized to test for homogeneity of proportions. The significance level was set to a value of $p < 0.05$.

RESULTS

The medical records of 28 patients were analyzed. Fifteen (53.6%) were men. The average age was 60.25 years old (39-89). Weight varied between 44 and 90 kg, with a mean value of 64.8 kg. Three types of surgical procedure were studied.

The majority of patients (53.6%) underwent duodenopancreatectomy. Biliodigestive derivations, for palliative treatment, were performed in 39.3%. In both groups the neoplasms were localized to the head of the pancreas. In 7.1% of the patients, pancreatectomy of the tail and body was performed, since the neoplasm was localized to the body/tail.

Comorbidities of the participants, smoking, diabetes mellitus, alcoholism and systemic arterial hypertension were studied (Table 1).

TABLE 1 – Lifestyle factors and associated comorbidities

Variable	N	%
Smoking		
Smoker	07	25.0
Non-smoker	15	53.6
Ex-smoker	06	21.4
Diabetes melitus		
Yes	09	32.1
No	19	67.9
Alcoholism		
Yes	06	21.4
No	22	78.6
Arterial hypertension		
Yes	11	39.3
No	17	60.7
Other	14	50.0

The tumor characteristics analyzed were histological type, T stage and N (lymph node) stage (Table 2).

Values of the tumor marker CA 19-9 were collected from 24 patients. The analysis demonstrated that 50% of the patients had values ≤ 37 U/ml; 20.8%, between 37.1 and 369.9 U/ml; 29.2%, ≥ 370 U/ml, and 14.2% had no information concerning the marker. The values varied between 1.2 and 84476.5 U/ml.

TABLE 2 – Tumor characteristics

Variable	N	%
Histological type		
Ductal adenocarcinoma	23	82.1
Acinar carcinoma	01	3.60
Cystic neoplasm	01	3.60
Endocrine neoplasm	02	7.10
Other	01	3.60
Localization of tumor		
Head	26	92.9
Body/tail	02	7.10
T stage		
T1	04	15.4
T2	04	15.4
T3	08	30.7
T4	10	38.5
N stage		
NX	09	33.3
N0	12	44.5
N1	06	22.2

The most common early surgical complications were intra-abdominal abscesses (32.1%), followed by delayed gastric emptying (25.0%), and pancreatic fistulas (21.4%). Among patients who underwent duodenopancreatectomy, four had a pancreatic fistula and two, pancreatic and biliary fistulas. Surgical reintervention for early postoperative complications of any kind occurred in five patients. Early non-surgical complications that stood out were respiratory (50.0%) – pneumonia and respiratory insufficiency – followed by cardiologic – acute myocardial infarction and atrial fibrillation – and renal – hypokalemia and metabolic acidosis (Table 3).

TABLE 3 – Early postoperative complications

Complication	n (%)
Surgical	
Intra-abdominal abscess	09 (32.1)
Delay in gastric emptying	07 (25.0)
Pancreatic fistula	06 (21.4)
Biliary fistula	05 (17.9)
Digestive fistula	04 (14.3)
Surgical wound infection	03 (10.7)
Abdominal sepsis	03 (10.7)
Postoperative hemorrhage	02 (7.10)
Other	05 (17.9)
Non-surgical	
Respiratory	14 (50.0)
Cardiologic	07 (25.0)
Renal	07 (25.0)
Other	09 (32.1)

Male patients experienced 55.6% of all early postoperative complications. The diabetics experienced 44.4% of the complications, and smokers, 33.3% (Table 4).

Among participants in stage T3, 35.4% showed complications; among T4 patients, only 17.6%; and all T1 and T2 patients showed early postoperative complications. There was a statistically significant association between the size of the tumor and all early postoperative complications ($p=0.018$) (Table 5).

Among patients undergoing duodenopancreatectomies, biliodigestive derivations, and body-tail pancreatectomies, 77.8%, 16.7%, and 5.6% showed complications, respectively. Diabetes mellitus was associated with the following postoperative complications: fistulas (the three types studied), infections (sepsis, surgical wound infections, and intra-abdominal abscesses), delayed gastric emptying and renal complications. Smoking was associated with surgical reintervention, fistulas and respiratory complications, and asthma was associated with fistulas (Table 6).

TABLE 4 – Association of gender and comorbidities with early postoperative complications

Variable	Complications		Total n (%)	p value
	Yes	No		
	n (%)	n (%)		
Gender				0.778
Female	08 (44.4)	05 (50.0)	13 (46.4)	
Male	10 (55.6)	05 (50.0)	15 (53.6)	
Total	10 (100)	18 (100)	28 (100)	
Smoker				0.112
Yes	06 (33.3)	01 (10.0)	07 (25.0)	
No	07 (38.9)	08 (80.0)	15 (53.6)	
Ex-smoker	05 (27.8)	01 (10.0)	06 (21.4)	
Diabetes melitus				0.098
Yes	08 (44.4)	01 (10.0)	09 (32.1)	
No	10 (55.6)	09 (90.0)	19 (67.9)	
Arterial hypertension				1.000
Yes	07 (38.9)	04 (40.0)	11 (39.3)	
No	11 (61.1)	06 (60.0)	17 (60.7)	
Alcoholism				1.000
Yes	04 (22.2)	02 (20.0)	06 (21.4)	
No	14 (77.8)	08 (80.0)	66 (78.6)	

TABLE 5 – Association between tumor characteristics and early postoperative complications

Variable	Complications		Total n(%)	p value
	Yes	No		
	n(%)	n(%)		
T Stage				0.018
T1	04 (23.5)	-	04 (15.4)	
T2	04 (23.5)	-	04 (15.4)	
T3	06 (35.4)	02 (22.2)	08 (30.7)	
T4	03 (17.6)	07 (77.8)	10 (38.5)	
N stage				0.570
NX	06 (33.3)	03 (33.4)	09 (33.3)	
N0	09 (50.0)	03 (33.3)	12 (44.5)	
N1	03 (16.7)	03 (33.3)	06 (22.2)	
Histological type				0.626
Ductal adenocarcinoma	14 (77.6)	09 (90.0)	23 (82.1)	
Acinar neoplasia	01 (5.60)	-	01 (3.60)	
Cystic neoplasm	01 (5.60)	-	01 (3.60)	
Endocrine neoplasm	01 (5.60)	01 (10.0)	02 (7.10)	
Other	01 (5.60)	-	01 (3.60)	
Location				1.000
Head	17 (94.4%)	09 (90%)	26 (92.9%)	
Body/Tail	01 (5.60%)	01 (10.0%)	02 (7.10%)	

TABLE 6 – Association between the type of surgery performed and early postoperative complications

Surgical procedure	Complications		Total n (%)	p value
	Yes	No		
	n (%)	n (%)		
Duodenopancreatectomy	14 (77.8)	01 (10.0)	15 (53.6)	0.002
Biliodigestive derivation	03 (16.7)	08 (80.0)	11 (39.3)	
Body/tail pancreatectomy	01 (5.60)	01 (10.0)	02 (7.10)	
Total	18 (100)	10 (100)	28 (100)	

DISCUSSION

Cancer of the pancreas is most prevalent in men^{14,17,22}. Lowenfels and Maisonneuve attribute this to the difference in the number of smokers, which is greater in males. This difference tends to disappear due to increases in women smokers²⁰ or the tendency of women to live longer than men^{17,9}. Several authors point out that the predominant age of patients with pancreatic cancer is above 60 years old^{14,22,18,11}. Rocha *et al.*²⁶, analyzing patients in Belo Horizonte, Brazil, reported a mean age of 59 years old, coinciding with world trends.

Cancers in patients undergoing duodenopancreatectomy progressed as far as stage II-B²⁹, and T3N1M0 occurred at the highest frequency. When isolated tumors were studied, it was found that the majority (38.5%) were grouped in stage T4. However, when the surgical procedure was analyzed, it was found that the majority of patients underwent duodenopancreatectomy because they were in stages T1-T3, that is, the sum total of the tumors staged in T1-T3 was greater than those staged exclusively in T4, explaining the prevalence of duodenopancreatectomy as the surgical procedure in this study rather than a palliative surgical procedure. Such data are in accordance with other studies^{14,11} that recommend resection up to stage II-B. However, Lefebvre *et al.*¹⁷ and Abraham *et al.*¹ demonstrated a similar likelihood of curative surgical operations in their studies, at around 11%.

Smoking is considered responsible for about 20-30% of pancreatic neoplasms in the western population¹⁶. Lowenfels *et al.*²¹ showed that smokers develop pancreatic cancer between three and four years before non-smokers. The smoking population has a 70% greater risk of developing a pancreatic malignancy than the non-smoking population. To stop or never start smoking is considered a preventive factor^{21,25}.

The incidence of diabetes melitus is higher in patients with pancreatic cancer, but the relationship between diabetes and cancer is controversial. Some studies indicate that diabetes is a risk factor for the development of pancreatic cancer, while others argue that diabetes could be a manifestation of cancer already in existence. Liao *et al.*¹⁹ demonstrated that diabetic patients, less than two years after their initial diagnosis, have an increased incidence of pancreatic cancer. However, at longer periods following the diagnosis, patients show no significant difference. Chiari *et al.*⁵ observed that diabetes melitus can be an early manifestation of pancreatic cancer rather than a risk factor.

Preoperative alcoholic participants made up ¼ of the total, but there were no records mentioning the quantity of alcoholic beverages consumed. The International Agency for Research on Cancer published a monograph on the evaluation of carcinogenic risks to humans and concluded that there was insufficient evidence to consider alcohol a risk factor for development of pancreatic cancer²⁷. However, Gupta *et al.*¹⁰ support the occurrence of pancreatic cancer in the subgroup of patients exhibiting excessive alcohol consumption, independently of smoking.

Studies demonstrate a higher incidence of adenocarcinomas in relation to other histological types² and localization to the head of the pancreas^{8,17,11}.

The tumor marker most commonly utilized in the diagnosis and prognosis of exocrine pancreatic cancer is the tumor-associated carbohydrate antigen 19-9 (CA 19-9). Around 70-90% of patients with pancreatic cancer express this marker in a manner sensitive to the stage of the disease²⁵. It is not uncommon to find patients with small tumors but normal values of CA19-9. It is thought that the marker is elevated in only half of the patients with tumors of 2 cm or less³. Kim *et al.*¹⁵ found that, at its cut-off value of 37 U/ml, its sensitivity and specificity were 76.7% and 87.1 %, respectively. Patients with very high levels of CA 19—9 (more than 1000 U/ml) are very likely to have inoperable cancer³.

Lermite *et al.*¹⁸ state that intra-abdominal abscesses are frequently associated with pancreatic and biliary fistulas. Diagnosis of a suspected fistula can be made by means of clinical data and confirmed by biochemical methods and imaging. In the present study, diagnosis of this complication was based solely on clinical observation, because the method used to confirm the diagnosis was not mentioned in the chart records, only the presence or absence of the complication. Therefore, in the diagnosis of a fistula, the characteristics of

the drained liquid were taken into account; except in a few cases in which amylase was measured in the drained liquid, no laboratory testing or imaging was used to study this. A digestive fistula was considered one whose liquid contained gastrointestinal secretions. A biliary fistula was considered one whose liquid was yellow-brown in color with crystals in the pancreatic liquid.

Pancreatic fistulas occur in 10-15% of patients subjected to duodenopancreatectomy, in agreement with Lermite *et al.*¹⁸. However, as this complication depends on various factors, there are investigators who report a lower rate. Kamphues *et al.*¹⁴ found them in 1.4% of 442 surgically treated patients and Amico *et al.*², in 50% of 54 surgically treated patients. Among the local factors related to the genesis of pancreatic fistulas, the consistency of the pancreatic remnant (soft, normal or hard) and the caliber of the pancreatic ducts are noteworthy. Subjective evaluation of the greater consistency of the pancreas, associated with ductal dilatation, contributed to a lower incidence of pancreatic fistulas²³. In the indicated study, this complication was unrelated to the consistency of the gland or to the type of anastomosis used (duct-to-mucosa or telescoping of the pancreatic stump).

Delayed gastric emptying is, by definition, persistent gastric stasis requiring nasogastric aspiration for a period of at least 10 days or solid food intolerance for up to 14 postoperative days. Various factors are related to the onset of this complication, notably previous abdominal operations, diabetes, malnutrition and postoperative intra-abdominal complications¹².

According to Kamphues *et al.*¹⁴, the most common non-surgical complication was of the cardiopulmonary type, occurring in 12.4% of the patients undergoing duodenopancreatectomy, and surgical reintervention took place in 10.3% of the cases. Already in the study of Rocha *et al.*²⁶, the nonsurgical complication that occurred the most was pneumonia (12.2%) along with surgical wound infection (12.2%). In the present study, total early postoperative complications came to 64.3%. This observation is at variance with Kamphues *et al.*¹⁴ and in harmony with Rocha *et al.*²⁶, who obtained values of 33.6 and 58%, respectively. In the study under discussion, 77.8% of the patients who underwent duodenopancreatectomy showed early complications postoperatively; among those subjected to biliodigestive derivation, only 16.7%; and among the remaining patients, who underwent corpocaudal pancreatectomy, 5.6%. Theoretically, one would expect to find a higher frequency of complications in patients undergoing duodenopancreatectomy when compared to those subjected to corpocaudal pancreatectomy. In the former case, the procedure is technically more complex, resulting in a longer period in surgery and the eventual need for a blood transfusion. In the latter case, the number of patients with tumors of the pancreatic body and tail was decidedly small, when compared with tumors of the head (based on the frequency of malignant tumors localized to the pancreas), and as a consequence, corpocaudal pancreatectomy was performed only a few times. Perhaps more instances of this procedure would reduce such a difference. A similar explanation may apply to cases in which the patients underwent biliodigestive derivation.

CONCLUSION

There is a need to encourage early detection of pancreatic tumors to increase the number of operations with curative potential. Refinements in surgical techniques and surgical teams could also diminish postoperative complications and thereby decrease operative morbimortality over time.

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