

COMPLICATIONS AFTER PANCREATECTOMIES: PROSPECTIVE STUDY AFTER ISGFP AND ISGPS NEW CLASSIFICATIONS

Complicações após pancreatectomias: estudo prospectivo após as novas classificações giedfp e giecp

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ABSTRACT – Background: Scientific publications focusing on the results of pancreatic resections in Brazil are scarce. **Aim:** To present the surgical results of pancreatic resections. **Methods:** Were analyzed prospectively 54 consecutive cases of patients undergoing consecutive pancreatectomy evaluating the occurrence of postoperative complications (pancreatic fistula, delayed gastric emptying and postoperative hemorrhage) based on the criteria of the International Study Group on Pancreatic Fistula Definition and International Study Group of Pancreatic Surgery. **Results:** Of the 54 pancreatectomy, 32 occurred in women (59,26%) and 22 in men (40,74%). The mean age of patients was 54,5 years. The most performed procedure was the Whipple operation, in 38 patients. In eight of those cases, mesenteric-portal confluence was resected. The mean period of hospitalization was 20,7 days. The hospitalization in 51% of patients was up to 10 days. A pancreatic fistula was observed in 50% of the cases submitted to the Whipple surgery. The postoperative hemorrhage and delayed gastric emptying in patients undergoing the surgery occurred respectively in 13,15% and 18,41%. The overall morbidity and mortality was respectively 62.9% and 5.5%. **Conclusion:** There is a need for the national publications to assimilate the concepts and criteria presented by the ISGFP² and ISGPS^{23,25} to enable comparison of the results obtained with surgical treatment of pancreatic disorders, in the Brazilian context. Who knows, therefore, whether the great advanced seen in the last 40 years in terms of the reduction in mortality rates associated with pancreatic resections may also occur with the persistently high levels of postoperative complications.

HEADINGS - Pancreatectomy.
Pancreaticoduodenectomy.
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RESUMO – Racional: No Brasil existe escassa publicação científica destinada à divulgação dos resultados das ressecções pancreáticas. **Objetivo:** Apresentar os resultados cirúrgicos das ressecções pancreáticas. **Métodos:** Analisou-se prospectivamente 54 casos consecutivos de pacientes submetidos à pancreatectomias. Foi avaliada a ocorrência de complicações pós-operatórias (fístula pancreática, retardo do esvaziamento gástrico e hemorragia pós-operatória) fundamentadas nos critérios dos Grupos Internacionais de Estudo sobre a Definição de Fístula Pancreática e de Cirurgia Pancreática. **Resultados:** Das 54 pancreatectomias, 32 foram realizadas em mulheres (59,26%) e 22 em homens (40,74%). A média de idade dos pacientes foi de 54,5 anos. O procedimento mais praticado foi à cirurgia de Whipple em 38 pacientes. Em oito destes, houve ressecção do eixo mesentérico-portal. O tempo médio de internação foi de 20,7 dias. A maioria dos pacientes (51%) esteve internada por até 10 dias. A fístula pancreática foi observada em 50% da amostra em 44,7% dos pacientes submetidos à operação de Whipple. O sangramento pós-operatório e o retardo do esvaziamento gástrico nos pacientes submetidos à essa operação ocorreram, respectivamente, em 13,15% e 18,41%. Na amostra a taxa global de morbidade e mortalidade foi respectivamente de 62,9% e 5,5%. **Conclusão:** Há necessidade das publicações nacionais assimilarem os conceitos e critérios apresentados pelas classificações GIEDFP e GIECP para permitir a comparação dos resultados obtidos com o tratamento cirúrgico de doenças pancreáticas, no contexto brasileiro. Quem sabe, se o grande avanço visto nos últimos 40 anos em termos de redução das taxas de mortalidade associadas com ressecções pancreáticas também pode ocorrer com os níveis persistentemente elevados de complicações pós-operatórias.

DESCRITORES - Pancreatectomia.
Pancreaticoduodenectomy.
Complicações pós-operatórias.

INTRODUCTION

Pancreatic resections are procedures involving high levels of morbidity¹⁴. The topography of the pancreas in the retroperitoneum close to the superior mesenteric vessels, the need for resections of adjacent organs, the high number of anastomoses that follow resection of its cephalic portion, and the high incidence of pancreatic fistula after any type of resection of the organ, make this a highly complex procedure.

In Brazil, there are few scientific publications that present the results of pancreatectomies^{10,12,13,20-22}. This is partly due to the small number of services specializing in these procedures. Associated with this, the majority of studies were published before the current standardization proposed by the International Study Group of Pancreatic Fistula (ISGPF) and the *International Study Group of Pancreatic Surgery* (ISGPS) for the definition of the main post-surgical complications.

Our surgical group has dedicated itself to the practice of pancreatic resections, working both in public hospitals and private clinics. This study presents the results for the last five years, in light of the publications of the ISGPF² and the ISGPS^{23,25}.

METHOD

This study was approved by the Ethics Committees of all hospitals involved where the surgical procedures were conducted: University Hospital Onofre Lopes, Riograndense Northern League Against Cancer and at the Casa de Saúde São Lucas, Natal, RN, Brazil.

Prospective analysis was carried out of 54 patients submitted to consecutive pancreatic resections, performed by the authors, from April 2007 to September 2012, for treatment of pancreatic or peripancreatic diseases.

For the cases of cephalic resection (gastroduodenopancreatectomy or Whipple procedure), the technical steps were: a) bilateral subcostal incision; b) inspection of the cavity and investigation of metastases and resectability of the lesion; c) resection of the surgical piece consisting of the gastric antrum, gallbladder, choledocus, pancreatic head (sometimes with venous segment of the mesenteric-portal axis) and duodenum with regional lymph nodes; d) pancreatojejunal anastomosis; e) hepaticojejunal anastomosis; f) gastrojejunal anastomosis; g) jejunostomy by the Witzel technique; and h) drainage by two tubulolaminar drains, with exit points on both flanks.

Three pancreatojejunal anastomosis techniques were used, depending on the characteristics of the residual pancreas. For pancreas with soft texture and normal or slightly enlarged duct of Wirsung (diameter < 5 mm), terminoterminal (telescopic type) or terminolateral (invagination) pancreaticojejunal

anastomosis were used. In both cases, simple separated sutures in 4-0 Prolene[®] thread were used. For the pancreas with hardened texture and enlarged duct of Wirsung (diameter > 5 mm), terminolateral duct to mucosa pancreatojejunal anastomosis was performed on two planes.

For the distal pancreatectomy, the technical steps were: a) left subcostal incision; b) inspection of the cavity with investigation of metastases and resectability of the lesion; c) resection of the surgical piece which, depending on the type of disease, may include the body and tail of the pancreas, or tail of the organ only, with or without concomitant removal of the spleen and regional ganglia; d) suture of the pancreatic stump with separated "U" stitches in 4-0 Prolene[®] thread; e) jejunostomy by the Witzel procedure; f) drainage with tubulolaminar drain, exiting on the left flank.

Octreotide was used in the majority of the patients, depending on its availability at the hospital, with prophylaxis to prevent pancreatic fistula, at a dose of 0.3 mg pd, divided into 8 h intervals, over a period of seven days. Drain output volume was recorded once a day, and drain amylase levels were measured on days 1, 3, 5 and 7 after surgery.

On postoperative day 7, ultrasonography or computed tomography of the abdomen was performed as control. The drains were removed on postoperative day 8 for cases with low values of drain amylase and no signs of abdominal collections in the image. In the presence of pancreatic fistula, the patient was kept nil-by-mouth, enteral feeding was introduced via jejunostomy, and subcutaneous octreotide was maintained.

For the diagnosis of pancreatic fistula, the ISGPF² criteria were used. Thus, pancreatic fistula was defined when on postoperative day 3, the amylase level in the drain liquid was more than three times the upper limit of serum amylase. The pancreatic fistula was graded, also based on the ISGPF² criteria, summarized as follows: Grade A – presence of no clinical complaints, or the appearance of the fistula has not led to changes in hospitalization time; Grade B – fasting, enteral or parental feeding is introduced, with repositioning of the drains, and the use of antibiotics, octreotide and other measures, as required, and with longer hospitalization time; Grade C – greater clinical repercussions, with sepsis, need for intensive care, reoperation, and risk of death.

The diagnosis of post-pancreatectomy hemorrhage and delayed postoperative gastric emptying was based on the definitions proposed by the ISGPS^{23,25}.

Thus, post-pancreatectomy hemorrhage was defined as blood loss via the abdominal drain, digestive tract or abdominal cavity, with a drop in serum hemoglobin levels after surgery. In regard to the stratification of bleeding, three levels were defined: Grade A – early bleeding (≤ 24 h after the end of surgery), mild, and without the need for transfusion;

Grade B – severe early bleeding (≤ 24 h after the end of surgery) or mild late bleeding (> 24 h after the end of surgery), both with good intermediary clinical condition, associated with the need for transfusional, endoscopic, radiological or surgical treatment; Grade C – severe late bleeding (> 24 h after the end of surgery), with severe clinical condition, risk of death, and need for transfusion, endoscopic, radiological or surgical treatment.

The diagnosis of postoperative delayed gastric emptying was established and graded as follows: Grade A – maintenance of the nasogastric tube for more than 3 days, or its reinsertion after postoperative day 4, or for patients in whom re-introduction of a solid oral diet was impossible up to postoperative day 7; Grade B – maintenance of nasogastric tube for 8 to 14 days, or its reinsertion after postoperative day 8, or for patients in whom reinsertion of a solid oral diet was impossible up to postoperative day 4; Grade C – maintenance of the nasogastric tube for more than 14 days, or its reinsertion after postoperative day 15, or for patients in whom re-introduction of a solid oral diet was impossible up to postoperative day 21.

Intra-hospital mortality was considered when the death occurred within 90 days of surgery.

RESULTS

The sample consisted of 54 patients being 32 women (59.26%) and 22 men (40.74%). The mean age was 54.5 years (16-90).

Fifty-four consecutive pancreatectomies were performed during the study period. The majority of the surgeries were performed at the University Hospital Onofre Lopes, (61.1%) followed by Casa de Saúde São Lucas (27.7%) and the Riograndense Northern League Against Cancer (11.1%).

The most frequent diseases were adenocarcinoma of the pancreas and duodenal papilla, each with sixteen cases (Table 1).

TABLE 1 – Distribution of pancreatic and peripancreatic diseases

DISEASES	INCIDENCE (%)
Adenocarcinoma of the pancreas	16 (29.63%)
Adenocarcinoma of the duodenal papilla	16 (29.63%)
Frantz's Tumor	8 (14.81%)
Cholangiocarcinoma of the choledocus	3 (5.55%)
Serous cystadenoma	3 (5.55%)
Pancreatic pseudocyst	2 (3.70%)
Adenocarcinoma of the duodenum	1 (1.85%)
Mucinous cystoadenoma	1 (1.85%)
Chronic pancreatitis	1 (1.85%)
Adenocarcinoma of the vesicle with infiltration of the choledocus	1 (1.85%)
Neuroendocrinal tumor	1 (1.85%)
Duodenal polyp	1 (1.85%)
Total	54

The surgical procedures performed most frequently were the Whipple procedure (70.37%) and distal pancreatectomy (20.37%) (Table 2).

TABLE 2 – Distribution of the types of pancreatic resection

TYPE OF PANCREATIC RESECTION	INCIDENCE (%)
Whipple Procedure	38 (70.37%)
Distal pancreatectomy (corpocaudal)	11 (20.37%)
Central pancreatectomy	3 (5.55%)
Uncinectomy	1 (1.85%)
Enucleation	1 (1.85%)
Total	54 (100%)

In eight patients submitted to the Whipple procedure, there was a need for full (seven cases) or partial (one case) resection of the mesenteric-portal axis. A polytetrafluorethylene prosthesis was implanted in two of these cases.

For the patient with adenocarcinoma of the gallblader, the Whipple procedure was associated with resection of hepatic segments IVb and V, as well as lymphadenectomy. In another two cases, the surgery was associated with a segmental resection of the transverse colon due to tumor invasion on the right side. Another case was associated with nephrectomy on the right side due to liver disease, with loss of function.

The pancreatojejunal anastomosis most frequently performed in patients submitted to the Whipple procedure was terminoterminal by telescopy (68.4% of cases) followed by terminolateral duct to mucosa anastomosis (21% of cases) and terminoterminal anastomosis by invagination (10.5%).

The second most common type of procedure was distal pancreatectomy, which was performed in eleven patients. The spleen was preserved in one of these cases. Laparoscopic access was used in one patient with Frantz's disease, who was submitted to distal pancreatectomy. In the majority of cases, the pancreatic stump was sutured with separated "U" sutures in 4-0 Prolene® thread. In just three cases, the pancreatic stump was stapled and reinforced with biological glue.

Central pancreatectomy was performed in three patients with small benign tumors (two cases of Frantz's Tumor and one case of neuroendocrine tumor) located in the pancreatic stump, in order to preserve the parenchyma. The pancreatic stump was preferably treated with separate "U" sutures in 4-0 Prolene® thread, and the pancreatojejunal anastomosis most commonly performed was the terminolateral type by invagination.

In 77.7% of the total case series, prophylactic octreotide was used for seven days.

The mean surgery times, for all the patients in the case series and for those submitted to the Whipple procedure, were 421.7 min (125-600) and 451.8 min (290-600), respectively.

The mean drop in serum hemoglobin values per patient in the case series during the first seven days after surgery was 2.07 mg/dl. Considering only the group of patients submitted to the Whipple procedure,

this figure was 2.19 mg/dl. Transfusion of red blood cell concentrate was required either intraoperatively, or in the first 24 h after surgery, in 48% of patients. Evaluating only the group submitted to the Whipple procedure, this value was 57.9% for all the 38 patients and 33.3% only for the last 19 cases.

The mean hospitalization time was 20.7 days (7-114). With the exception of the three patients who died, 51% of the remaining patients were hospitalized for up to 10 days.

Some type of complication occurred in 62% of the patients, the most common being pancreatic fistula (Table 3). Not including grade A fistulas, which do not represent clinically evident complications for the patients, the global morbidity was 46.2%.

TABLE 3 – Distribution of postoperative complications

COMPLICATIONS	INCIDENCE (%)
Pancreatic fistula	27 (50,00)
Delayed gastric emptying	7 (12,96)
Hemorrhage	5 (9,26%)
Acute renal failure	3 (5,55%)
Biliary fistula	2 (3,70%)
Intra-peritoneal collection	2 (3,70%)
Peritonitis	2 (3,70%)
Plural effusion	2 (3,70%)
Septic shock	1 (1,85%)
Coagulopathy	1 (1,85%)

The levels of pancreatic fistula for the case series as a whole, and only for the patients submitted to the Whipple procedure, were 5% (n=27) and 44.7% (n=17), respectively. Most of the patients who developed pancreatic fistula were classified as Grade A (27.7%) (Table 4).

Post-pancreatectomy hemorrhage and postoperative delayed gastric emptying were only found in the patients submitted to the Whipple procedure.

Thus, the majority of cases that evolved with post-pancreatectomy hemorrhage (80%) were classified as grade B, and the majority that developed delayed gastric emptying (85.7%) were classified as grades A or B (Table 4).

Three patients of the overall case series died (5.5%). They had all undergone Whipple procedure, resulting in a mortality of 7.9% for this procedure. Cases that evolved to death were the 5th, 15th and 19th patients. There were no mortalities in the last 35 cases of the present series.

The first case, died of renal failure and coagulopathy on the 12th day after surgery; the second developed refractory shock and died on the 6th day and in neither case amylase drains dosages evidenced pancreatic fistula; the third died for septic shock. There were no deaths in the remaining 35 cases.

TABLE 4 – Distribution of the three most common postoperative complications, according to the criteria of the ISGFP² and ISGPS^{23,25} and surgical procedures performed in the 54 patients

COMPLICATION	GRADE	PROCEDURES			TOTAL
		Pancreatectomy Whipple	Distal pancreatectomy	Others	
		(n=38)	(n=11)	(n=5)	
PANCREATIC	A	9 (23,68%)	4 (36,36%)	2 (40%)	15 (27,77%)
FISTULA	B	4 (10,53%)	0 (0%)	2 (40%)	6 (11,11%)
	C	4 (10,53%)	2 (18,18%)	0 (0%)	6 (11,11%)
	Total	17 (44,74%)	6 (54,54%)	4 (80%)	27 (50%)
HEMORRHAGE	A	1 (2,63%)	0	0	1 (1,85%)
	B	4 (10,52%)	0	0	4 (7,41%)
	C	0 (0%)	0	0	0 (0%)
	Total	5 (13,15%)	0 (0%)	0 (0%)	5 (9,26%)
DELAYED	A	3 (7,89%)	0	0	3 (5,55%)
GASTRIC	B	3 (7,89%)	0	0	3 (5,55%)
EMPTYING	C	1 (2,63%)	0	0	1 (1,85%)
	Total	7 (18,41%)	0 (0%)	0 (0%)	7 (12,96%)

DISCUSSION

Although the literature includes publications of reference Brazilian services in pancreatic surgery on the treatment of specific diseases, such as chronic pancreatitis¹⁰, pancreatic adenocarcinoma¹⁹ and pancreatic trauma²⁰, there are few national publications dedicated to the overall results of pancreatectomies carried out for various diseases in a single service.

Rocha et al.²¹ evaluated 41 patients submitted to the Whipple procedure with various diseases, at a public hospital in Belo Horizonte over an eight-year period. The morbidity rate was 58% and the mortality rate was 21.9%. Although the majority of patients in the case series were aged over 60 years, the mortality rate was high, even considering the last patients operated on.

Orlando et al.²² analyzed 39 patients submitted to the Whipple procedure at a university hospital in Maranhão state. The level of complications cannot be correctly evaluated, as the authors only described the term "major complications", without adequately defining it. The mortality rate was 10.2%.

Better results were found by Junior et al. (2005)¹³ in a retrospective study with 64 patients, carried out at the National Cancer Institute. The mortality rate evaluated in the first 30 days after surgery was 3.12%. Two years later, in a new publication by this author in the same service, with a smaller case series, this level had doubled to 6.25%¹².

In the present series, the global mortality rates and those found in the patients submitted to the Whipple procedure were 5.5% and 7.9%, respectively. Although higher than the levels found in large North American centers²⁶, there may be a tendency in this casuistic for these values to decrease, since the three causes of death occurred in the first 19 cases, suggesting an inverse relationship between surgical experience and mortality rate. This fact has been extensively

described by the literature for 30 years, prompting the "regionalization" in the care of patients with diseases requiring major surgical procedures, as is the case with pancreatectomies^{6,16}

Pancreatic fistula continues to be the main concern for surgeons involved with surgery of the pancreas^{1,15}. In a bibliographic review on pancreatic anastomoses spanning more than 50 years in the Pubmed database, 1700 publications¹ were found relating to this complication. Up to 2004, at least 26 different definitions of the term "pancreatic fistula" were found in the medical literature, making comparison between the studies unfeasible. An important development, in this regard, was the standardization of the definition of the term "pancreatic fistula" by the ISGFP, divulged in 2005². The concept of "pancreatic fistula" established in this publication was rapidly popularized in practically all subsequent studies.

As the currently-accepted term is very broad, and includes cases of patients with a small drained volume rich in amylase (grade A) without any other occurrence and with similar hospitalization time to the other non-complicated patients, it is unlikely that the publications that used patients prior to 2005 reflect the real incidence of postoperative pancreatic fistulas. This was the case of the three Brazilian series cited previously. While [Rocha et al](#)⁵ do not define the term "pancreatic fistula", [Orlando et al](#)⁶ and [Júnior et al](#)⁷ consider it only if the leakage of amylase-rich liquid occurs after postoperative days 8 or 7, respectively.

In only one Brazilian study, apparently involving two institutions, with retrospective analysis of 117 patients submitted to pancreatic resection between 2000 and 2006, [Haddad et al](#)¹¹ using the currently-accepted concept for the diagnosis of pancreatic fistula, report a 30% incidence of this complication. The type of pancreatic anastomosis was defined by the surgeon's preference, with pancreaticogastrostomy being performed in the majority of cases (55.6%). The residual pancreas was described by the authors as having a hard texture (57%) containing a principal dilated pancreatic duct (51%) in the majority of patients¹¹

In this series, the global levels of pancreatic fistula, and the level of the cases submitted to the Whipple procedure, were 50% and 44.7%, respectively, this being the main type of complication of the series by far, with comparatively higher values than those found in international publications¹⁵. Some possible reasons for these high levels were: a) systematic use of measurements of amylase of the liquid from the abdominal drains on predetermined postoperative days (postoperative 3, 5 and 7), which enabled the diagnosis of a high number of subclinical fistulas (grade A); b) high level of residual pancreas with soft texture and thin duct of Wirsung (76% of cases submitted to the Whipple Procedure) and c) inefficacy of the technique of terminal-terminal anastomosis in telescopic, performed in most of the patients submitted to the Whipple procedure.

The question of which is the best technique for pancreatic-enteral anastomosis remains inadequately elucidated⁹. At least two meta-analyses and seven prospective, randomized clinical trials are available in the literature comparing pancreatoenteral anastomosis with the stomach, or with the jejunum, or comparing different types of pancreatojejunal anastomosis (duct to mucosa vs invagination techniques)^{3,5,7,9,17,18,24,27}. In the prospective study of the largest case series on the best type of pancreaticojejunostomy after duodenopancreatectomy, 197 patients were randomized between duct to mucosa anastomosis and the terminal-lateral technique by invagination⁵. A significantly smaller number of fistulas was identified with the terminal-lateral technique in patients with soft-textured pancreas. The authors concluded that there is a need for additional studies for adequate clarification of the theme⁵. Inspired by this study, our group has recently given preference to pancreatojejunal terminal-lateral anastomosis by invagination in cases of pancreas with a high risk of fistula. Due to the small number of cases in which this type of anastomosis was performed, it was not possible to recommend this type of construction.

Whatever our knowledge, the present study represents the first national case series involving a prospective series of consecutive patients submitted to pancreatic resections analyzed based on the current criteria of the ISGFP² and ISGPS^{23,25}.

CONCLUSION

There is a need for the national publications to assimilate the concepts and criteria presented by the ISGFP² and ISGPS^{23,25} to enable comparison of the results obtained with surgical treatment of pancreatic disorders, in the Brazilian context. Who knows, therefore, whether the great advanced seen in the last 40 years in terms of the reduction in mortality rates associated with pancreatic resections may also occur with the persistently high levels of postoperative complications.

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