Laparoscopic management of pancreatic cancer.
Our experience

Ann. Ital. Chir., 2015 86: 518-523
pii: S0003469X15023830

Paolo Ialongo, Marialessia Milella, Bianca Pascazio, Antonio Prestera, Oronzo Pannarale, Annunziata Panebianco, Annalisa Volpi, Nicola Palasciano

Department of Emergency and Organ Transplantation, II General Surgery Unit, University of Bari, Policlinico General Hospital, Bari, Italy

Laparoscopic management of pancreatic cancer. Our experience

AIM: *Minimally invasive techniques have a definite role in the surgical treatment of several gastrointestinal tract cancers but there is still no widespread use of the laparoscopic approach for cancers of the head of the pancreas. The aim of this retrospective study is to review our experience from 2003 to 2013 in the management of pancreatic cancer with particular emphasis on the clinical application of minimally invasive techniques.*
METHODS: *One hundred fifty-eight pancreatic cancer patients (median age 69,7±12,6 years) with obstructive jaundice were enrolled in our study. One hundred eighteen (74,7%) had an endoscopic biliary stent, 68 patients (43,03%) were eligible for surgery. Only 22 of the patients eligible for surgical intervention underwent pancreaticoduodenectomy (PD): 14 had open PD and 8 had laparoscopic PD (LPD). Thirteen of the PD patients had a pylorus-preserving procedure (8 open and 5 laparoscopic procedures) whereas in 9 the pylorus was not preserved (6 open and 3 laparoscopic procedures). The other 46 patients had un-resectable tumors and 34 of them underwent palliative surgery consisting of gastrojejunal and hepatojejunal anastomosis (18 open and 6 laparoscopic procedures), and gastrojejunal anastomosis in 10 patients (4 open and 6 laparoscopic procedures). Ten patients had only explorative laparoscopy and 2 only explorative laparotomy.*
RESULTS: *The resectability rate was 13,9%. The median age in patients treated with an endoscopic biliary stent was significantly higher than in those who underwent surgery (73,2±13,3 years vs 64,4±9,6 years; $p < 0,05$). Operative time in LPD patients was significantly longer than in PD patients (521±68 minutes vs 381±88 minutes; $p<0.05$). The hospital stay of patients who underwent PD was significantly longer than that of those who underwent palliative surgery (27±4 days vs 10±5 days; $p < 0.05$). in PD patients the morbidity rate was 22,72 % and the mortality rate 4.5%.*
CONCLUSIONS: In *recent years laparoscopic surgery has become very important in oncologic surgery because it is minimally invasive and reduces postoperative complications and because there is sufficient evidence based data showing that results in terms of complications and survival are as good as the results of conventional surgery. However the learning curve for laparoscopic cancer surgery of the head of the pancreas is steep and our results indicate that in LPD operative time is significantly longer than in PD, and moreover the laparoscopic approach is not associated with a shorter hospital stay. Therefore LPD should be performed only in well-established laparoscopic and oncological centers with a multidisciplinary team.*

KEY WORDS: Laparoscopy, Pancreatic cancer, Pancreaticoduodenectomy

Introduction

Pancreatic cancer (PC) is rare but the incidence of this cancer continues to rise probably due to the increase in the average age of the general population as well as an increased exposure to various risk factors including cigarette smoking and alcohol abuse and to a higher inci-

Pervenuto in Redazione Febbraio 2015. Accettato per la pubblicazione Giugno 2015
Correspondence to: Paolo Ialongo, Piazza Eroi del Mare 13, 70121 Bari, Italy (e-mail: ialongopaolo@gmail.com)

Abbreviations

PD	Pancreaticoduodenectomy
OPD	Open pancreaticoduodenectomy
LPD	Laparoscopic pancreaticoduodenectomy
SPD	Standard pancreaticoduodenectomy
LSPD	Laparoscopic standard pancreaticoduodenectomy
PPPD	Pylorus preserving pancreaticoduodenectomy
LPPPD	Laparoscopic pylorus preserving pancreaticoduodenectomy

TABLE I - *Distribution of surgical patients according to the 6th edition of the TNM staging system of the UICC.*

TNM staging	Patients	%
Stage I – Local disease	3	4,4
Stage II – Local invasion (duodenum, portal vein and mesenteric vessels)	6	8,8
Stage III – lymph node metastasis	27	39,7
Stage IV – Invasive disease (liver and peritoneal metastasis)	32	47,1
Total	68	100

dence of underlying disease associated with PC, notably chronic pancreatitis. Moreover, due to the widespread use of powerful diagnostic tools, more cases of PC are being diagnosed.

In Europe and the United States, PC is the10th most common solid tumor [1]. The incidence of PC is highest in the United States, especially among black men. There is strong evidence that factors that increase accumulation of body fat (such as a low level of physical activity and a high calorie intake), are linked to increased PC risk. Therefore diabetes mellitus and obesity play an important role in the etiology of PC. The disease has such a poor prognosis that although it is rare it is the 4thleading cause of cancer-related death in Western countries [2].

In spite of the progress made in diagnostic imaging as new imaging modalities have been perfected (ultrasound (US), computed tomography (CT) scanning, and magnetic resonance imaging (MRI)), PC is often diagnosed late and 80-90% of patients already have locally advanced cancer or distant metastases.

However, surgical resection, when feasible, gives the best chance for a cure.

The aim of this retrospective study was to analyze our experience over the past 10 years with PC surgery in light of the dominant role laparoscopy has come to play in both diagnosis and treatment.

Patients and Methods

In the period from January 2003 to December 2013, 158 patients (88 men, 70 women) with obstructive jaundice due to pancreatic cancer caused by PC were admitted to our unit (Department of Surgery III, Polyclinic, University of Bari).

Preoperative investigations included routine CA 19.9 levels, US and abdominal CT scan or MRI.

Patients with high serum bilirubin underwent endoscopic retrograde cholangiopancreatography (ERCP) with placement of a biliary stent in the common bile duct. This was the only procedure performed in patients who had advanced disease with metastases, or were in poor clinical condition, and high-risk for general anesthesia.

Staging was done according to the 6th edition of the Union for International Cancer Control (UICC) TNM classification [3] (Table I).

The decision to perform open surgery or use a minimally invasive approach was made collectively after discussion of the case with the anesthesiologist. From 2004 on all patients without contraindications to the use of anesthesia, underwent laparoscopy with curative intent (in the most favorable cases of localized disease when resection or a bypass procedure was possible) or a staging laparoscopy (in patients with advanced disease).

All patients were given antithrombotic prophylaxis (enoxaparin 4000 U.I. sc) and short-course antibiotic therapy (piperacillin-tazobactam 4.5g x 4 iv). In the postoperative period they were put on gabexate mesilate (600 mg/day iv) and octreotide (0.3 mg/day sc) for 1 week.

Demographic and physiological parameters of PD patients as well as tumor stage, type of treatment, operative time, length of hospital stay, morbidity and mortality were assessed. In-hospital mortality was defined as death from any cause within 30 days after surgery or before discharge.

To define pancreatic fistula we used the criteria proposed by Gouillat in 2002: postoperative drainage of at least 100ml of liquid with concentration of amylase in the drainage 5 times the serum amylase level, starting after day 3 and persisting after day 12. The patients with pancreatic fistula who were in good clinical condition were discharged with a Jackson-Pratt drain in place.

Surgical Treatment

From October 2004 on, if patients had no contraindications for anesthesia, we always performed diagnostic laparoscopy. In patients with resectable tumors the resection phase was carried out laparoscopically and the reconstruction phase (anastomosis) was performed via a minilaparotomy. It is our practice to construct a termino-lateral pancreaticojejunal anastomosis using two (anterior and posterior) semicontinuous 3/0 Biosyn® sutures and to place a stent in the duct of Wirsung.

More recently, from 2010 on, even the reconstruction phase was carried out in laparoscopy.

Statistical Analysis

Analysis of ordinal variables was performed with the chi-square test with Yates' correction for small numbers. Fisher's exact test and Student's t-test were used for analysis of continuous variables (expressed as average ± standard deviation (SD)).
A p-value <0.05 was considered significant.

Results

In the period from January 2003 to December 2013, 158 patients (88 men and 70 women) were admitted to our unit for obstructive jaundice caused by PC. The average age was 69,7±12,6 years (range 36-89 years). One hundred and eighteen patients (74,7%) underwent endoscopic placement of a biliary stent. In 90 of them (57%), because of their poor clinical condition or advanced disease, this was the only procedure performed. The average age of the patients who underwent the endoscopic procedure was significantly greater than that of the patients who underwent surgical treatment (73.2±13,3 years vs 64.4±9.6 years; p<0,05) (Table II). Only 22 (32.4%) of the 68 patients who underwent surgery could be treated with pancreaticoduodenectomy (PD) (14 cases of open PD (OPD)), 8 cases of laparoscopic PD (LPD)), which meant that only 13.9 % of the patients in the study could benefit from radical surgery.
Pylorus-preserving PD (PPPD) was performed in 13 of these patients (8 open procedures (OPPPD) and 5 laparoscopic procedures (LPPPD)) whereas in 9 the pylorus was resected in a standard PD (SPD) (6 open procedures (OSPD) and 3 laparoscopic procedures (LSPD)) (Table III) .
The indications for PD are listed in Table IV.
In 24 patients a double bypass was made (gastro- and hepatojejunal) and in 10 who had undergone endoscopic placement of a biliary prosthesis in the common bile

Table II - *Patient demographics*

Variable	Surgical group	Endoscopic group	p value
Age, mean±SD, years	64,4±9,6	73,2±13,3	<0,05
Sex, n (%)			
Male	42 (61,8)	46 (51,1)	NS
Female	26 (38,2)	44 (48,9)	NS
Total	68	90	

Table III - *Surgical treatments*

Variable	Open		Laparoscopic		p value
	n	%	n	%	
Surgical approach					
SPD	6	(8,8)	3	(4,4)	NS
PPPD	8	(11,8)	5	(7,4)	NS
Double bypass	18	(26,5)	6	(8,8)	<0,05
Gastroenteric bypass	4	(5,9)	6	(8,8)	NS
Explorative laparoscopy	/		10	(14,7)	/
Explorative laparotomy	2	(2,9)	/		/
Total	38	(55,9)	30	(44,1)	

Table IV - *Types of pancreatic tumors*

	Patients	%
Pancreatic adenocarcinoma	13	59,1
Intraductal pancreatic mucinous neoplasm	3	13,6
Ampullary adenocarcinoma	3	13,6
Pancreatic neuroendocrine tumor	2	9,1
Colangiocarcinoma	1	4,6
Total	22	100

Table V - *Mean postoperative hospital stay of surgical patients*

Variable	PD	Other procedures	p value
Length of stay, mean±SD, days	27±4	10±5	< 0.05

Table VI - *Complications of PD*

	Patients	%
Pancreatic fistula	4	18.2
Abdominal hernia	1	4.5
Total	5	22.7

Table VII - *Operative time of PD*

Variable	OPD (n 14)	LPD (n 8)	p value
Operative time, mean±SD, minutes	381±88	521±68	< 0.05

duct a gastrojejunal anastomosis was constructed. Ten patients underwent only explorative laparoscopy and 2 only explorative laparotomy .

Average hospital stay for patients who had undergone PD was 27±4 days and therefore significantly longer than for those who underwent other surgical procedures (27±4 days vs 10±5; $p<0.05$) (Table V).

The major morbidity rate after PD was 22,7 %. In particular, pancreatic fistula developed in 4 patients (18.2%) after PD and in one case was associated with dehiscence of the laparotomy wound (in a patient with a tracheostomy from prior laryngectomy for cancer) (Table VI). Laparocele repair was required.

Operative time in LPD patients was significantly longer than in PD (521±68 minutes vs. 381±88 minutes, $p<0.05$) (Table VII).

Three patients (4.4%) one of whom (4.5%) had undergone PD, died in the postoperative period. One was a patient who had undergone diagnostic laparoscopy, who died on day 6 of hemoperitoneum caused by liver metastases from a poorly differentiated neuroendocrine tumor of the head and tail of the pancreas. Another patient, with intestinal occlusion and peritoneal carcinosis, who had been treated with a laparoscopic gastrojejunal bypass after undergoing internal biliary bypass at another hospital, died on day 9 of septic shock. The third patient, who had undergone PD, died of severe respiratory failure on day 63.

Discussion

Although advanced radiologic imaging modalities (ultrasound, CT scan, MRI) and invasive imaging modalities (ERCP) have facilitated the diagnosis of cancer of the head of the pancreas, the disease is often diagnosed late. Accurate preoperative staging of PC is difficult in spite of the sophisticated imaging techniques available (CT scan and MRI), and historically, in the majority of centers specialized in hepatobiliary and pancreatic surgery only laparotomy made it possible to make a correct diagnosis and above all to determine whether the lesion was resectable.

The high percentage of radiologically occult metastases, which according to the literature is circa 20%, is a problem in patients with pancreatic cancer. However laparoscopic staging, performed by an expert surgeon, can permit the detection of microlesions not identified on preoperative imaging studies and detailed examination of the abdominal cavity and provide the opportunity to take biopsies and thus avoid unnecessary laparotomies which are associated with complications, especially in patients in poor clinical condition.

Laparoscopy may be better than open surgery for identifying small lesions because of the magnification of the operative field. Moreover, when laparoscopy shows that the tumor is unresectable, it is possible to perform a laparoscopic gastrointestinal bypass and when indicated, endoscopic placement of a biliary stent.

When PD can be performed it is the best treatment for cancer of the head of the pancreas. Whipple proposed this technique in 1935. In 1944, Watson introduced PPPD, but over 30 years went by before this technique was popularized, by Tranverso and Longmire (1978) [4].

PPPD provides a better quality of life. The modification described by Traverso and Longmire is characterized by better postoperative weight gain and more regular gastrointestinal function as well as a lower incidence of dumping syndrome.

In our experience, most patients were diagnosed late, i.e. they had advanced disease and so very few could be treated with radical resection (resectability rate: 13.9%).

Five-year survival has improved in the past decade and ranges from 15% to 20% [5]. In the literature, prognostic factors for 5-year survival after curative resection include tumor size (better prognosis: ≤ 3 cm), lymph node involvement (14% survival if positive nodes vs.40% if negative nodes), status of resection margins (8% survival if positive margins vs 26% if negative margins) and histotype (1.3% survival for adenocarcinoma, 7.7% for papillary carcinoma, 67% for neuroendocrine tumors) [6].

As regards postoperative pancreatic fistula, incidence rates are reported to range from 5% to 15% [5,6]. Main risk factors are a small-caliber duct of Wirsung and a pancreatic remnant with a soft consistency [7]. There is still controversy about what type of pancreaticojejunostomy to use since none has been shown to be significantly superior in terms of postoperative morbidity. As a result, in the majority of cases the type of anastomosis made is an indication of where the surgeon did his/her training. It is our practice to construct a terminolateral pancreaticojejunostomy and place a stent in the duct of Wirsung.

The issue of vascular resection in cases of tumor infiltration is equally controversial. In qualified centers venous resection in particular has been shown to be feasible and improve survival [8].

However arterial resection has not yet been shown to provide any benefits in terms of survival and in fact has been associated with an increase in morbidity and mortality even when performed in highly qualified centers [8].

Unfortunately less than 20% of patients with cancer of the head of the pancreas can be treated with surgical resection, but it is possible to perform palliative procedures to cause resolution of the jaundice or the duodenal obstruction.

Obstructive jaundice can be treated surgically, endoscopically or percutaneously. Surgical bypass, often carried out during explorative laparoscopy, consists of construction of a choledochojejunal or, less commonly, a choledochoduodenal anastomosis. Cholecystoenteric bypass is no longer performed.

The other two procedures, endoscopic or percutaneous stenting, are used in patients who are considered inoperable because of their poor clinical condition.

The duodenal obstruction is treated at the same time because otherwise, as reported in the literature [9], it will require treatment within 8 months in 13% of patients and, if the duodenal obstruction is treated when there are signs of intestinal occlusion, mortality is 25% [10,11]. Therefore double bypass (biliary and gastric), which is associated with a success rate of 90% and a low morbidity rate, is recommended.
Limitations of this study include its retrospective nature and the small sample size.

Conclusions

In recent years the laparoscopic approach has become very important in oncologic surgery because it is minimally invasive and reduces the incidence of postoperative complications and because there is sufficient evidence-based data showing that results in terms of complications and survival are as good as the results of conventional surgery.
However the learning curve for laparoscopic cancer surgery of the head of the pancreas is steep and our results indicate that in LPD operative time is significantly longer than in PD, and moreover the laparoscopic approach is not associated with a shorter hospital stay. Therefore it is our opinion that LPD should be performed only in well-established laparoscopic and cancer care centers with a multidisciplinary team.

Riassunto

OBIETTIVO: La laparoscopia riveste oggi un ruolo ormai ben definito nel trattamento di neoplasie dell'apparato gastroenterico; tuttavia il suo impiego in neoplasie della testa del pancreas è ancora limitato. Obiettivo di questo lavoro retrospettivo è analizzare la nostra esperienza nel trattamento chirurgico del carcinoma pancreatico con riferimento all'esperienza relativa agli ultimi 10 anni e alla luce dell'utilizzo ormai routinario della laparoscopia a fini diagnostici e terapeutici.
METODI: Nel periodo compreso tra gennaio 2003 e dicembre 2013 sono stati ricoverati in regime d'urgenza 158 pazienti affetti da ittero ostruttivo da neoplasia pancreatica; 88 erano di sesso maschile e 70 di sesso femminile. L'età media era di 69,7±12,6 anni (range 36-89 anni). In 118 pazienti (74.7%) è stata posizionata una protesi biliare per via endoscopica e in 90 di essi (57%), date le compromesse condizioni cliniche o la stadio di malattia avanzato, questo è stato l'unico tipo di trattamento effettuato. Dei 68 pazienti sottoposti a procedura chirurgica, solo in 22 (32,4%) è stato possibile effettuare una duodenocefalopancreasectomia (DCP), in 8 casi per via laparoscopica (LDCP). Per quanto concerne i pazienti sottoposti a DCP, in 13 casi è stato preservato il piloro (in 5 di essi l'intervento è stato effettuato in laparoscopia) e in 9 invece è stata effettuata anche una resezione del piloro (in 3 casi in laparoscopia).
In 24 pazienti è stata effettuata una doppia derivazione (gastrica ed epatico-digiunale; in 6 casi in laparoscopia) ed in 10, già sottoposti a posizionamento endoscopico di protesi nella via biliare, è stata confezionata una anastomosi gastro-digiunale (6 per via laparoscopica).
In 10 casi è stata eseguita soltanto una laparoscopia diagnostica ed in 2, infine, una laparotomia esplorativa.
RISULTATI: Il tasso di resecabilità è risultato del 13,9%. L'età media dei pazienti sottoposti a procedura endoscopica è risultata significativamente maggiore rispetto a quelli sottoposti a trattamento chirurgico (età media 73,2±13,3 anni vs 64,4±9,6; p<0,05). La degenza ospedaliera media è risultata di 27±4 giorni nei pazienti sottoposti a DCP e dunque significativamente maggiore rispetto a quelli che hanno beneficiato di altra procedura chirurgica (27±4 giorni vs 10±5; p<0,05).
La durata dell'intervento chirurgico, nei pazienti sottoposti a DCP, è risultata significativamente maggiore in quelli operati per via laparoscopica (521±68 minuti vs 381±88; p< 0,05).
La morbilità e mortalità nei pazienti che hanno beneficiato di DCP è risultata rispettivamente del 22,7% e del 4,5%.
CONCLUSIONI: La laparoscopia riveste oggi un ruolo importante per il trattamento chirurgico di neoplasie pancreatiche avendo dimostrato, con sufficiente evidenza clinica, risultati comparabili a quelli della chirurgia tradizionale in termini di complicanze e di sopravvivenza.
Tuttavia il suo impiego, in neoplasie della testa del pancreas, è ancora limitato poiché la curva di apprendimento è complessa, i tempi chirurgici sono notevolmente superiori e la degenza ospedaliera invariata contrariamente a quanto accade per altre patologie. Il suo impiego pertanto, a nostro avviso, andrebbe limitato a centri di riferimento per la chirurgia laparoscopica.

References

1. Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P: *Estimates of the cancer incidence and mortality in Europe in 2006*. Ann Oncol, 2007; 18:581-92.

2. Jemal A, Siegel R, Xu J: *Cancer statistics, 2010.* CA. Cancer J Clin, 2010; 60:277-300.

3. UICC (International Union Against Cancer): *TNM classification of malignant tumours*. In: Sobin LH, Wittekind Ch, (eds). 6th ed. New York, Chichester, Weinheim, Brisbane, Singapore, Toronto: Wiley-Liss., 2002.

4. Giordano G, Ingrosso M, Tumolo R, Carrassa G, Olfati A, Brescia V, Ialongo P: *Sulle neoplasie dell'ampolla di Vater (contributo d'esperienza).* Chir Gastroent, 1994; 28 (4):351-58.

5. Yeo CL: *Management of complication following pancreaticoduodenectomy*. Surg Clin North Am, 1995; 75:913-24.

6. Yeo CJ: *Pylorus preserving pancreaticoduodenectomy*. Surg Oncol Clin North Am, 1998; 78:143-56.

7. Tersigni R, Capaldi M, Ialongo P, Grillo LR, Anselmo A: *Surgical treatment of the pancreatic stump: Preventive strategies of pancreatic fistula after pancreaticoduodenectomy for cancer*. G Chir, 2014; 35: 213-22.

8. Vicente E, Quijano Y, Ielpo B: *Arterial resection for pancreatic cancer: A modern surgeon should change its behavior according to the new therapeutic options.* G Chir, 2014; 35:5-14.

9. Sarr MG, Cameron JL: *Surgical management of unresectable carcinoma of the pancreas*. Surger, 1982; 91:123-33.

10. Iskikawa O, Ohigashi H, Imaoka S, et al.: *Preoperative indication for extended pancreatectomy for locally advanced pancreas cancer involving the portal vein*. Ann Surg 1992; 215:231-36.

11. Watanapa P, Williamson RCN: *Surgical palliation for pancreatic cancer: Development during the past two decades*. Br J Surg, 1992; 79: 8-20.

12. Bardaxoglu E, Landen S, Maddern GJ, Buard JL, Meunier B, Campion JP, Terblanche J, Launois B: *Total pancreatectomy and subtotal duodenopancreatectomy for the management of carcinoma of the head of the pancreas: an institutional experience and evolving trends.* Dig Surg, 1996; 13:12-1.

13. Mason GR, Freeark RJ: *Current Experience with Pancreatogastrostomy.* Am J Surg, 1995; 169:217-19.

14. Yeo CJ, Cameron JL, Lillemoe KD: *Pancreaticoduodenectomy for cancer of the head of pancreas. 201 patients.* Ann Surg, 1995: 221:721-33.

15. Anderson JR, Sorensen SM, Kruse A, et al.: *Randomized trial of endoscopic endoprothesis versus operative by pass in malignant obstructive jaundice*. Gut, 1989; 30:1132-135.

16. Borman PP, Harries-Jones EP, Tobias R, et al.: *Prospective controlled trial of transhepatic biliary endoprothesis versus biliary by pass surgery for uncurable carcinoma of the head of pancreas*. Lancet, 1986; I: 69.

17. Aranha GV: *A tecnique for pancreaticogastrostomy*. Am J Surg, 1998; 175:328-29.

18. Bobin JY: *La chirurgie du cancer du pancréas exocrine.* Cahiers d'Oncologi, 1998; 7(8):25-29.

19. Gagner M, Inabnet WB, Biertho L, Salky B: *Laparoscopic pancreatectomy: a series of 22 patients*. Annales de Chirurgie, 2004 (129): 2-7.

20. Mabrut JF, Fernandez-Cruz L, Azagra JS, Bassi C, Delvaux G, Weert, Fabre JM, Boulez J, Baulieux J, Peix JL, Gigot JF: *Laparoscopic pancreatic resection: Results of a multicenter European study of 127 patients*. Surgery, 2005; 137 (6):597-60.

21. Palanivelu C, Jani K, Senthilnathan P, Parthasarathi R, Pajapandian S, Madhankumar MV: *Laparoscopic pancreaticoduodenectomy: Technique and outcomes*. J Am Coll Surg, 2007; 205 (2):222-30.

22. Patterson EJ, Gagner M, Salky B, Inabnet WB, Brower S, Edye M, Gurland B, Reiner M, Pertsemlides D: *Laparoscopic pancreatic resection: Single-institution experience of 19 patients.* J Am Coll, 2001 193 (2):281-87.

23. Sasco AJ, Gendre I, Couris C: *Epidémiologie du cancer du pancréas*. Cahiers d'oncologie, 1998; 7(8):5-19.

24. Asbun HJ, Stauffer J: *Laparoscopic vs open pancreaticoduodenectomy: Overall outcomes and severity of complications using the accordion severity grading system*. J Am Coll Surg, 2012; 215 (6): 810-19.

25. Williamson RCN: *Pancreatic cancer: The greatest oncological challenge*. Br Med J, 1988; 296: 445-46.

26. Ialongo P, Ferrarese F, Pannarale O, Panebianco A, Volpi A, Palasciano N: *The role of laparoscopy in surgical treatment of pancreatic cancer*. Ann Ital Chir, 2010; 81(4):295-99.