

Which Laparoscopic Treatment in Pancreatic Pathology?

Giorgio Maria Paolo Graziano, Antonio Di Cataldo, Antonino Graziano

Abstract— Pancreatic cancer is in Italy the fourth place among the causes of death in women, which still maintains a poor prognosis with only 7% of men and 9% of women who have a 5-year survival. the highest incidence of the disease is between 6 and 7 decade of life. the aim of this study is to obtain treatment indications that are well codified with the possibility of extending their applications to perform both derivative and resective interventions .Materials and methods: From January 2010 to December 2017 at the department of specialized surgical science II of the AOU Policlinico di Catania were observed in 32 patients with pancreatic neoplasm of which women 22 and 10 men, with a mean age of 65 (58-72.a) The symptomatology was characterized by jaundice, weight loss, steatorrhea, onset of diabetes without an apparent reason, impaired intestinal motility (constipation and diarrhea), intolerance to fatty foods. 10% of the cases had a family history defined with at least 2 degree relatives affected by pancreatic neoplasm. the histological study obtained before the oncology therapy and with an endoscopic ultrasound method that was essential in defining the nature of non-neoplastic lesions, and we obtained a diagnosis of: ductal adenocarcinoma in 8 cases, of serous cystadenoma in 2 cases, cystic mucinous in 6 cases , intraductal in 3cases, acinar cells in 4 cases, similar papillary in 3cases, and neuroendocrine in 6 cases. Results : In the preoperative diagnosis the immunophenotypic profile was necessary to define the histological typology characterized by the ductal differentiation for the production of mucus. acinar differentiation for enzyme production, and neuroendocrine for chromogranin positivity. The tumor marker ca19.9 was positive in 100% of the cases observed with metastatic disease with a positive prognostic value of decrement in the postoperative period in those cases in which the resection of the tumor was carried out. Diagnostic-stapling laparoscopy was indispensable, at the time of diagnosis, were: 1) laparoscopy exploration revealed in 30% of cases the presence of metastases not shown with the usual procedures of preoperative staging. 2) The laparoscopic evaluation showed a positive predictive index of 100%, of the cases, and negative in 97% of the cases observed with a diagnostic accuracy of 97%. 3) Unsurpreted metastatic diffusion was more specifically reported in body-caudal tumors (30%) and cephalic lesions (20%). 4) Staging diagnostic laparoscopy Study the M parameter of tumor disease, with visualization of the surface of the abdominal cavity and of the liver, in order to exclude the presence of small, often multiple, peritoneal or sub-glissonian metastases which, if present , made the intervention useless.Discussion: Laparoscopic pancreatic surgery interventions, regardless of the tumor site and the type

of intervention, even in the feasibility, are not yet fully accepted on the oncological level. This is due to both the reduced number of cases of resectable pancreatic carcinoma and the reduced number of laparoscopist surgeons dedicated to pancreatic surgery. (25,26,27,28) All this makes it more difficult to undertake multi-center studies that can demonstrate the oncological correctness of the method. The diagnosis then becomes mandatory in those cases in which the suspected tumor is high where the histological material is obtained before the intervention with a tissue sampling with trans cutaneous biopsy with multiple thin needle with a risk of low complications, in the presence of lesions resection. (29,30,31,32), Conclusions: From the results obtained, the indication emerges definitively to a standard diagnostic-stadiative laparoscopy, which allows to define with considerable accuracy the TNM action steps, with a modest impact on the time of use of the operating room. Laparoscopy in expert hands is a useful tool for pancreatic surgery not only for diagnosis but also for resective and palliative surgery.

Index Terms— pancreas laparoscopy.

I. INTRODUCTION

Pancreatic cancer is in Italy the fourth place among the causes of death in women, which still maintains a poor prognosis with only 7% of men and 9% of women who have a 5-year survival. the highest incidence of the disease is between 6 and 7 decade of life. At present, no screening studies have yet been carried out in the subjects considered to be at risk since there is no concordance on which are the common risk factors to be evaluated since the latter are completely non-specific such as: smoke with the presence of nitroderivatives, capable of inducing genetic modifications, is responsible in 30% of cases of the onset of the tumor, the diet rich in dietary fat, obesity in relation to the alteration of the glucose metabolism. Patients with type I and II diabetes mellitus, chronic pancreatitis with a risk of onset of the tumor of 7.2 and finally exposure to solvents and oil and pesticide derivatives (DDT). Bernheim (1.2.3.4.5) and Merchant (6.7.8), reports that he used laparoscopy for the evaluation of pancreatic tumors thought to be resection. The applications of laparoscopy to pancreatic pathology have been evaluated successively and at the end of the pre-operative diagnostics are well coded through O to a simple diagnostic exploration or to a resection surgery. (9,10,11,12) However, this last therapeutic option is burdened by the high technical difficulty, due to the close relations of contiguity between the pancreas and the vascular structures, associated with the need for manual palpation, in the case of injuries found in the gland, with the absence of standardization in the laparoscopic treatment of the residual tract of the pancreas, which is associated with the failure to achieve oncological radicality and the low percentage of patients eligible for laparoscopic resections. These factors explain the reduced favor of

Giorgio Maria Paolo Graziano, Researcher fellow University of Catania, Medical School Italy Dpt Sciences Medical of Surgery and Technologies Advanted via S Sofia 86 cap 95125 Catania

Antonio Di Cataldo, University of Catania, Medical School Italy Dpt Sciences Medical of Surgery and Technologies Advanted via S Sofia 86 cap 95125 Catania

Antonino Graziano, University of Catania, Medical School Italy Dpt Sciences Medical of Surgery and Technologies Advanted via S Sofia 86 cap 95125 Catania

surgeons towards this methodology, and the skepticism of the scientific community, due to the execution of unnecessary resection surgery for tumor pathology (13.14.15.16) In surgical staging, although it may be accurate, weighs the unknown diagnostic identification of peritoneal carcinomatosis with the presence of little mts below 1 cm they are often diagnosed only or with a laparoscopic evaluation that precludes the curative resection, even if it reduces the execution of the surgical exploratory open by 20%. (17,18,19,20) In addition, the pancreas surgery is burdened by a high index of postoperative complications, which we try to remedy with the centralization of patients towards operating units with a high volume of pathology in an attempt to reduce them. the need for a particularly long laparoscopic training, in order to be able to deal with the due safety of pancreatic surgery by minimally invasive, associated with the need to standardize laparoscopic techniques, with the limitation of the surgical procedure to selected cases and to surgeons with experience of laparoscopy advanced aimed at being able to better face this delicate surgery. All this means that the possible applications of laparoscopy in this pathology are evaluated from time to time (21,22,23,24). The purpose of this study is to obtain indications for treatment that are well codified with the possibility of enlarging the applications of the same to perform both derivative and resection interventions.

II. MATERIALS AND METHODS

From January 2010 to December 2017 at the Department of Specialized Surgical Science II of the AOU Policlinico of Catania, 32 patients with pancreatic tumor were observed, of which women were 22 and 10 men, with a mean age of 65 (58-72.a) The symptomatology was characterized by jaundice, weight loss, steatorrhea, onset of diabetes without an apparent reason, alteration of intestinal motility (constipation and diarrhea), intolerance to fatty foods. In 10% of cases there was a family history defined with at least 2 first-degree relatives with pancreatic tumor, a genetic evaluation of BCRA2 and P16 was carried out in this group. Patients with a history of chronic pancreatitis and newly developed diabetes accounted for a further 30% of cases. Tumor markers were also evaluated, such as Cea, Ca19.9 both in the pre and post-operative phase and for diagnostic and prognostic purposes. the TNM staging of the neoplasm was obtained through the execution of a first method abdominal ultrasound examination for the differential diagnosis with the other pathologies in the presence of jaundice. Multislide CT scan was performed in which the pre-contrast study evaluated the presence of calcifications obtaining a differential diagnosis with chronic pancreatitis. The arterial phase allowed to identify the tumor between hyperdense healthy tissue and hypodense tumor tissue, fig 1,2

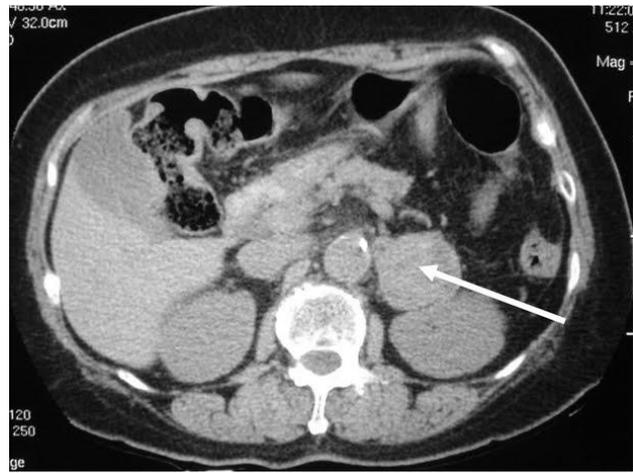


Fig 1 neoplasm head of the pancreas (hypodense)

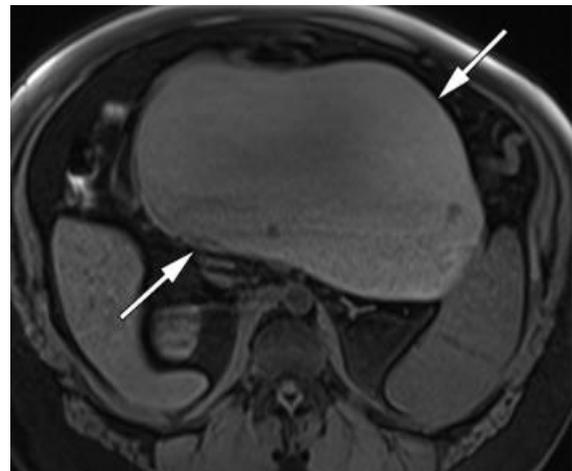


fig 2 cystic neoplasm of the pancreas

in addition to evaluating the parenchyma ratios with vascular structures and in the venous phase, the possible presence of metastatic follicular (2mm) was evaluated. It was associated with the RNM that demonstrated the eventual near pancreatic infiltration obtaining information on the involved vessels and lymph nodes. These instrumental exams were aimed at obtaining the critiques that can be decreed that in adenocarcinoma reached a predictive value that ranged between 89-97% of cases. PET found an indication both in revealing the MTS and in obtaining confirmation of complete remission after treatment. a complementary instrumental examination was a methodological endoscopy that allowed an ultrasound probe to evaluate the organs in close contact with the gastro wall, providing additional vessel and lymph node and bile duct data as well as characterizing the pancreatic cystic lesions. Finally, the study cites histologic obtained before the therapy oncology and with endoscopic ultrasound methodology that was essential in defining the nature of not tumor lesions, and we obtained a diagnosis of: ductal adenocarcinoma in 8 cases, of serous cystadenoma in 2 cases, cystic mucinous in 6 cases, intra ductal in 3cases, acinar cells in 4 cases, near papillary in 3 cases, and neuroendocrine in 6 cases. with the TNM stage we had in the stadium: TIM0N0 in 10 cases (33%), in the T2-T3M2 Nx stage in 6 cases (17%) and in the T4 MxNx stage in 16 cases (50%). In the presence of jaundice in this last group the ColangioRMN offered an important role in defining the nature of the stenosis (10% of the cases n 2 patients) i Finally

an exploratory laparoscopy was performed especially in patients at the IV stage TNM in order to select the patients to undergo radical surgery by diagnosing MTS or at an hepatic or peritoneal.

III. RESULTS

In pancreatic tumors, it is appropriate to distinguish pancreatic adenocarcinoma, in which at the time laparoscopy still had almost exclusively diagnostic-stadiative purposes, compared to neuroendocrine and cystic tumors, in which the method plays a therapeutic role. In the pre-operative diagnosis the immunophenotypic profile was necessary to define the histological typology characterized by the ductal differentiation for the production of mucus. acinar differentiation for enzyme production, and neuroendocrine for chromogranin positivity. The tumor marker ca19.9 was positive in 100% of the cases observed with metastatic disease with a positive prognostic value of decrement in the postoperative period in those cases in which the resection of the tumor was carried out. The indications for the treatment with the diagnostic-stadiative Laparoscopy that became indispensable, at the time of the diagnosis, were: 1) the laparoscopy scan revealed in 30% of the cases the presence of metastases not shown with the usual procedures of preoperative staging. 2) The laparoscopic evaluation showed a positive predictive index of 100%, of the cases, and negative in 97% of the cases observed with a diagnostic accuracy of 97%. 3) Unsurpreted metastatic diffusion was more specifically reported in body-caudal tumors (30%) and cephalic lesions (20%). 4) Staging diagnostic laparoscopy Study the M parameter of tumor disease, with visualization of the surface of the abdominal cavity and of the liver, in order to exclude the presence of small, often multiple, peritoneal or sub-glissonian metastases which, if present, made the intervention useless. To this end, the use of a single access was sufficient, with the introduction of a 30 ° laparoscopic optic. In the presence of a peritoneal and / or hepatic picture of unambiguous interpretation, it is possible to complete the procedure by introducing other trocar operators, to perform the biopsy of the suspected new formations or the LUS (Laparoscopic Ultra-Sonography) which was able to improve the accuracy diagnosis in cases with dubious hepatic localizations not immediately sub-glisson. The ultrasound probes were provided with an operative channel, and therefore an eco-guided biopsy of intra-parenchymal new formations was performed., 5) The indication for the withdrawal of liquid possibly present in the abdomen, for an extemporaneous cytological examination; in the presence of a small ascitic film, it was performed with a sterile saline solution wash, the cytological examination on the peritoneal fluid was specific if positive, and had a high predictive value in determining the resection. 6) In addition to the definition of the M parameter, the laparoscopic examination aimed to evaluate the T and N. parameters due to the local invasion of the neoplasm; this in spite of a pre-operative diagnostic of high accuracy, which required longer operative times and involved technical difficulties, which involved both vascular and lymph node involvement., in patients "doubts" on the CT the study required the contribution of an expert sonographer and the results obtained were moderately reliable, considering the high number of false positives (peritumoral flogistic reaction towards tumor involvement). 7). The study of the N parameter provided for sampling of inter-aorto-caval

lymph nodes, whose tumor involvement is a sure contraindication to resection. This maneuver required ample mobilization, not always easy, even in traditional surgery, and a high laparoscopic ability. 8) If in the absence of univocally accepted parameters, the indications to laparoscopy were considered justified in patients with: 1) new formation of the body-tail of the pancreas with a diameter > 3 cm; 2) locally advanced tumor; 3) presence of ascites; 4) evaluation of CA19-9 > 400 U / ml or hypoalbuminemia; 5) marked weight loss and / or presence of posterior pain. 6) patients judged borderline resection for locally advanced disease. With indication for the use of preoperative radiochemotherapy. The minimally invasive approach in pancreatic resection surgery with regard to indications, they have been limited to benign and benign or borderline tumor pathologies (cystic and endocrine tumors). Laparoscopic pancreatic resections for carcinoma were sporadic (11% of cases in 4 cases) Laparoscopic duodenopancreasectomy It had high average operating times (610 minutes), with a conversion rate of 60%, an average post-operative hospital stay of > 32 days and a high morbidity, whose limits of the laparoscopic surgical method have been beyond the precise oncological motivations, also to the difficulties technical reasons, due to the packaging of bilio-digestive and pancreatic-jejunal anastomoses during the reconstructive phase, mainly performed for adenocarcinoma. Therefore, although the feasibility of the surgical technique is possible. the intervention in our opinion remains not advantageous compared to open surgery, even today the most reliable and safe. In the review of patients undergoing laparoscopic pancreatic resection surgery, 50% of cases had undergone distal pancreatectomy without splenectomy (20). in 25% of cases the intervention was performed for a cystic tumor (benign or malignant) and in 25% for a neuroendocrine tumor (not working) that, for this intervention, represent the elective indications (22,23,24). The results of this review show that left pancreatectomy is a reproducible procedure, even though it is burdened by a morbidity that can be compared to that of the traditional surgical approach. These data confirm that although there are no statistically significant differences between the patients treated with laparoscopy technique those operated in open., The onset of fistulae and the positivity of the resection margins. and prolonged operating times in addition to the blood loss overlapping the open surgery indicates how this method requires further innovative technology. the elective indication was represented by solitary, small, apparently benign tumor, preferably located on the periphery of the gland or on the surface of the parenchyma, such as insulinomas (2 cases 5%) Enucleation conducted by laparoscopy allows the complete removal of the tumor, while avoiding excessive loss of pancreatic parenchyma. The procedure exposes you to the risk of an R1 in case of malignant lesions. The revision on postoperative complications, after this procedure, the most common was the pancreatic fistula. Which according to the severity of the clinical picture. had a greater onset of fistulas after enucleation due to was in the section of some vessels during exposure maneuvers of the distal part of the pancreas. For the resection of the pancreatic parenchyma, the most used technique involved the use of a mechanical stapler. used in 80% of cases and the ultrasonic dissector in 10% of cases, with the use of a manual reinforcement suture in 10% of cases,. The effectiveness of hemostatic glues or sealants in

the prevention of post-operative bleeding or fistulas has not been demonstrated. Near the resection shredder, he applied a 24 mm tubular drainage. The operative piece was removed through a little laparotomy, inside an endobag . (fig 3,4)



Fig 3 tumor pancreas resection



fig 4 tumor laparoscopic vision

The supra-pubic incision guaranteed the cosmetic result, necessary to perfect haemostasis or suture of the pancreatic stump, the incision site was the sub-costal left

IV. DISCUSSION

Laparoscopic pancreatic surgery, regardless of the tumor site and the type of intervention, even in the feasibility, are not yet fully accepted on the oncological level. This is due to both the reduced number of cases of resection pancreatic carcinoma and the reduced number of laparoscopic surgeons dedicated to pancreatic surgery. (25,26,27,28) All this makes it more difficult to undertake multi-center studies that can demonstrate the oncological correctness of the method. The diagnosis then becomes mandatory in those cases in which the suspected tumor is high where the histological material is obtained before the intervention with a tissue sampling with trans cutaneous biopsy with multiple thin needle with a risk of low complications, in the presence of lesions resection . (29,30,31,32) The choice of the guided method, US or CT guided, was conditioned both by the possibility to visualize

the biopsy lesion, and by the experience of the operators (33,34,35,36). The main disadvantage was the dependence on the operator, whose experience can considerably influence the diagnostic quality of the method, and the feasibility (38,39,40,41). The diagnosis obtained on the excised tissue provided information on the action stage. The laparoscopy technique proved to be necessary and reliable in achieving the required results with regard also in the incidental pancreatic solid or cystic lesions found by chance with the Imaging technique. (42,43,44,45) These injuries are not foreseen clinically. present the need for a diagnostic diagnostic evaluation because of their potential malignancy, so the laparoscopic approach performed to obtain a biopsy or a cystic fluid test is optimal (46,47,48,49,50) in planning the strategy more suitable therapy, allowing to differentiate the adenocarcinoma from other less frequent pathologies (neuroendocrine tumors, lymphoma, metastasis). In operable tumors: in these cases the need for a pre-operative cyto-histological diagnosis is shared in the presence of a pancreatic lesion solid (which rarely simulates other diseases) considered resection by imaging and in the absence of systemic manifestations, surgery is the only potentially curative treatment (51,52,53) techniques, performed for resection interventions in laparoscopy they have not currently accepted unanimous consent, however the single out resection technique: conducted under general anesthesia, and that p is accepted for the simplicity of execution and with indication For lesions located at the level of the body-tail, the procedure begins with the opening of the gastro-colic ligament, to obtain the pancreas exposure. (54,55,56,) Intra-operative ultrasound allows the lesion to be identified, confirming the presence of an intact capsule and the distance of the lesion from the main pancreatic duct and from the vessels of the region, in particular from the spleno-mesenteric-portal confluence. We find the boundaries of the lesion from the healthy parenchyma and we proceed to the single out resection of the tumor. the dissection The ultrasonic dissector is effective and manageable and aims to remove the lesion with the entire capsule , without deepening too much in the parenchyma, and not risking to damage the pancreatic duct of Wirsung. The apposition of hemostatic glues or sealants, with appropriate laparoscopy dosers, can sometimes be useful to perfect haemostasis. For derivative procedures it is possible to perform surgical interventions by performing digestive and biliary derivative interventions. As the gastro entero anastomosis ante lateralateral isoperistaltic colic. For biliary and relatively simple derivation procedures to implement a fast-acting stomy fasting cholecystus the indication for endoscopic surgical intervention by the affixing of stents in the biliary pathway was due to the failure of the endoscopic., Finally a further indication to laparoscopic treatment is in pancreatic cysts with a packaging of a lateralateral anastomosis fasting cistys. Finally, in the localized disease surgery which represents the potentially curative treatment with a tumor diameter <2 cm, in the absence of lymph node mts susceptible to surgery resection, which can be performed in a high volume center, the complications are less than 5% with the aim of perform a laparoscopic pancreatic resection with a multidisciplinary TNM that evaluates the extent of the disease. The increase in the incidence of such lesions is indicative to begin to obtain results that demonstrate the usefulness of this laparoscopic surgical treatment.

V. CONCLUSIONS

From the results obtained, the indication emerges definitively to a standard diagnostic-stadiative laparoscopy, which allows the TNM action stage to be defined with considerable accuracy, with a modest impact on the operating theater usage time. In fact, the method envisages a minimum lengthening of the operating times for patients who will ultimately be resection and allows to avoid, in at least 10% of cases, an unnecessary laparotomy. In consideration of the additional costs of the method, even if reduced, it emerges however the necessity to select the patients, to identify as accurately as possible, the patients at high risk of metastatic disease, among those judged pre-operatively resection, in order to limit only to them laparoscopic staging For tumor pathology, resection laparoscopic surgery is currently elective indication in neuroendocrine and cystic tumors (benign and borderline) to body-caudal localization (distal pancreatectomy with or without preservation of the spleen) and in small endocrine tumors cephalic localization, susceptible to resection sing out resection and in small pancreatic incidentaloma if malignancy is defined. Laparoscopy in expert hands is a useful tool for pancreatic surgery not only diagnostic but also for resection and palliative surgery.

REFERENCES

[1] Pierce RA, Spittler et al BD. Outcome analysis of laparoscopic resection of pancreatic neoplasms. *Surg Endosc* 2007; 21:579-586

[2] Yeo CJ, Cameron JL, et al . Six hundred fifty consecutive pancreaticoduodenectomies in 1990s: pathology, complications and outcomes. *Ann Surg* 1997; 226(3):248-257 discussion 257-260

[3] Bernheim BM. Organoscopy: Cystoscopy of the abdominal cavity. *Ann Surg* 1911; 53(6):764-7

[4] Cuschieri A, Hall AW, Clark J. Value of laparoscopy in the diagnosis of pancreatic carcinoma. *Gut* 1978; 19:672-77

[5] Conlon KC, Dougherty E, Klimstra DS, Coit DG, Turnbull ADM, Brennan MF. The value of minimal access surgery in the staging of patients with potentially resectable peripancreatic malignancy. *Ann Surg* 1996; 223(2):134-40

[6] Merchant NB, Conlon KC, Saigo P, Dougherty E, Brennan M. Positive peritoneal cytology unresectability of pancreatic adenocarcinoma. *J Am Coll Surg* 1999; 188:421-426

[7] Jimenez RE, Warshaw AL, Rattner DW, Willett CG, McGrath D, Fernandez-del Castillo C. Impact of laparoscopic staging in the treatment of pancreatic cancer. *Arch Surg* 2000; 135(4):409-14

[8] Nieveen van Dijkum EJM, Romijn MG, et al . Laparoscopic staging and subsequent palliation in patients with peripancreatic carcinoma. *Ann Surg* 2003; 237(1):66-73

[9] White R, Winston C, Gonen M, D'Angelica M, Jarnagin W, Fong W, Conlon KC, Brennan M, Allen P. Current utility of staging laparoscopy for pancreatic and peripancreatic neoplasm. *J Am Coll Surg* 2008; 206:445-450

[10] Mayo SC, Austin DF, Sheppard BC, Mori M, Shipley DK, Billingsley KG. Evolving preoperative evaluation of patients with pancreatic cancer: does laparoscopy has a role in the current era? *J Am Coll Surg* 2009; 208(1):87-95

[11] Graziano g (2016). Which treatment in cystic tumors of the pancreas: conservative or resection . *International journal of current advanced research*, vol. 5, p. 1190-1198, issn: 2319-6505, doi: doi: 12.24327/ijcar

[12] Graziano g, et al (2017). Congenital anomalies of the kidney and urinary tract neoplasms and in the elderly. *International journal of advanced research*, vol. 5, p. 265-273, doi: doi url: <http://dx.doi.org/10.21474/ijar01/3512>

[13] graziano g, et al (2017). Lithiasis in urinary diversions or post prostatectomy . *International journal of recent scientific research*, vol. 8, p. 16357-16363, doi: <http://dx.doi.org/10.24327/ijrsr.2017.0804.0136>

[14] graziano g, et al (2017). Papillary bladder tumor. *International journal of recent scientific research*, vol. 8, p. 18485-18490, , doi: <http://dx.doi.org/10.24327/ijrsr.2017.0807.0518>

[15] graziano g, e al (2016). Renal ureteroscopy treatment of kidney and bladder stones . *International journal of new technology and research*, vol. 2, p. 135-138,

[16] graziano g, e al (2016). Vascular thoracic fibrous adipose tissue (new disease). *Journal of pharmaceutical and biomedical sciences*, vol. 6, p. 419-424, , doi: <http://dx.doi.org/10.20936/jpbms/160265>

[17] graziano g, et al (2016). Clinical and molecular anatomy of gastrointestinal stromal tumors (gist) *international journal of new technology and research*, vol. 2, p. 110-114,

[18] Menack MJ, Spitz JD, Arregui ME. Staging of pancreatic and ampullary cancers for resectability using laparoscopy with laparoscopic ultrasound. *Surg Endosc* 2001; 15:1129-34

[19] Yekebas EF, Bogoevski D, et al . En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels. *Ann Surg* 2008 Feb; 247:300-309 14.

[20] Colon Cancer laparoscopic or Open Resection study Group, Buunen M, Veldkamp R, Hop WC, Kuhry E, Jeekel J, Haglind E, Pahlman L, et al . Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol* 2009 Jan; 10(1):44-52

[21] Gagner M, Pomp A. Laparoscopic pylorus-preservin pancreaticoduodenectomy. *Surg Endosc* 1994 May; 8(5):408-410

[22] Dulucq JL, Wintringer P, Mahajna A. Laparoscopic pancreaticoduodenectomy for benign and malignant disease. *Surg Endosc* 2006; 20(7):1045-1050

[23] Briggs DC, Mann CD, Irving GRB, Neal CP, Peterson M, Cameron IC, Berry DP. Systematic review of minimally invasive pancreatic resection. *J Gastrointest Surg* 2009 Jan; 13:1129-1137

[24] Lukish JR, Rothstein JH, Petruzzello M, Kiteley R, Denobile J, Soballe P. Spleen-preserving pancreatectomy for cystic pancreatic neoplasms. *Am Surg* 1999; 65:596-599

[25] Fernandez-Cruz L, Martinez I, Cesar-Borges G, Astudillo E, Orduna D, Halperin I, Sesmilo G, Puig M. Laparoscopic surgery in patients with sporadic and multiple insulinomas associated with multiple endocrine neoplasia type I. *J Gastrointest Surg* 2005 Mar; 9(3):381-388

[26] Fernandez-Cruz L, Blanco L, Cosa R, Rendòn H. Is laparoscopic resection adequate in patients with neuroendocrine pancreatic tumors? *World J Surg* 2008; 32:904-917

[27] Giorgio Maria Paolo Graziano *et al.*2018, The Radical Anal Trans Excision In The Initial Neoplasm of The Rectum. *Int J Recent Sci Res.* 9(2), pp. 24013-24017. DOI: <http://dx.doi.org/10.24327/ijrsr.2018.0902.1581>

[28] Giorgio Maria Paolo Graziano *et al.*2018, Local Recurrences After Ultra Low Resection of The Rectum. *Int J Recent Sci Res.*9(2), pp. 24119-24124. DOI: <http://dx.doi.org/10.24327/ijrsr.2018.0902.1601>

[29] GRAZIANO G, et al (2017). The antibiotic is needed in clean surgery? . *INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH*, vol. 8, p. 22339-22342, , doi: <http://dx.doi.org/10.24327/ijrsr.2017.0812.1247>

[30] Graziano G, A Dicaldo (2017). COMPLICATIONS IN LAPAROSCOPIC CHOLECYSTECTOMY *INTERNATIONAL JOURNAL OF CURRENT ADVANCED RESEARCH*, vol. 6, p. 3855-3859, doi: <http://dx.doi.org/10.24327/ijcar.2017.3859.0382>

[31] Kooby DA, Gillespie T, Bentrem D, Nakeeb A, Schmidt MC, Merchant NB, Parikh AA, Martin R 2nd, Scoggins CR, Ahmad S, Kim HJ, Park J, et al . Left-sided pancreatectomy a multicenter comparison of laparoscopic and open approaches. *Ann Surg* 2008 Sep; 248(3):438-446

[32] Edwin B, Mala T, Mathisen O, et al . Laparoscopic resection of the pancreas: a feasibility study of the short-term outcome. *Surg Endosc* 2004 Mar; 18(3):407-411

[33] Berends FJ, Cuesta MA, et al. Laparoscopic detection and resection of insulinoma. *Surgery* 2000 Sep; 128(3):386-391

[34] Bassi C, Dervanis C, Butturini G, et al. International study group on pancreatic fistula definition. *Surgery* 2005 Jul; 138(1):8-13

[35] Eom BW, Jang YJ, Lee SE, Han HS, Yoon YS, Kim SW. Clinical outcomes compared between laparoscopic and open distal pancreatectomy. *Surg Endosc* 2008 May; 22(5):1334-1338

[36] Matsumoto T, Shibata K, Ohta M, Iwaki K, Uchida H, Yada K, Mori M, Kitano S. Laparoscopic distal pancreatectomy and open distal pancreatectomy: a nonrandomized comparative study. *Surg Laparosc Endosc Percutan Tech* 2008 Aug; 18(4):340-343

[37] Graziano G, e al (2016). Early Epithelial Ovarian Carcinoma Treatment (IF 2.995). *INTERNATIONAL JOURNAL OF NEW TECHNOLOGY AND RESEARCH*, vol. 2, p. 69-74, ISSN: 2454-4116

[38] Graziano G, e al (2016). On Traumatic Lesions of The Pancreas (IF 2.09). *WORLD JOURNAL OF RESEARCH AND REVIEW*, vol. 2,

p. 24-28, ISSN: 2455-3956

- [39] Assalia A, Gagner M. Laparoscopic pancreatic surgery for islet cell tumors of the pancreas. *World J Surg* 2004; 28:1239-1247
- [40] Graziano G, et al (2015). The Neuroendocrine Cancer. Personal Comments and Operational Remarks. *JOURNAL OF SURGERY AND SURGICAL RESEARCH*, vol. 1, p. 53-58, doi: DOI: 10.17352/2455-2968.000014
- [41] GRAZIANO G, et al (2017). ROLE OF GENETIC MUTATIONS IN THE DIAGNOSIS OF GALLBLADDER NEOPLASMS . *INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH*, vol. 8, p. 20908-20913, DOI: <http://dx.doi.org/10.24327/ijrsr.2017.0810.0982>
- [42] GRAZIANO G, et al (2017). THE USE OF BAR IN COLORECTAL SURGERY IN THE ELDERLY . *INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH*, vol. 8, p. 19950-19954, DOI: <http://dx.doi.org/10.24327/ijrsr.2017.0809.0793>
- [43] Graziano G, et al (2015). The Stent Evolution in Colo-Rectal Emergencies. *JOURNAL OF SURGERY AND SURGICAL RESEARCH*, vol. 1, p. 45-48, doi: 10.17352/2455-2968-000012
- [44] Giorgio Maria Paolo Graziano. et al 2016, Diagnostic and Therapeutic In the Intestinal Duplication. *Int J Recent Sci Res.* 7(8), pp.13000-13003.
- [45] Graziano Giorgio maria paolo et al Which Therapeutic Treatment in Gastric Lymphoma *World Journal of Research and Review (WJRR)* ISSN:2455-3956, Volume-2, Issue-6, June 2016 Pages 06-09
- [46] Giorgio Maria Paolo Graziano et al On Traumatic Lesions of The Pancreas *World Journal of Research and Review (WJRR)* ISSN:2455-3956, Volume-2, Issue-6, June 2016 Pages 24-28
- [47] Fernandez-Cruz L, Martinez I, et al . Laparoscopic distal pancreatectomy combined with preservation of spleen for cystic neoplasm of the pancreas. *J Gastrointest Surg* 2004 May-Jun; 8(4):493-501
- [48] Erturk SM, Mortelè KJ, Tuncali K, Saltzman JR, Lao R, Silverman SG. Fine-needle aspiration biopsy of solid masses: comparison of CT and Endoscopic sonography guidance. *AJR* 2005; 187:1531-1535
- [49] Volmar EK, Vollmer RT, Jowell PS, Nelson RC, Xie HB. Pancreatic FNA in 1000 cases: a comparison of imaging modalities. *Gastrointest Endosc* 2005; 61(7):854-861
- [50] Hartwig W, Scheneider L, Diener MK, Bergmann F, Büchler MW, Wernwer J. Preoperative tissue diagnosis for tumours of the pancreas. *British Journal of Surgery* 2009; 96:5-20
- [51] Zech CJ, Helmberger T, Wichmann MW, Holzknnecht N, Diebold J, Reiser M. Large core biopsy of the pancreas under CT fluoroscopy control: results and complications *Journal Computer Tomography* 2002; 26(5):743-749
- [52] Paulsen SD, Nghiem HV, Negussie E, Higgins EJ, Caoili EM, Francis IR. Evaluation of Imaging guided core biopsy of the pancreas. *AJR* 2006; 187:769-772
- [53] Li L, Liu LZ, Wu KL, Mo YX, Liu XW, Cui CY, Wan D. CT guided core needle biopsy in the diagnosis of pancreatic diseases with an automated biopsy gun. *J Vasc Intervent Radiol* 2008; 19:89-94
- [54] Bhatia P, Srinivasan R, et al. 5-year review and reappraisal of ultrasound-guided percutaneous transabdominal fine needle aspiration of pancreatic lesions. *Acta Cytol* 2008; 52(5):523-9
- [55] Brandt KR, Charboneau JW, Stephens DH, Welch TJ, Goellner JR. CT and US -guide biopsy of the pancreas. *Radiology* 1993; 187:99-104
- [56] Amin Z, Theis B, Russell RCG, House C, Novelli M, Lees WR. Diagnosing pancreatic cancer: the role of percutaneous biopsy and CT. *Clinical Radiology* 2006; 61:996-100