

AISP - 34th National Congress. Peschiera del Garda, VR (Italy). October 7-9, 2010

(The abstracts are published as submitted by the authors)

ORAL COMMUNICATIONS

Clinical and Morphological Aspects of Autoimmune Pancreatitis Associated with Ulcerative Colitis

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Context Ulcerative colitis (UC) is associated with type II AIP and low relapse rate has been described. **Objective** To evaluate aspects of patients suffering from AIP with (AIP-UC+) or without UC (AIP-UC-). **Methods** from our prospective AIP database, we selected 64 patients (44 males, 20 females; mean age 47±17 years) with a definitive diagnosis of AIP in the period 2003-2010, all in follow-up. Clinical findings at onset, clinical outcome, imaging, need for surgery, serum IgG4 levels were evaluated. **Results** Twelve out of 64 AIP patients (19%) had a histological diagnosis of UC (5 males and 7 females; mean age 30±12 years), 4 with focal and 8 with diffuse AIP. Table 1 shows the main features of AIP-UC- vs. AIP-UC+. Age at onset, sex, jaundice, biliary involvement, and serum IgG4 higher than 135 mg/dL were significantly different between the two groups at clinical onset. Surgery was performed only in AIP-UC- group, but the difference was not statistically significant. On the contrary, pancreatic relapses documented at instrumental

investigation (MR or CT) were similar in both groups. However, immune-suppressant drugs were used only in AIP-UC- group. **Conclusions** AIP associated with UC presents peculiar epidemiological and morphological aspects and seems to be a less aggressive form of AIP.

Table 1.

Variables	All AIP patients (n=64)	AIP-UC- (n=52)	AIP-UC+ (n=12)	P value
Sex (males)	69%	75%	42%	0.038
Age at onset (years)	47±17	51±15	30±12	<0.0001
Focal type	38 (59%)	34 (65%)	4 (33%)	0.055
Jaundice	35 (54%)	34 (65%)	1 (8%)	0.001
Serum IgG4 (>135 mg/dL)	29 (45%)	27 (52%)	2 (17%)	0.016
Biliary involvement	19 (30%)	19 (36%)	0	0.013
Steroid treatment	59 (92%)	47 (90%)	12 (100%)	NS
Surgery	10 (16%)	10 (19%)	0	NS
Pancreatic relapses	19 (30%)	16 (31%)	3 (25%)	NS
Immune-suppressant drug	12 (19%)	12 (23%)	0	NS

Pancreatoblastoma in an Adult Male with Recurrent Pancreatitis. A Case Report and Review of the Literature

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Context Pancreatoblastoma is an extremely rare neoplasm. It represents the most common pancreatic tumor in children (200 cases described in literature), but it is rare in the adult population, with only 21 reported cases. **Case report** A 44-year-old male, previously healthy, was referred to our Institute after several episodes of mild acute recurrent pancreatitis, with a negative MRI and CT scan. He was investigated through laboratory tests (cancer markers were normal,

and antibody set with ANA, ASMA and AMA was negative) and endoscopic ultrasonography, with the finding of a suspect invasive IPMN at pancreatic isthmus; cytology suggested the diagnosis of adenocarcinoma. A CT scan was repeated and the tumor appeared to be limited to the pancreas. The patient underwent laparoscopic left pancreatectomy with splenectomy; following postoperative course was normal. At the histological examination the pathologist

reported large representation of acinar structures, in association with squamoid-like cells, in a context of mixed exocrine-endocrine differentiation suggestive of a pancreatoblastoma diagnosis; an high proliferative index was described (Ki67: 20%) and the final TNM was pT3, pN0. **Conclusion** Pancreatoblastoma is a slow-growing tumor, more frequently symptomatic in adult patients, whose clinical manifestations appear mainly due to mass effect of the neoplasm and impairment of pancreatic exocrine function: abdominal pain, steatorrhea and weight loss. The differential diagnosis includes acinar adenocarcinoma, ductal adenocarcinoma, non-functioning endocrine pancreatic tumors and solid pseudopapillary tumor; however radiological findings are not really diriment in most

cases, and the percutaneously or endoscopically run FNAB is rarely diagnostic. The definitive histological examination of the specimen appears the only reliable way to make a correct diagnosis. The mean survival of this neoplasm in adult population is 18.5 months, with a 51-month maximal survival described. Among the reported cases, 26% had already metastatic disease at diagnosis and 43% died of the disease. According to literature radical resection offers the best results in long-term survival; the tumor has an evident metastatic potential, and according to some authors metastasis should be treated surgically. Medical therapy, performed until now on unresectable patients or on relapsed cases, generally gave weak results.

Autologous Pancreatic Islet Cell Transplantation for Improved Glycemic Control After Pancreatectomy

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Context In some patients candidates to pancreatic resections the removal of a normal portion of the gland is needed. These procedures may result in a type of insulin-dependent diabetes. Post-pancreatectomy diabetes is relatively difficult to control and requires the daily injection of exogenous insulin. **Objective** To assess the feasibility and the short-term efficacy of pancreatic islet autotransplantation (IAT) after total or extended pancreatectomy, when a healthy part of the gland must be removed for technical reasons. **Methods** From November 2008 to June 2010, 13 non diabetic patients underwent IAT. Indications were: 1) re-laparotomy with completion pancreatectomy because of pancreatic anastomosis leakage after pancreaticoduodenectomy (PD) (6 patients); 2) removal of the distal pancreas to avoid a high-risk pancreatic anastomosis (6 patients: 4 patients candidates to PD, 2 patients to median pancreatectomy); 3) subtotal pancreatectomy for chronic pancreatitis (1 patient). A frozen section examination of the resection margin was obtained before isolation and microbiological analyses were performed as well. The isolation of the endocrine component was obtained with standard procedure. IAT was carried out during the same day of operation in two cases, the other 11 patients underwent IAT within

24 h. The islet cells were transplanted into the liver (portal infusion) in 10 patients and in the bone marrow (iliac crest) in 3 patients. **Results** Normalized to weight of pancreatic tissue processed, we isolated $2,823 \pm 1,547$ islet (IEQ)/gram and transplanted $2,314 \pm 1,300$ IEQ/kg body weight. Two patients had IAT-related complications: 1 portal vein thrombosis, 1 partial thrombosis of the left portal branch; both were treated successfully with anticoagulant therapy. A patient undergoing completion pancreatectomy died for surgical complications unrelated to IAT. All patients showed positive basal and stimulated C-peptide levels. At present, 6/12 patients are insulin-free (range: 2-19 months): 3 cases of total pancreatectomy, 3 cases of subtotal pancreatectomy. Daily mean insulin requirement for the rest of the patients is 19.5 ± 5.7 UI. The current mean glycated hemoglobin value in all patients is $6.23 \pm 0.54\%$. In patients who underwent total pancreatectomy no episodes of symptomatic hypoglycemia were recorded. **Conclusions** Islet autotransplantation may become a common procedure to be offered to pancreatic surgery patients. It improves glycemic control in patients who undergo extended pancreatectomy, when a part of non-neoplastic parenchyma is removed.

Preoperative F-18 Fluorodeoxyglucose-Positron Emission Tomography Predicts Survival After Pancreatic Cancer Resection

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Context The identification of prognostic factors useful in selecting patients with pancreatic cancer who will benefit from surgery or other treatments, is still debating. Preliminary reports showed that 18-fluorodeoxyglucose positron emission tomography (18-FDG PET) was predictive of prognosis in patients resected on for pancreatic adenocarcinoma [1].

Objective The aim of this study is to evaluate the role of 18-FDG PET as a prognostic factor for patients who underwent resection for pancreatic cancer. **Methods** From January 2003 to July 2009, a total of 90 patients who underwent resection for pancreatic cancer, were examined with 18-FDG PET (with CT acquisition) in their preoperative work-up. The standardized uptake value (SUV) of 18-FDG was calculated and the patients were divided into high (>3.8) and low (≤3.8) SUV groups. They were also evaluated according to the tumor node metastases, stage (TNM), tumor grade and radicality of resection. **Results** Forty-six cancers showed low and 44 high SUVs. Disease free survival (DFS) was significantly influenced by tumor stage (P=0.009), nodes status (P=0.03), radicality of resection (P=0.01), SUV (P=0.02) and grading (P=0.0004). Multivariate analysis showed that only

grading (P=0.01) and radicality (P=0.02) were independent predictors of DFS. Overall survival was significantly influenced by node status (P=0.02), radicality of resection (P=0.007), stage and SUV (P=0.002) and grading (P=0.0001). Multivariate analysis showed that grading (P=0.009), stage and radicality (P=0.01) were independent predictors of survival. When patients analyzed for SUV were stratified according to stage, FDG uptake was related to DFS (P=0.02) and overall survival (P=0.001) in tumor's stage I-II. In these patients, multivariate analysis confirmed that SUV was independent predictor of survival. **Conclusion** This study confirms that tumor grading is the strongest independent factor influencing disease-free and overall survival after resection for pancreatic cancer. The SUV, calculated with 18-FDG PET, is an important prognostic parameter in stage I-II pancreatic carcinoma and may be useful in selecting patients for neo-adjuvant therapy.

Reference

1. Sperti C, Pasquali C, Chierichetti F, Ferronato A, Decet G, Pedrazzoli S. 18-Fluorodeoxyglucose positron emission tomography in predicting survival of patients with pancreatic carcinoma. J Gastrointest Surg 2003; 7:953-9. [PMID 14675704]

Alimentary Residuals in Pancreatic Ductal System in Surgery Specimens. Report of Two Cases After Pancreatic Endoscopic Stenting

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Context Transient ductal damages are reported after insertion of pancreatic stent positioned for different reasons especially in patients with "normal" pancreas. In literature no reports had shown the presence of alimentary fibres in ductal pancreatic system after pancreatic stenting. We reported here two cases of severe inflammation due to alimentary fibres detected in surgical specimens after pancreatic stenting. The role of fibre residuals are discussed in the genesis of pancreatic inflammation and ductal damages. **Case report** Case#1: A 60-year-old male underwent endoscopic drainage for obstructive jaundice caused by suspected papilla tumor, diagnosed by MRI. A biliary (11.5 Fr, 5 cm) and a pancreatic stent (10 Fr, 5 cm) were inserted to drain the opacified biliary and

pancreatic ducts. A duodeno-cephalo-pancreatectomy (DCP) pylorus-preserving was performed with complications. Histological examination of surgical specimen showed a poor differentiated pancreatic adenocarcinoma. A severe abscessual inflammation of pancreatic tissue around the pancreatic duct associated with fibre residuals and pancreatic stent was observed.

Case#2: A 69-year-old male underwent ERCP with insertion of a biliary stent for obstructive jaundice in another hospital with a new diagnosis of chronic pancreatitis. After 2 months a new CT showed a 2.5 cm mass in the head of the pancreas, missed at the first CT. In our hospital a new ERCP was performed showing a double duct sign. Intraductal biliary biopsies were positive for neoplasia; a biliary (10 Fr, 5 cm) and a

pancreatic stents (7 Fr, 5 cm) were inserted to drain the opacified ducts. The histological examination after pylorus preserving DCP confirmed pancreatic adenocarcinoma and showed a severe abscessual inflammation of pancreatic tissue associated with fibre residuals and pancreatic stent. **Conclusion** Pancreatic duct stent-induced ductal injuries are reported in literature. Precise risk factors for this complication have not been clearly defined. Characteristics of stents

like flange, diameter similar to pancreatic duct, occlusion of side branch or tearing of the pancreatic ductal mucosa during insertion could explain the reported ductal abnormalities. In patients who underwent stenting of main pancreatic duct, abscessual periductal inflammation of pancreatic parenchyma associated with alimentary fibres in pancreatic ductal system could be another cause of stent-induced pancreatic ductal injuries.

Circulating Tumor Cells in Resectable Pancreatic Cancer

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Context Pancreatic adenocarcinoma has a really poor prognosis even in resected patients. Nowadays, no markers have been found to predict such an awful trend before surgery. Circulating tumor cells (CTCs) represent a new attractive frontier in oncological decision making. **Objective** To investigate the presence of CTCs in systemic and portal circulation, and if they could represent a reliable marker of relapse in patients undergoing pancreatic resection for malignancy. **Methods** We enrolled 20 patients (from February 2009 to January 2010) undergoing pancreaticoduodenectomy, distal pancreatectomy or total pancreatectomy for malignancy. Ten mL blood samples were collected intraoperatively both from systemic and portal circulation (PC) at the same time. Blood sample were analyzed for CTCs with J&J Veridex CellSearch® within 72 hours from collection. We started a strict follow-up 1 month after surgery, using CT and/or PET scan once every 3 months, and we have collected 12-month data for the first 11 patients. **Results** We found CTCs in 9 patients: 3

patients had cells both in portal circulation (PC) and in systemic circulation (SC); 1 patient had cells only in SC; 5 patients had cells only in PC. In CTCs positive group, 1 patient died 3 weeks after surgery due to surgical complications, 1 patient had peritoneal, liver and local relapse after 13 months and died 1 month later, while the other 4 patients are still cancer-free. In CTCs negative group, 1 patient had peritoneal, liver and local relapse after 3 months from surgery and died soon after, 1 patient had lymphatic, liver and peritoneal relapse after 5 months and died 2 months later, 1 patient had lung and pleural relapse after 8 months and died 6 months later, while 2 patients are cancer-free so far. **Conclusion** We found an extremely high frequency of CTCs (45%) in patients with non-systemic disease. However, preliminary results show that there is little correlation between presence and number of CTCs, and postoperative pattern of relapse in patient undergoing pancreatic resection for malignancy.

Endoscopic Management of Pseudocysts Following Resection for Pancreatic Neoplasia Is a Suitable Technique. Our Results with Long-Term Follow-up

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Context Data regarding the treatment of post surgical pancreatic pseudocysts (PP) are lacking in the English literature. **Objective** To contribute to the assessment of safety and efficacy of endoscopic treatment of PP in patients who underwent pancreatic surgery for neoplasm. **Methods** Between January 1999 to June 2008, 25 patients were included in this study. All

clinical charts regarding patients were retrospectively reviewed. We also compared the results with those obtained in 30 patients endoscopically treated for post inflammatory PP in the same period (acute severe pancreatitis in 28 patients and chronic pancreatitis in 2). **Results** During follow-up (median 34 months) the success rate of the endoscopic treatment was mildly

higher in the post surgical group (84%) than in the post inflammatory one (73%). In 4 patients of the post-surgical group the procedure was unsuccessful. One percutaneous drainage, one laparotomy to remove an infected PP, one laparotomy for gastric bleeding and one further endoscopic drainage were needed, respectively. The procedure was not successful in 8 cases of the post-inflammatory group; in 6 cases surgical intervention was needed. One patient died of

severe hemorrhage from a false pseudo aneurysm of the gastroduodenal artery. In other 6 patients PP recurrence occurred and a second endoscopic treatment was needed in 5 cases with definitive successful outcome. **Conclusion** Endoscopic treatment of pseudocysts following resection for pancreatic neoplasm is a safe and efficient technique, associated to low complication and high success rate.

Riedel's Lobe of the Liver Mimicking a Malignant Pancreatic Mass. Case Report

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Context Riedel's lobe is a rare anatomical variation which consists in an abnormal extension of the caudate lobe. In literature only few cases are described, especially mimicking right renal or adrenal mass. Most cases are detected during pediatric age and are associated with other malformation like diaphragmatic hernias. **Case report** We report a case of a 57-year-old man admitted to our Department for occasional finding of a solid pancreatic head mass. The patient was totally asymptomatic excepting for vague abdominal discomfort. Ultrasound showed a 3 cm pancreatic head mass with no dilation of the pancreatic duct. The mass

was adherent to superior mesenteric vein. The patient underwent MRCP, which showed the presence of an accessory hepatic lobe (Riedel's lobe) mimicking a pancreatic head mass. **Conclusions** The finding of a huge pancreatic head mass without cancer-related signs or symptoms (pain, weight loss, jaundice) may lead to diagnostic errors. In case of unusual upper abdominal right side masses and of disagreement between clinical and radiological findings, additional rare diagnostic options (such as Riedel's lobe), have to be taken into account.

Usefulness of Dindo-Clavien Classification After Pancreaticoduodenectomy

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Context There is a lack of a unified grading system for severity of complications after pancreaticoduodenectomy (PD). **Objective** To evaluate the usefulness of Dindo-Clavien classification (DCC) in patients who underwent PD. **Methods** From January 2006 to June 2010, data such as sex, age, co-morbidities, ASA, type of resection, pathological diagnosis, morbidity and mortality were prospectively collected from 85 consecutive PD. All complicated patients were classified according to DCC and each grade was compared with the length of postoperative stay and the rate of the most important complications. Analysis was carried out with multi-way ANOVA test with simple and repeat contrast analysis. The linear-by-linear chi squared and Spearman rank tests were used when appropriate. **Results** Mean age of patients was 66.3±10.2 years. There were 34 (40%) females and 51

(60%) males. One or more co-morbidities were present in 58 (68.2%) patients; 19 (22.4%) patients were ASA 2, 58 (67.1%) ASA 3 and 9 (10.6%) ASA 4. An extended resection was carried out in 8 (9.4%) cases. Malignant disease was present in 74 (87.1%) cases. Twenty-eight (32.9%) patients had no complications and 57 (67.1%) resulted complicated. Four (4.7%) patients had grade I, 34 (40%) grade II, 7 (8.3%) grade III, 8 (9.4%) grade IV and 4 (4.7%) grade V. Rate of pancreatic fistula (POPF), postoperative pancreatic haemorrhage (PPH), and delayed gastric emptying (DGE) were 30.6%, 36.5% and 17.6%, respectively. There was a significant progressive increase in length of postoperative stay from patients without complications to those with grade 4 (in patients with grade II, III, IV, P=0.011, P<0.001, and P<0.001, respectively). Comparing different grades, mean

postoperative stay was significantly different between grade II and III ($P<0.001$), whereas between patients with grade III and IV we did not find any significant difference ($P=0.318$). The rate of POPF, PPH and DGE was related to DCC ($P=0.046$, $P=0.006$, and $P=0.040$, respectively). The severity of POPF and PPH was

related to DCC ($P=0.004$ and $P=0.003$). **Conclusion** DCC appears a reproducible classification system in patients who underwent PD. It allows distinguishing a normal postoperative course from any deviation and the severity of complications.

Use of ISGPS Definition of Delayed Gastric Emptying in a Middle-High Volume Center for Pancreatic Resections

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Context Delayed gastric emptying (DGE) is one of the most common complications after pancreaticoduodenectomy (PD) and it has been reported in about 20-60% of PD patients. Recently, the International Study Group of Pancreatic Surgery (ISGPS) has proposed an objective definition of DGE, based on the duration of nasogastric intubation and the postoperative day (POD) of solid food intake. Three different grades (A, B, C) were defined. **Objective** To determine the incidence of DGE in patients undergoing PD for pancreatic adenocarcinoma in a middle-high volume surgery department and to compare the rate of postoperative complications (pancreatic fistula, intra-abdominal abscess), postoperative hospital stay and need of postoperative intensive care for more than 2 days, among patients with or without DGE. **Methods** All patients that underwent PD for pancreatic adenocarcinoma from January 2003 to December 2009 were reviewed. DGE was evaluated according to the ISGPS definitions. Patients' complications, hospital stay and need of intensive care were determined

retrospectively from our database. Our policy was to take out the nasogastric tube in third POD and to restart oral food intake in fourth POD. **Results** Patients with available complete data were 56. The overall DGE incidence was 58%: 24 patients were grade A (42%), 5 grade B (8.9%) and 4 grade C (7.1%). Furthermore, patients with DGE had significantly higher rates of postoperative complications (48% vs. 4.3%), longer postoperative hospital stay (22 vs. 14 days) and more frequent need of prolonged intensive care (18% vs. 8.5%). Among patients with complications, overall DGE incidence resulted to be 94%, while among patients without complications it was 43%. **Conclusions** Our results show that the proposed ISGPS definition of DGE seems to be applicable in the clinical practice of a middle-high volume center for pancreatic resection. Notwithstanding, this new definition does not allow a distinction between primary DGE from DGE due to other surgery-related complications, such as pancreatic fistula and intra-abdominal abscess.

Robotic Pancreatectomies.

A Single Institution Preliminary Experience

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Context The "Da Vinci Surgical System" (DSS) is a promising minimally invasive technique in pancreatic surgery. Today few data are available on literature on it. **Objective** To analyze the short-term results of robotic pancreatectomies (RP). **Methods** From October 2008 to May 2010, 38 robotic pancreatectomies were performed at our institution. There were 11 males (28.9%) and 27 females (71.1%). The mean age was 59.4 years (range: 24-80 years). The mean BMI was 24.6 kg/m². Nineteen patients (50%) received a previous abdominal surgery. Fourteen patients (36.8%) underwent pancreaticoduodenectomy, 1 (2.6%) total pancreatectomy, 17 (44.8%) distal pancreatectomy, 3

(7.9%) central pancreatectomy, 3 (7.9%) enucleation. **Results** A histological diagnosis of cystic tumor of the pancreas was found in 22 cases (57.8%), periampullary tumor in 6 (15.8%), neuroendocrine tumor in 5 (13.2%), ductal adenocarcinoma in 2 (5.3%), Frantz tumors in 2 (5.3%), and chronic pancreatitis in 1 (2.6%). There were no postoperative deaths. Twenty patients (52.6%) developed postoperative complications including 16 cases (43.2%) of pancreatic fistula. Only one patient (2.6%) required a re-laparotomy. The mean postoperative stay was 14.4 days (range: 6-37 days). The postoperative stay was significantly shorter in patients with an uneventful post

operative course (9.8 days) on respect to patients with complications (17.4 days) ($P=0.0042$). **Conclusions** From our preliminary results robotic pancreatectomy

seems to be safe and feasible. Potential advantages, indications and impact on the quality of life should be evaluated in larger prospective randomized trials.

Medium-Term Outcome of Endotherapy for Pancreas Divisum in Patients with Acute Recurrent Pancreatitis

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Context Pancreas divisum (PD) is the most common congenital variant of pancreatic ductal development occurring in approximately 6% of general population, but it was more common (up to 25%) in patients with acute recurrent pancreatitis (ARP). In these patients, the role of the endoscopic therapy for preventing the recurrences of the disease and the development of endoscopic signs of chronic pancreatitis (CP) is still debated. **Objective** To investigate the recurrence of AP and signs of CP in patients with PD and ARP submitted to endoscopic minor papilla therapy. **Methods** Between 2005 and 2008 all patients evaluated in our division for ARP and PD were enrolled into the study. PD was diagnosed by MRCP (with or without secretin). Patients with ARP and other known causes or signs of CP were excluded. Patients with relapses in the year before the time of enrolment were submitted to endoscopic therapy, those free of recurrences were conservatively managed except in case of relapses during follow-up. Endoscopic therapy was performed with minor papilla sphincterotomy with a temporary 5 or 7 Fr stent. A successful ERCP was defined as the absence of a further recurrence after endoscopic therapy. In all patients, the development of CP during follow-up was investigated by repeated EUS (one per year). The diagnosis of CP was established when a total of 4 or more EUS pancreatic abnormalities were detected (Wiersema criteria). Fisher exact and t

tests were performed for comparisons of proportions and continuous variables, respectively. **Results** Thirty-four patients with ARP and PD were studied: 24 females and 10 males with a mean age of 51.8 years (range: 26-69 years). 20 patients were submitted to endoscopic therapy and 14 conservatively managed. ERCPs were successful in 14/20 patients (70%): the first section in 8/20 (40%), the second in 13/20 (65%), the third in 14/20. The median follow-up time in the group of treated and untreated patients was not significantly different. One patient with unsuccessful ERCP was lost during follow-up. CP was diagnosed in overall 19/33 patients (60.6%): 11/19 (57.9%) treated and in 8/14 (57.1%) untreated patients (P NS). In the group of treated patients, CP development was significantly lower in those submitted to successful (6/14, 42.8%) than unsuccessful ERCPs (5/5, 100%) ($P=0.04$). **Conclusions** Minor papilla endotherapy can be effective for reducing relapses in patients with pancreas divisum and recent episodes of acute recurrent pancreatitis. In these patients, when effective, endotherapy can prevent the progression to chronic pancreatitis with a similar rate of those observed in patients without recent episodes of pancreatitis. When endotherapy for pancreas divisum is not effective, an accurate and complete etiological investigation should be recommended.

Contrast-Enhanced Ultrasound of Focal Pancreatic Lesions. A Multicenter Study (PAMUS: Pancreatic Multicenter US Study)

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Objective The aim of this multicenter study was to describe the typical contrast-enhanced ultrasound

(CEUS) pattern of pancreatic lesions and to evaluate the diagnostic accuracy of CEUS in the

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characterization of the most common focal pancreatic lesions. **Methods** From 2003 to 2008, all US and CEUS examinations of focal pancreatic masses performed in six centers were reviewed. Inclusion criteria were: focal pancreatic mass pathologically proved, visible at ultrasound (US) and studied with CEUS. All lesions were then evaluated for size, echo-structure and enhancement pattern. Sensitivity, specificity, positive and negative predictive values with 95% CIs were calculated to define diagnostic accuracy of CEUS in respect to pathology. Diagnostic confidence of US and CEUS, discerning between benignancy and malignancy, were represented by using receiver operating characteristics (ROC) curves. Agreement was evaluated by means of kappa statistics.

Results One-thousand and 439 pancreatic lesions were included. At CEUS the lesions were divided into solid (89%) and cystic (12%) masses and classified into six and eight categories, respectively. Among the solid lesions, the adenocarcinoma was characterized with an accuracy of 87.8%. Among the cystic lesions, the cystic tumor was diagnosed with an accuracy of 97.1%. The area under the ROC curve increased from 0.637 for US to 0.877 for CEUS ($P<0.0001$). Inter-observer agreement was slightly higher for solid ($\kappa=0.78$) than cystic ($\kappa=0.62$) lesions. In none of the centers side effects were reported. **Conclusions** CEUS is accurate in the characterization of pancreatic lesions. CEUS should be considered as a complementary imaging method for pancreatic lesions characterization.

Serum Biomarkers of Pancreatic Cancer (PC) and Pancreatic Cancer Derived Diabetes Mellitus (DM)

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Objective To verify whether discontinuous SDS-PAGE, performed in the conditions which allowed the isolation of NT-S100A8 from PC tissues, can identify potential serum markers of PC and PC induced DM. **Methods** We collected sera from 42 PC patients (17 with and 25 without DM) and from 11 healthy controls (C). **Results** In the low MW range (15,000-1,000 Da), nine protein bands were identified and numbered 1 to 9 from heaviest to lightest. Only band number 2 (14,200 Da approximately) was correlated with PC diagnosis, being present in 10/11 C and absent in 37/42 cancer cases ($\chi^2=26.8$, $P<0.001$). Two bands, 4 and 9, MW 10,000 and 1,000 Da respectively, correlated with each other ($\chi^2=4.8$, $P<0.05$). In PC, the absence of both bands correlated with the presence of DM ($\chi^2=8.6$, $P<0.01$ for band 4 and $\chi^2=6.6$, $P<0.05$ for band 9) and was significantly associated with higher fasting plasma glucose levels ($P<0.05$ for band 4 and $P<0.01$ for band 9). The absence of band 9 was also significantly associated with HbA_{1c} ($P<0.05$) and with glucose/C-peptide ratio ($P<0.05$). To characterize the protein inversely correlated with PC diagnosis, we performed a MALDI-TOF analysis of the tryptic in-gel digestion of band 2. The identified peaks were analyzed by Mascot Peptide Mass Fingerprint and showed a high homology with human hemoglobin subunit b (score 76, $P<0.05$). **Conclusion** SDS-PAGE analysis of the low MW serum proteins allowed the detection of peptides correlated with PC derived DM and the identification of free beta globin as a potential PC serum marker.

Radiofrequency Ablation of Stage III Pancreatic Cancer Does not Lead to Peritoneal Seeding. Our Experience

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Context Radiofrequency ablation (RFA) has been recently applied to stage III pancreatic cancer. We recently demonstrated its feasibility and safety. RFA is an invasive procedure where a needle is placed into a tumor with the potential risk of tumor seeding.

Objective The aim of the study is to analyze the possibility of peritoneal cancer cell seeding during the procedure. **Results** Between February 2007 and April 2010, 125 patients with stage III pancreatic cancer underwent RFA. From April 2009 to November 2009

13 consecutive patients were investigated for the aim of this study. Male/female ratio was 12/1 with a median age of 55 years. Tumor was located in the head-uncinate process in 10 patients and in the body-tail in 3 patients. All patients underwent preoperative CT scan or MRCP and US guided biopsy to confirm diagnosis and staging. The procedure was performed by introducing the needle under US guide and withdrawing it performing a correct thermal track

ablation. We perform peritoneal lavage before and after the procedure and cytological analysis of the peritoneal fluid was done by an expert pathologist. No neoplastic cells were detected in peritoneal fluid before and after RFA. **Conclusions** RFA is a safe and feasible procedure which does not lead to peritoneal cancer cell seeding. Further studies that show the impact of RFA on survival are being developed.

Loss of Heterozygosity (LOH) Status of D9S105 Marker Is Associated with Down-Regulation of Kruppel-Like Factor 4 (KLF4) Expression in Pancreatic Ductal Adenocarcinoma and PanINs

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Context Homozygosity suppression of Kruppel-like factor 4 (KLF4) placing this gene as putative tumor suppressor gene in gastric, bladder and colorectal cancer. Experimental data suggest that KLF4 may be over-expressed or down-regulated in pancreatic ductal adenocarcinoma (PDAC) and its role in this pathology is unclear. **Objective** This study was aimed at evaluating the association between loss of 9q31-32 region and gene expression of KLF4 in PDAC. **Methods** We investigated the loss of heterozygosity (LOH) in the 9q region and the expression of KLF4 gene in 35 PDAC, 6 PanINs, 6 normal ducts and 4 primary cell culture of PDAC (PCC). Epithelial cells were isolated by laser microdissection. We used 4 microsatellite markers (D9S127, D9S53, D9S105, D9S106) flanking KLF4 locus, while mRNA gene

expression was performed by RT-PCR. **Results** In 46.9% of PDAC and 83.3% of PanIN lesions there was a loss of the D9S105 marker, which resulted to be the most deleted marker. The PCC wild-type for D9S105 marker had mutated in K-ras gene at codon 12 and expressed KLF4. Lack of KLF4 expression was found to be significantly associated with: 1) genomic deletion flanking KLF4 in PDAC (P=0.018) and in PanINs (P<0.01); 2) LOH of D9S105 marker (P=0.014); 3) presence of low-grade of PDAC-associated PanIN (P=0.021). We identified a relation between D9S105 deletion and loss of KLF4 expression in PDAC. **Conclusion** Our results suggested that the KLF4 gene can switch its role between tumor suppressor gene and oncogene depending on the biological context of PDAC.

Duplication and Protein Expression of PMP22 Gene in Pancreatic Ductal Adenocarcinoma. Association with Charcot-Marie-Tooth 1A (CMT1A) Syndrome?

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Context The peripheral myelin protein 22 (PMP22) gene is usually expressed in nervous systems, but both PMP22 mRNA and protein expression have been also

observed in pancreatic ductal adenocarcinoma (PDAC) tissues. DNA amplification of 17p11.2-12 region related to Charcot-Marie-Tooth 1A syndrome

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(CMT1A) is associated with a duplication of PMP22 gene. Some authors observed this genetic condition in different tumor types such as osteosarcoma, glioma and glioblastoma, but no data are available on PDAC.

Objective To evaluate the presence of CMT1A-like genomic condition associated with a duplication of PMP22 gene in PDAC patients. **Methods** We analyzed 16 PDAC frozen tissues and 3 primary pancreatic tumor cell cultures (PPTCCs). We used as positive controls 3 patients affected by CMT1A neuropathy and we used 3 normal subjects (genetically unaffected) as negative controls. DNA extraction was performed in all 21 cases by standard procedure. The duplication of 17p11.2-12 region related to CMT1A syndrome, was evaluated by PCR reaction and digestion by two endonucleases (EcoRI and NsiI). We also evaluated DNA amplification in blood samples from PDAC cases and the protein expression in both tissues and cell cultures by immunohistochemistry scoring (range: 0 absent, 1 low, 2 middle, and 3 high). **Results** The

positive cases (CMT1A patients) harbored a 1.7 Kbp specific DNA fragment. This alteration was not present in the negative controls. However, the specific DNA fragment associated with a duplication CMT1A-like was observed in 44% (7/13) PDAC patients and 2 out of the 3 PPTCCs. All amplified PDAC samples and PPTCCs (9/9) showed a 2.1 Kbp additional fragment while no DNA amplification was detectable in blood samples. PDAC amplified samples showed high score of PMP22 protein expression with respect to non amplified samples ($P=0.0262$). **Conclusion** This is the first study showing that the genetic alteration of CMT1A syndrome is also detectable in PDAC tissues and cells. No CMT1A amplification was observed in the correlative blood samples, excluding the association between CMT1A and PDAC. PMP22 protein is involved in cellular growth and further studies are warranted in order to understand its role in PDAC.

Involvement of Bile Duct in Autoimmune Pancreatitis. ERCP Verona Experience

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Context Autoimmune pancreatitis (AIP) is a rare pancreatic disease with an incidence of 0.71/100,000 people in Japan. There are two morphological form of AIP: a diffuse form, characterized by an enlargement of the entire pancreatic gland, and a focal one, characterized by focal enlargement of the pancreas, sometimes mimicking pancreatic tumor. Jaundice is the major symptom at onset reported in 44-54% of patients. Two are the reasons for jaundice: edema of pancreatic gland and the IgG4 sclerosing cholangitis associated with AIP (IAC). This is an extrapancreatic manifestation of AIP characterized by infiltration of IgG4-plasmacells within and around bile ducts that caused stenosis in biliary tree, both intra- and extra-pancreatic. Biliary strictures can be isolated or involve non-contiguous segment of bile duct. Frequency of IAC differed greatly (17-98%) among different experiences reported. We report here our experience in patients with AIP diagnosed in our Department from 1993 to 2010. **Patients** One-hundred and nine patients with AIP were diagnosed. 54 (49.5%) presented jaundice as initial symptom. Seventeen patients (11 males, 6 females; mean age 49.9 years, range: 26-72 years; 10 focal forms) underwent ERCP. Three patients

suffered from ulcerative colitis and 2 from Sjogren syndrome. Four out of 11 (36.4%) presented an elevated IgG4 serum level (>135 mg/dL). **Results** Only in 2 cases (2/17, 11.7%) intrahepatic stenosis were diagnosed. Six patients underwent duodenocephalo-pancreatectomy for the suspect of pancreatic cancer ($n=5$) or cholangiocarcinoma ($n=1$). Two of these patients with intrahepatic strictures suffered from cholangitis after surgery, disappeared after introduction of steroid/immunosuppressive therapy. Two patients underwent hepaticojejunum anastomosis. Nine patients were treated only endoscopically with stent insertion and do not present relapse of biliary stricture after a mean follow-up of 5.4 years (range: 6 months to 16 years). Mean duration of stent treatment was 6.4 months (range: 2 weeks to 19 months). **Conclusions** AIP is a difficult diagnosis especially when patients presented with jaundice. With the introduction of CP-RMN endoscopic drainage should be limited to patients affected by AIP with dominant bile duct stricture with high level of bilirubin or in jaundice patients who necessitate further work-up to clarify the correct diagnosis. Patients with multiple intrahepatic strictures must be treated with medical therapy.

Total Pancreatectomy for Distal Bile Duct Cancer Complicated by Post-ERCP Infected Acute Pancreatitis

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Context A young man affected by malignant common bile duct neoplasm and suffering from severe acute pancreatitis post-ERCP. **Case report** In March 2010 a 50-year-old male patient affected by ischemic cardiac disease, diabetes and antecedent laparoscopic cholecystectomy presented with jaundice. He underwent at a peripheral hospital US abdomen and CECT that demonstrated dilatation of the biliary tree, common bile duct diameter 1.4 centimeter without a focal mass; ERCP evidenced a 2 cm long distal stricture of the common bile duct, the brushing was positive for adenocarcinoma; a plastic biliary stent was inserted. The patient developed a post-ERCP necrotic acute pancreatitis. He was discharged in acceptable clinical condition, waiting for recovery of pancreatitis and pancreaticoduodenectomy at our center. One month later he developed epigastric pain, early satiety, weight loss and fever. A CECT showed progression of pancreatic necrosis to multiple fluid collections. A FNA revealed infection by Gram negative bacteria. A

laparotomy was then performed: an infected necrotic pancreatitis involving the body-tail of the pancreas but sparing the head was found; a total pancreatectomy to treat both the distal bile duct cancer and the infected pancreatitis was done. The procedure was highly demanding (13 h, 4,500 mL blood loss) but technically successful. The postoperative period was initially characterized by sepsis and presence of infected fluid from abdominal drainages; clinical pictures then improved and the patient was discharged 22 days after surgery. The histology revealed adenocarcinoma of the common bile duct, pT3 G3 pN1. Three months after surgery the patient is in good clinical condition and he is receiving adjuvant systemic chemotherapy. **Conclusion** Preoperative endoscopic biliary stenting can sometimes impairs surgical treatment of periampullary neoplasm. In this situation total pancreatectomy can represent a possible high demanding solution.

Resection After Radiofrequency Ablation of Stage III Pancreatic Cancer

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Context Stage III pancreatic cancer (PC) is a very aggressive entity and the results of chemo and/or radiotherapy are so far disappointing. Experiences of radiofrequency ablation (RFA) in pancreatic cancer are very limited and the specific effects on PC tissue are still unknown. **Objective** We report our findings on resected PC specimens after chemo-radiotherapy and RFA. **Methods** Only patients with histologically proven stage III PC were consecutively treated with RFA and followed by different association of chemo-radiotherapy. Follow-up (consisting in clinical examination, abdominal CT scan and serum CA 19-9) was planned at 1, 3, 6 and 12 months. **Results** Between February 2007 and April 2010, 125 patients with stage III PC underwent RFA. Five patients underwent radical resection after combined treatment of RFA+CT-RT. Male/female ratio was 3/2 with a median age of 67 years. Tumor was located in the head or uncinate process in 4 patients and in body-tail in 1 patient. Two patients underwent resection because of complications occurred after RFA: one patient because of duodenal necrosis and the other for duodenal bleeding. The first

received CT-RT after resection, the second underwent CT-RT before RFA. In 3 patients resection was performed for downstaging after combined treatment of RFA and CT-RT. Two patients received RFA as up front treatment, the other underwent RFA because of stable disease after CT neoadjuvant. All patients received CT-RT after RFA. Histopathology shows the presence of different degrees of fibrosis (related to different timing of resections) with some isolated neoplastic aggregate. In one case no residual tumor was found at histopathology. Two patients are alive without progression at 21 and 29 months, respectively. One patient is alive at 35 months with hepatic progression. Two patients died: one of progression after 28 months, one of cardiovascular accident after 15 months. **Conclusions** RFA in PC does not impair a radical resection and, in some cases, seems to provide an early downstaging. In our experience for the first time we were able to achieve an histological specimen of an ablated pancreatic tumor. The impact on survival and the histopathological effects of RFA are currently being studied.

MicroRNA-21. An Oncomir Under the Spotlight as a Potential Biomarker of Clinical Outcome and Determinant of Chemoresistance in Pancreatic Cancer

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Context MicroRNAs are noncoding RNAs with key role in control of cellular proliferation and apoptosis. Recent data showed that miRNAs affect cancer prognosis, and influence response to chemotherapy. In particular microRNA-21 (miR-21) was reported to be overexpressed and contribute to gemcitabine resistance in PDAC. **Objective** This study was aimed to evaluate whether miR-21 is associated with overall-survival (OS) of PDAC patients and provide mechanistic insights on its role in chemoresistance. **Methods** MiR-21 expression was evaluated in cells (7 PDAC cell lines, 7 primary cultures, and a normal ductal cell line) and tissues (specimens from 77 PDAC patients treated with gemcitabine and 5 normal ductal samples) isolated by laser-microdissection. The role of miR-21 on gemcitabine and 5-fluorouracil (5-FU) activity was studied with specific miR-21 precursor and inhibitors (pre-miR-21 and anti-miR-21). **Results** Patients with high miR-21 expression had significantly shorter OS both in the metastatic and in the adjuvant setting.

Multivariate analysis confirmed the prognostic significance of miR-21. MiR-21 expression in primary cultures correlated with expression with both gemcitabine and 5-fluorouracil resistance. Pre-miR-21 transfection significantly decreased gemcitabine antiproliferative and pro-apoptotic effects, while metalloproteinase-2/-9 and VEGF expression were up-regulated. The transfection with anti-miR-21 resulted in an increased activity of 5-FU. Similarly, the addition of inhibitors of PI3K and mTOR decreased phospho-Akt and prevented pre-miR-21 induced resistance to the pro-apoptotic effects of gemcitabine. **Conclusions** MiR-21 expression correlated with outcome in PDAC patients treated with gemcitabine, and with resistance toward both gemcitabine and 5-FU. Modulation of apoptosis, Akt phosphorylation, and expression of genes involved in invasive behavior, may contribute to miR-21 role in PDAC chemoresistance and to the rational development of targeted combinations.

NT-S100A8 Inhibits Insulin Release and Activates Akt and NF-KappaB Cell Signalling in Pancreatic Cancer (PC) Cells

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Objective To verify whether NT-S100A8, a peptide isolated from PC tissue of diabetic patients: 1) alters Akt and NF-kappa B signaling in PC cells; 2) interferes with insulin signaling; and 3) alters insulin response to glucose stimulation. **Methods** PC cell lines (BxPC3, Capan1, MiaPaCa2) remained unstimulated or were stimulated with 50 mU insulin for 10 minutes with/without 50 and 500 nM NT-S100A8 for 5, 10, 15 and 30 min. Immunoblots of the cell lysates were performed with pI-kappa B-alpha, pAkt (Ser⁴⁷³ and Thr³⁰⁸), Akt, pPDK1 (Ser²⁴¹), p-mTOR (Ser²⁴⁴⁸) and beta-actin antibodies. Beta-TC6 rat insulinoma cells

were left untreated or treated 30 min daily for one week with 50, 200 and 500 nM NT-S100A8 alone or with 20 mM glucose. Cells were then stimulated with 20 mM glucose and insulin was measured in the at 2, 3, 5, 10, 15 and 30 min. **Results** Both insulin and NT-S100A8 independently induced Akt Ser⁴⁷³ phosphorylation in BxPC3 and MiaPaCa2, not in Capan1. Akt Thr³⁰⁸ phosphorylation in all PC cell lines was induced by insulin, not by NT-S100A8. NT-S100A8 time and dose-dependently induced p-mTOR in BxPC3, but it did not induce pPDK1. To study NF-kappa B signaling we assessed the phosphorylation of

its cytoplasmic inhibitor I-kappa B-alpha. In all cell lines I-kappa B-alpha was constitutively phosphorylated. Insulin determined a significant reduction of pI-kappa B-alpha in Capan1 and MiaPaCa2 and an enhancement in BxPC3, effects not counteracted by NT-S100A8. In BxPC3 and Capan1, NT-S100A8 caused an increase in pI-kappa B-alpha after 5 min, followed by a reduction at 10 and 15 min and a recovery at 30 min. pI-kappa B-alpha in MiaPaCa2 cells was not modified. Glucose induced early (2 min) and late (15-30 min) insulin release in control beta-TC6 cells. The amount of insulin release

was progressively reduced when cells were stimulated with glucose for one week and almost completely abolished when glucose was given with NT-S100A8 (repeated measures analysis of variance: $P < 0.001$). **Conclusions** NT-S100A8 in PC cells induces Akt phosphorylation through mTOR signaling pathway not PDK1 pathway and it activates NF-kappa B signaling. These findings support for a role of NT-S100A8 in promoting PC cell survival. This peptide does not counteract insulin signaling, but its chronic exposure abolishes insulin response to glucose and this supports for its role as a diabetogenic factor.

Perioperative and Long-Term Results of Laparoscopic Spleen Preserving Distal Pancreatectomy with or Without Splenic Vessels Resection

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Context Distal pancreatectomy (DP) with splenectomy is the procedure of choice for tumors of the body-tail of the pancreas. Growing interest in the immunological role of the spleen led surgeons to avoid splenectomy during DP for benign tumors. Surgical techniques for spleen-preserving distal pancreatectomy (SPDP) include conservation of the splenic vessels (SPDP-SVP) as well as their resection with preservation of the short gastric vessels (SPDP-SVR). **Objective** To describe our experience with laparoscopic SPDP and to compare perioperative and long-term outcome of patients who underwent SPDP-SVP and SPDP-SVR. **Methods** We retrospectively analyzed demographic, pathology, surgical details and long-term outcomes of patients who underwent laparoscopic SPDP from January 1999 to December 2007 at our institution. Follow-up included a thorough medical examination, routine blood tests, and a contrast-enhanced CT-scan or a magnetic resonance imaging at one year from the index operation. Follow-up was stopped in October 2009. **Results** We performed 43 SPDP for benign tumors. Mortality was nil. Median operative time was 160 minutes (range: 75-310 min). The rate of

abdominal complications and of pancreatic fistula was 51.1% and 32.5%, respectively. SPDP-SVP were 36, SPDP-SVR were 7. No significant differences were observed between the two techniques as per demographic and surgical details. One patient in SPDP-SVR group required splenectomy on postoperative 10 for splenic infarction. In SPDP-SVP group 3 patients needed reoperation. In particular, a splenectomy for splenic infarction (on postoperative day 14) and two drainage operations for infected collections (both on postoperative day 15) were performed. Seventeen patients accepted the follow-up protocol (4 in SPDP-SVR and 13 in SPDP-SVP group). At 12 months, perigastric varices were found in 3 patients (75.0%) after SPDP-SVR and in 2 patients (15.3%) after SPDP-SVP ($P = 0.052$). No gastrointestinal bleeding was observed at a median follow-up of 44 months (range: 31-102 months). **Conclusion** SPDP is safe, either with SVP and SVR. However, a moderate risk of postoperative splenic infarction has to be taken into account. The formation of perigastric varices has to be interpreted as a paraphysiologic phenomenon after SVR.

Evaluation Of M-ANNHEIM Classification in an Italian Series of Patients Suffering from Chronic Pancreatitis

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Context M-ANNHEIM classification is the first attempt to correlate etiological, clinical, functional and

radiological findings in CP. **Objective** To evaluate M-ANNHEIM classification in a consecutive series of

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patients suffering from CP in Italy. **Methods** Patients with a definitive, probable or borderline diagnosis of CP in the period 2007-2010 were enrolled. Data on etiological, clinical, functional and radiological aspects were achieved, following criteria previously published. **Results** Three-hundreds and two patients (194 males, 108 females; mean age 48.3 ± 15.4 years) were enrolled. In 123 patients (41%) we found a single etiologic factor, 158 (52%) more than one and in 21 (7%) none. CP was definitive in 225 patients (75%), probable in 37 (12%) and borderline in 40 (13%). Frequency of male sex was higher in patients with definitive diagnosis of CP (70%), compared with those with probable (54%) or borderline (42%) diagnosis ($P=0.002$). Age at onset was different in patients with definitive (43 ± 16 years),

probable (39 ± 16 years) or borderline (36 ± 15 years) diagnosis of CP ($P=0.006$). Clinically, 51 patients (17%) were in stage 0, 131 (43%) in I, 75 (25%) in II, 39 (13%) in III, and 6 (2%) in IV. Disease duration was different in the 5 groups ($P<0.0001$). One-hundred and twenty-five patients (41%) were in disease severity stage A, 97 (32%) in B, 55 (18%) in C, 22 (7%) in D, and 3 (1%) in E. Disease duration was different in the 5 groups ($P<0.0001$). Clinical and severity stages did not differ in absence or presence (single and multiple) of the etiologic factors, except for autoimmune pancreatitis. **Conclusions** M-ANNHEIM classification is able to evaluate the clinical and severity stages of CP. The number of clinical and severity stages may be reduced for a better assessment of the disease.

Fractalkine Receptor (CX3CR1) Switch-on in Pancreatic Ductal Adenocarcinoma and Precursor Lesions

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Context Ductal pancreatic adenocarcinoma (PAD) expresses chemokine receptors, which can promote migration, invasion and metastasis. The fractalkine receptor CX3CR1, involved in neural adhesion, is a candidate mediator for PAD neural invasion (NI).

Objective To assess whether 1) PAD expresses CX3CR1, and 2) neural invasion correlates with CX3CR1 expression and genotypes. **Methods** The study series included 85 consecutive pancreatic cancers (65 PAD, 14 ampullary, and 6 endocrine), of known stage (TNM classification), grade and NI (27 PAD+). Fifteen PAD specimens also contained early ductal neoplastic lesions (pancreatic intraductal neoplasia, PanIN). CX3CR1 expression, assessed by immunohistochemistry, was scored as negative/low (L) and high (H). **Results** Thirty (46%) PAD showed H-CX3CR1, but 2 (14%) ampullary ($P=0.02$), and 0

endocrine ($P=0.03$) cancers did. In the 15 PAD with PanIN (13 H-CX3CR1), the H-expression rate increased from normal ducts and PanIN1 (19/66, 29%), to PanIN2 (27/41, 66%) and PanIN3 (29/38, 76%) ($P<0.001$). NI was seen in 15 (50%) H- and in 12 (34%) L-CX3CR1 PAD ($P=0.02$). Among 25 PAD with no lymph-node metastasis (N0), NI was present in 8 of 12 (75%) H- but in 3 of 13 (23%) L-CX3CR1 ($P=0.03$). **Conclusions** CX3CR1 expression increases selectively in PAD, and anticipates malignant transformation and invasion, potentially contributing to neoplastic progression. Our data also suggest that H-CX3CR1 participates to PAD NI early, before lymph node invasion. CX3CR1 contribution to local PAD progression and NI deserves further investigation in the light of its potential to discriminate a subgroup of locally, neural-invasive PAD.

Patients with Chronic Asymptomatic Hyperenzymemia. Which MRCP Findings?

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Context Persistent increases in serum concentrations of pancreatic enzymes without clinical evidence of pancreatic disease are a relatively common finding in

clinical practice. In healthy subjects, the rise is considered a benign idiopathic biochemical abnormality and is called "non-pathological chronic

pancreatic hyperenzymemia". But recent studies show that MRCP yielded pancreatic findings in more than 50% of patients with asymptomatic pancreatic hyperenzymemia. **Objective** To analyze the spectrum of MRCP findings in patients with asymptomatic hyperamylasemia and/or hyperlipasemia. **Methods** From March 2009 to March 2010, 23 consecutive patients (12 females and 11 males) having chronic hyperenzymemia were scheduled to undergo MRCP. Seven patients (31%) had pancreatic hyperamylasemia, 4 (17%) hyperlipasemia and 12 (52%) an increase of both enzymes. The increase of pancreatic enzymes was found occasionally and was confirmed by three laboratory tests. None of the subjects had any symptoms or signs of pancreatic or other diseases (renal, celiac disease, viral hepatitis, hypercholesterolemia). All patients were no drinker or at least <40 g/day of alcohol. **Results** Four out of 23

patients (17%) had a normal pancreatic ductal three at MRCP. In the remaining 19 patients (83%), 6 patients (32%) showed pancreatic cysts, 5 (26%) pancreatic changes compatible with IPMN, 1 (5%) a dilated Wirsung with Kinking, 1 (5%) IPMN and chronic pancreatitis, 1 (5%) IPMN and cancer, 2 (11%) a chronic pancreatitis, 1 (5%) an autoimmune pancreatitis and 2 (11%) an anatomic abnormality (pancreas divisum). **Conclusions** Patients with asymptomatic hyperamylasemia and/or hyperlipasemia showed abnormal MRCP in 83% of cases. MRCP is the most effective and non invasive imaging technique in these patients because it gives more detailed morphological information about the pancreaticobiliary ductal system. In more of 50% of cases we found clinical relevant diseases (IPMN, cancer, pancreatic cysts). A long-term follow-up is necessary to set up the clinical meaning of some of the MRCP alterations.

The Protease Inhibitor Gabexate Mesylate Reduces Invasiveness and Angiogenesis in Pancreatic Cancer Cell Lines, Enhancing Gemcitabine Action

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Context Pancreatic cancer cells produce various proteases involved in invasion, angiogenesis and metastatic spread. Gabexate mesylate (GM), a serine protease inhibitor, may reduce invasive capabilities and enhance chemotherapy effects. **Objective** To evaluate the effect of treatment with GM and gemcitabine (GEM) alone or combined. **Materials and methods** Studies have been performed on cancer cell lines PANC-1, SW1990 and endothelial cell EA.hy926. Treatment consisted of GM (50-100 µM for 24 h), alone or followed by GEM (250 µM for 24 h). Aspects studied included: cell viability (MTT assay), cell invasiveness and migration (Boyden chambers chemoinvasion and chemotaxis assay), angiogenesis (endothelial tube formation assay) and VEGF levels (ELISA) in EA.hy926 cell, MMP-2 and MMP-9 activity (gelatin zymography). **Results** Cell viability: this parameter decreased by 40% with GM alone only in EA.hy926 cells (P<0.05). Cell invasiveness: GM alone inhibited SW1990 and EA.hy926 cell line

invasiveness by about 75% (P<0.001). GM and GEM reduced invasiveness of PANC-1 and SW1990 cells by 55-65%. Angiogenesis and VEGF: inhibition of angiogenesis (from 60 to 90%) was observed in EA.hy926 cells incubated with the supernatant of PANC-1 and SW1990 cells treated with GM, alone or followed by GEM. Similar result was found for VEGF levels, strongly decreased in all cell lines treated with GM, alone or followed by GEM (P<0.001). The inhibitory effect of GM on PANC-1 and SW1990 was superior to bevacizumab (P<0.05). MMP-9 and MMP-2 activity: MMP-9 and MMP-2 activities were decreased by 40% after combined treatment (GM and GEM) in both PANC-1 and SW1990 cells. In EA.hy926 cells GM alone was more effective than the combination in inhibiting MMP-2 (P<0.001). **Conclusion** These *in vitro* data indicate that GM can effectively inhibit pancreatic cancer cell invasiveness and angiogenesis, also enhancing the effect of gemcitabine.

Linear Ultrasonography Clinical Impact in Patients Suspected of Neuroendocrine Pancreatic Tumor

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Context Endoscopic ultrasonography (EUS) is a valuable diagnostic tool for evaluating pathologies in or in relation to the GI tract. To detect pancreatic neuroendocrine tumors (PNETs) EUS is an accurate technique to provide high-resolution imaging in close proximity to the pancreas and to allow cytology aspiration from pancreatic lesions by operative fine needle aspiration (FNA). **Objective** The aim of this study was to evaluate the diagnostic yield of EUS in patients suspected of PNETs. **Methods** From November 2006 to September 2009, 21 patients were referred to our Endoscopic Unit for EUS evaluation due to suspected PNETs. All patients were studied by two skill endoscopists, using a linear ultrasonography probe. Helical-CT (h-CT) scan was performed in all patient as a first diagnostic work-up. Retrospective analysis of obtained data was performed. SPEC and SENS of chromogranin related to NETs, were also evaluated. **Results** Twenty-one patients were enrolled in the study and data were retrospectively analyzed. Nine females and 12 males were the study group; the median age was 48 years (range: 14-93 years). Eleven patients had symptoms (7 hypoglycemia, 3 diarrhea, and 1 jaundice) and 10 patients were asymptomatic. Chromogranin level, available for all patients, was greater than 18 ng/mL (range: 0-18 ng/mL) in 12 patients: 8 asymptomatic and 4 symptomatic patients. In 9 patients chromogranin levels were in range; 7

patients were symptomatic while 2 patients had no symptoms suitable with a neuroendocrine syndrome and diagnosis was placed under an incidental finding on h-CT. In 11/21 patients, h-CT scan showed normal findings. Four out of 21 lesions were located in the head of pancreas, 4/21 in the in the isthmus, 8/21 in the body, and 5/21 in the tail. The mean size of lesions was 1.7 cm (range: 0.7-4 cm). All patients underwent FNA biopsies, 10/21 patients with 22 G needle, 11/21 with 25 G needle. As regard the cytohistological typing, 10 lesions were well differentiated carcinoids, 4 lesions were poorly differentiated carcinoids, 5 lesions were insulinomas and 2 were glucagonomas. Nineteen patients subsequently underwent surgical resection (11 wedge resection, 5 distal pancreatectomy and 3 duodeno-cephalo-pancreatectomy). Two patients were unfit for surgery because of advanced neoplasm and elderly age, respectively. No malignancy recurrence and no symptoms NETs related were recorded after 6 months of post-surgical follow-up. SENS and SPEC of chromogranin were 70% and 30%, respectively. **Conclusion** EUS may detect PNETs which have not being visualized by other imaging modalities. EUS should be performed early in the diagnostic work-up if a PNETs is suspected. Chromogranin serum level is not useful as a diagnostic test when PNTs in suspected because of its low accuracy rate.

Aquaporin Kinetic and Related Gene Expression May Help Predicting the Outcome of Experimental Acute Oedematous Pancreatitis. Clues to Clinics?

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Context The clinical course in some cases of edematous form of acute pancreatitis (AP) seems to follow pathophysiological mechanisms to be fully predicted and unfolded as yet. Marked edema of the parenchyma is observed in virtually all cases and such changes are displayed by the classical experimental cerulein-induced AP. Aquaporins (AQPs) are widely distributed in mammals and represent a family of membrane proteins controlling water channel,

regulating cellular permeability and transport in health as well as in disease. Recently, it has been shown an upregulation of AQP1 expression seen in pancreatic ducts of patient with autoimmune pancreatitis. To the best of our knowledge, there is a paucity of data regarding AQPs status in acute pancreatitis. **Objective** The aim of the present investigation was to study and to monitor AQPs localization and functional genomic expression in early cerulein-induced AP in view of

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getting further insights into their possible role in phenotypic expression of the disease. **Methods** Male Wistar rats weighing 200-230 g and aged 8 months were housed in individual cages in an environmental-controlled vivarium. Under phenobarbital anesthesia 10µg/kg/h of cerulein was infused for 3 h to induce AP and sacrifices were made at 3 h and 72 h afterwards. Pancreases were excised and examined for histology. In particular, the expression of AQP1 and AQP8 was examined by specific RT-PCR (AQP1: 5'-CTGGGTGGGACCATTCATTG-3' and 5'TGCGGTC TGTAAGTCGCTG-3'; AQP8: 5'-GCCTAATGAGC AGTCCCACAA-3' and 5'-TGGATCTCACTGGCTG GGCCAGCTC-3'). **Results** Control pancreases showed AQP1 and AQP8 localized in pancreatic ductal cells together with capillary endothelia and in acinar cells, respectively. During early phase (3 h) of AP, AQP1 expression significantly decreased in all sites

and further worsened later (72 h) despite overall histological improvement of AP. The same pattern was observed with AQP8 at 3 h but this level remained stable at the 72 h observation. On the other hand, immunoblot showed unchanged band densitometry for protein level of AQP1 but decreased for AQP8 (at 3 h and 72 h). At immunohistochemistry, AQP1 disappeared in ductal cells (looking normal at histology) but strongly increased in capillary endothelia. AQP8 disappeared in the apical membrane of acinar cells at 3 h but less than 50% was detected at 72 h. **Conclusion** The gene expression/protein level discrepancy noted for AQP1 and AQP8 are likely due to different turnover and half life. On the other hand, "normal" histology may still hide significant prolonged epigenomic abnormalities which warrant further studies aimed in view of possible implication for the clinical course of AP.

Spleen-Preserving Distal Pancreatectomy. The Procedure of Choice in Case of Benign or Low-Malignant Pancreatic Neoplasms

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Context Distal pancreatectomy with preservation of the spleen and of the splenic vessels is a technically demanding operation, because of the close relationship of the pancreas with the splenic vessels. It can be indicated in case of benign or low-malignant pancreatic neoplasm, as an alternative to distal pancreatectomy with splenectomy. Splenectomy significantly increases the risk of severe infections, being sepsis' incidence in asplenic patients about 600 times higher than in the general population. **Objective** To evaluate the feasibility and safety of spleen-preserving distal pancreatectomy (SPDP) in case of benign or borderline neoplasm of the pancreas, by comparing the outcome of SPDP with that of distal pancreatectomy with splenectomy (DPS). **Methods** From January 1999 to December 2009, overall 141 patients underwent distal pancreatectomy for benign or borderline neoplasm in our institution. Data were prospectively collected in our electronic pancreatic surgery database. Basing on preoperative findings, 87 patients were candidate to SPDP, whereas 54 patients to DPS. In 13 out of 87 patients (15%) spleen preservation was not successful and splenectomy was performed. Therefore, overall 74 patients underwent SPDP and 67 patients DPS. In all cases of SPDS, the spleen was preserved along with the

splenic vessels; no ligation of the vessels (Warshaw operation) was performed. **Results** Both groups were similar when considering the nature and average diameter of the lesion (4.5 cm SPDP vs. 4.7 cm DPS). Intraoperative data in the two groups were similar as well: no difference was found in operative time (SPDP 245 min vs. DPS 235 min), blood loss (SPDP 674 mL vs. DPS 518 mL) and transfusion rate. Comparable results were also found for the postoperative data: no mortality was observed; the reoperation rate was 2.7% in case of SPDP and 3% in case of DPS; pancreatic fistula rate was 32.5% and 38.3%, respectively (P=0.304). The fistulas were mainly grade A (31.2%) and grade B (5%); all of them were treated conservatively. Hospital stay was significantly shorter in SPDP group (8 days vs. 10 days, P=0.04). **Conclusion** When indicated, spleen-preserving distal pancreatectomy with preservation of the splenic vessels can be successfully accomplished in 85% of cases. Patients undergoing this procedure had a shorter length of stay without any other impairment of postoperative course with respect to patients in which splenectomy was associated. We suggest that spleen-preserving left pancreatectomy is the procedure of choice in case of benign or borderline neoplasm of the pancreas.

Exocrine Pancreatic Insufficiency After Pancreatic Resection in Patients with Benign or Low Grade Malignant Pancreatic Tumors

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Context We evaluated the incidence of exocrine pancreatic insufficiency (EPI) after partial pancreatic resection in patients with benign or low grade malignant pancreatic tumors. **Objective** We re-evaluated the clinical and functional data related to exocrine pancreatic function of patients undergoing partial pancreatic resection from 1996 to 2007, with follow-up greater than two years. We excluded patients with chronic pancreatitis or cancer of the exocrine pancreas. **Results** We performed 342 partial resections of the pancreas (enucleations excluded). Among 99 selected patients with low grade malignant or benign neoplasm, 9 were excluded for follow-up less than two years and 2 for pre-operative pancreatic exocrine insufficiency. In the remaining 88 patients (46 neuroendocrine tumors (NET), 25 serous or mucinous cystadenoma (CA), 13 benign intraductal tumors (IPMN) and 4 pseudopapillary cystic tumors (PCT)), 12 had a pancreaticoduodenectomy (PD), 12 duodenum preserving pancreatic head resection (DPPHR), 20 central resections (CR) and 44 left pancreatectomy

(LP). The median follow-up was 77.1 months (range: 24-168 months). Twenty-one out of 88 patients had an EPI (23.8%). Among the patients receiving a PD, 10/12 (83.3%) had an EPI (median follow-up 57.6 months). Among DPPHR, 8/12 (66.6%) developed an EPI (including one with simultaneous LP) with median follow-up of 74.1 months. The CP had 10.0% rate of EPI (1 of them received later even a LP) with median follow-up of 80.5 months. Only 1/44 LP (2.2%) had an EPI (mean follow-up of 79.4 months). Stratified by disease, we found an EPI in 13/46 NET (28.2%), 4/25 CA (16.0%), 4/13 IPMN (30.7%), and 0/4 PCT. Among the 21 patients with postoperative EPI, diabetes mellitus was found in only 4 patients (2 DPPHR, 1 PD, 1 CP), with normal preoperative OGTT. In 4 out of 18 patients with EPI who received a PD or DPPHR, a dilated Wirsung was evident at MR/CT. **Conclusion** The rate of patients with EPI after operations such as PD or DPPHR is from 66% to 83%. This fact should be considered in case of resection of the pancreatic head for patients with neoplasms with long life expectancy.

Effect of Surgeon Volume on Outcome Following Pancreaticoduodenectomy in a High-Volume Hospital

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Context The impact of surgeon volume on pancreaticoduodenectomy (PD) outcome is still controversial. So far, available data are from retrospective multi-institutional reviews, considering in-hospital mortality as the only outcome variable. **Objective** To assess the independent impact of surgeon volume on outcome after PD in a single high-volume institution. **Patients and methods** Demographics, clinical, and surgical variables were prospectively collected on 610 patients who underwent PD from August 2001 to August 2009. Cut-off value to categorize high and low-volume surgeons (HVS and LVS, respectively) was 18 PD/year. Primary endpoint was operative mortality (death within 30-day post-discharge). Secondary endpoints were morbidity, pancreatic fistula (PF), and length of hospital stay (LOS). Postoperative complications were graded according to Clavien-Dindo classification, validated in pancreatic surgery. Complications requiring either intervention under general anesthesia or ICU

management, or causing death were considered as major (Clavien-Dindo grade 3b-5). Postoperative PF was defined according to ISGPF definition. **Results** In the whole series mortality was 4.1%, overall morbidity was 61.3%, and PF rate was 27.5%. Two HVS performed 358 PD (58.6%) while six LVS performed 252 PD (41.4%). Mortality was 3.9% for HVS and 4.3% for LVS ($P=0.84$). Major complication rate was similar for HVS and LVS (9.3% vs. 9.6%). PF rate was higher for LVS (32.4% vs. 24.1%, $P=0.03$). Reoperation was necessary in 29 (8.1%) patients of the HVS group and in 20 (7.9%) patients of the LVS group ($P=0.92$). Mean LOS was 15.5 days for HVS vs. 16.9 days for LVS ($P=0.11$). At multivariate analysis, risk factors for PF occurrence were LVS, soft pancreatic stump, small duct diameter, and longer operative time. **Conclusion** Low-volume surgeons had a higher pancreatic fistula rate. However, this did not increase mortality and major complications because of the protective effect of high-volume hospital.

Patient Reported Outcomes After Pancreaticoduodenectomy for Different Diseases. A Follow-up Study

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Objective To evaluate clinical features and quality of life (QoL) in a 2-year follow-up study in subjects who underwent pancreatic head resection (PHR). **Patients** One-hundred and ninety-seven patients with benign and malignant diseases. **Investigations** A dedicated clinical form and the EORTC QLQ-C30 questionnaire were administered immediately before and 6, 12, 18 and 24 months after surgery. **Reference group** A sample of 197 sex- and age-matched norms. **Results** The final pathological diagnoses were: 145 pancreatic neoplasms (73.6%; mainly represented by 97 ductal carcinoma and 35 IPMN), 33 neoplasms of the papilla of Vater (16.8%), 8 chronic pancreatitis (4.1%), 11 other periampullary neoplasms (5.6%). Malignant diseases were present in 164 patients (83.2%) and

benign in 33 (16.8%). Before surgery, global health was significantly lower ($P=0.001$) in the study population as compared to the norms. Sixty-two (31.5%) patients died during the follow-up (all of them with malignant disease) while 33 patients (16.8%) were lost. There was a significant progressive improvement of the global health during the follow-up. At the end of the study, the QoL was not significantly different from the norms, even if the 30 patients with benign disease had a significant better QoL than the 72 patients with malignant diseases. **Conclusions** The QoL before PHR was impaired as compared to the normative population, while it significantly improves in the 2 years following surgery.

Synchronous Association of Two Carcinoids of the Foregut, Adenocarcinoma of the Caecum and Meckel's Diverticulum with Pancreatic Ectopic Mucosa. A Case Report

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Context Neuroendocrine gastroenteropancreatic (NE-GEP) constitute a heterogeneous group of neoplasms with location of the primary tumors in the gastric mucosa, pancreas, small and large intestine. Duodenal carcinoids are rare tumors and show extremely variable biological behavior and clinical course. According to several large series of patients with primary

gastrointestinal carcinoids, the incidence of second primary malignancies can exceed 50%. **Case report** We report a case of concurrent colonic carcinoma, a couple of two carcinoids of the duodenum and the presence of Meckel's diverticulum, which proved at histology harbor pancreatic ectopic mucosa.

Identification and Validation of an Individual Risk Score for Acute Post-ERCP Pancreatitis

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Context There are many risk factors which expose patients to develop acute post-ERCP pancreatitis

(PEP), the worst complication of this medical procedure. The complications can either be of a clinical

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type, depending on the patient's features, or of a technical type, resulting from the ERCP procedure. Being able to discriminate between the patients with a high risk of developing pancreatitis from the low risk ones is nowadays crucial in order to establish which patients would receive the best benefits from a prophylactic treatment, which considers pharmacological medications or a pancreatic stent placement. **Objective** To identify and to validate, in a large prospective series, an individual i.e. "*ad personam*" score model, to establish which patients are at high risk of developing PEP. **Methods** Three independent different ERCP Italian databases have been considered, one of which to build the score model (2,651 patents), and the other two ones to validate it (1,796 patients). During the score model "derivation phase", the risk variables significantly linked to PEP were identified (multivariate analysis). Then, the identified variables were inserted into a mathematical model (logit) which allowed to calculate, for each patient, a score representing the risk of developing PEP. A ROC curve was used to measure the predictive performance of this model. Subsequently, a cut-off 8 score value was found, in order to stratify patients in two classes, one with a high PEP risk and the other with a low risk. During the "validation phase", the

score has been calculated for each patient, then categorized in one of the two risk-classes previously identified. **Results** The variables significantly linked to PEP were: "previous PEP" (OR=7.2; P<0.0001), "difficult cannulation of Vater's papilla" (OR=2.9; P<0.0001), "pancreatic duct cannulation" (OR=2.2; P=0.02), "precut sphincterotomy" (OR=1.9; P=0.03) and "younger age" (OR=1.8; P=0.006). The area under the curve (AUC) was equal to 0.78 (95% IC: 0.71-0.85; P<0.0001), and the best cut off value to separate the high risk patients from the low risk ones was equal to 3. During the "validation process" significant differences were detected with regards to the distribution of the two validation cohorts patients, concerning that these three samples showed different clinical and epidemiological features. The "clinical effectiveness" of the risk score obtained for every single patient has been confirmed because, in each analyzed case study, no significant differences were found between the observed and expected PEP frequencies. **Conclusions** This study identified for each patient subjected to ERCP a PEP risk score, which may be easily applied in the clinical practice. The identification of a high risk for PEP allows to select the patients who can better benefit from a prophylaxis.

Is Pancreaticoduodenectomy a Feasible Procedure in Patients over 80-Year Age?

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Context Postoperative results after pancreatic surgery in elderly patients remain still unclear. **Objective** To evaluate the postoperative results in patients over 80 years age who underwent pancreaticoduodenectomy (PD). **Methods** From January 2006 to June 2010, 85 PD were performed. Data regarding sex, age, co-morbidities, ASA score, type of resection, characteristics and management of pancreatic remnant, pathological diagnosis, morbidity and mortality were collected in a prospective database. The main outcomes were overall postoperative complications rate, medical, postoperative pancreatic fistula (POPF), postoperative pancreatic hemorrhage (PPH), delayed gastric emptying (DGE) and mortality. Patients were divided into two groups: 9 elderly patients 80 years or more (G1) and 76 patients less than 80 years (G2). Univariate analysis was carried out with appropriate test. Logistic regression was carried out to evaluate risk factors related to main outcomes. **Results** The two groups were similar for sex, co-morbidities, ASA score, type of resection, extension of resection, texture of pancreatic remnant, presence of dilated main pancreatic

duct and presence of malignant disease. The closure of pancreatic stump was performed more frequently in G1, than in G2 (66.7% vs. 27.6%; P=0.026). Overall postoperative medical complication rate in G1 was higher than G2 (44.4% vs. 28.9%) but this difference was not statistically significant (P=0.446). POPF rate was similar in the two groups (33.3% and 30.3% in G1 and G2, respectively; P=1.000). PPH rate was lower in G1 than G2 (22.2% vs. 38.2%; P=0.476). DGE rate was significantly higher in G1 respect to G2 (44.4% vs. 14.5%; P=0.048). Mortality in G1 was lower than in G2 (0% vs. 5.3%; P=1.000). Logistic regression showed a significantly increased risk of DGE in patients over 80 years old (OR: 9; 95% CI: 1-64; P=0.026). Multivariate analysis also demonstrated that ASA IV score increased the risk of medical complications (OR: 5; 95% CI: 1-28; P=0.039) and mortality rate (OR: 37; 95% CI: 3-417; P=0.003). Risk of POPF increased in patients with soft pancreatic stump (OR: 4; 95% CI: 1-16; P=0.034). **Conclusion** PD is a feasible surgical procedure for elderly patients over 80 years age without major medical diseases.

Risk Factors of Complications After Pancreaticoduodenectomy

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Context The rate of complications after pancreaticoduodenectomy (PD) remains still high.

Objective To evaluate the presence of risk factors related to postoperative morbidity and mortality in patients who underwent pancreaticoduodenectomy (PD). **Methods** From January 2006 to June 2010, data from 85 PD were collected. The main outcomes were postoperative overall complications rate, medical, postoperative pancreatic fistula (POPF), postoperative pancreatic hemorrhage (PPH), delayed gastric emptying (DGE) and mortality. The following potential risk factors were evaluated: sex, age, co-morbidities, ASA score, type of resection, characteristics and management of pancreatic remnant, pathological diagnosis, morbidity and mortality were collected in a prospective database. Univariate analysis was carried out with appropriate test. Multivariate analysis was performed with logistic regression. **Results** Overall complications rate was 67.1%. Medical complications were in 30.6% cases, POPF, PPH and DGE in 30.6%, 36.5%, and 17.6% respectively. Postoperative mortality

was 4.7%. At univariate analysis, ASA score was related to medical complications rate (ASA II, 10.5%; ASA III, 31.6%; ASA IV, 66.7%; $P=0.003$) and to mortality rate (ASA II, 0%; ASA III, 1.8%; ASA IV, 33.3%; $P=0.002$). POPF was significantly more frequent in patients with soft pancreatic stump ($P=0.001$), dilation (>3 mm) of Wirsung duct ($P=0.008$) and in patients without pancreatic anastomosis ($P=0.001$). We did not find risk factors in patients with PPH and DGE. Multivariate analysis demonstrated that ASA IV score increased the risk of medical complications (OR: 5; 95% CI: 1-28; $P=0.039$) and mortality rate (OR: 37; 95% CI: 3-417; $P=0.003$). Age increased significantly the risk of DGE (OR: 1.1; 95% CI: 1-1.2; $P=0.020$). POPF increased in patients with soft pancreatic stump (OR: 4; 95% CI 1-16; $P=0.034$). **Conclusion** The only risk factor related to postoperative mortality and medical complications was ASA score. Soft pancreatic stump and age were risk factors for POPF and DGE respectively.

Laparoscopic Distal Pancreatectomy.

The Learning-Curve in a High-Volume Pancreatic Surgery Hospital

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Context Laparoscopic distal pancreatectomy (LDP) for benign and borderline pancreatic lesions is becoming the treatment of choice. **Objective** The purpose of this study was to estimate the learning curve for LDP. **Patients and methods** From March 2009 to May 2010, 46 consecutive patients with pancreatic neoplasms (22 benign, 24 malignant) underwent distal pancreatectomy in our institution. Exclusion criteria for laparoscopy were: cancer contact with major vessels ($n=12$), comorbidity ($n=4$), BMI >35 kg/m² ($n=2$), refusing LPS ($n=1$), absence of dedicated team ($n=6$). To evaluate the learning-curve we considered two periods: first 3 months ($n=8$) and subsequent months ($n=13$). Clinical characteristics as well as intra- and postoperative data were prospectively recorded. All patients received an early recovery after surgery protocol. Postoperative pancreatic fistula (POPF) was defined according to ISGPF definition. **Results** Of the 21 patients in which laparoscopy was attempted, LDP was carried out successfully in 15 patients, while in 6 cases (28.5%) conversion to laparotomy was needed. The conversion rate was 75% in the first period and 0% in the

subsequent one ($P=0.001$). In the first period the mean operative time was 271 ± 59 min, then it was 189 ± 44 min ($P=0.006$). Mean operative time of complete laparoscopic resection was 210 ± 47 min (range: 120-300 min) versus converted procedures 283.3 ± 65 min (range: 180-360 min) ($P=0.006$). Mean operative time of spleen preserving LDP was 188 ± 49 min whereas of LDP with splenectomy was 221 ± 16 min. Overall mean blood loss was 330 mL (range: 0-1,800 mL); it was 210 mL (range: 0-1,000 mL) in the complete LDP and only one patient needed intra-operative blood transfusion. Ten patients experienced POPF (grade A: 6 patients; grade B: 3 patients; grade C: 1 patient). Overall morbidity was 47.6% with no mortality. The median hospital stay of LDP was 5 ± 2.2 days. Eight out of 24 patients affected by malignancies were treated laparoscopically (16 were ruled out due to exclusion criteria) with a conversion rate of 37.5%. The mean number of lymph nodes harvested was 16.7 (range: 3-32). **Conclusion** The learning curve appears to be short in a high-volume pancreatic surgery hospital. LDP can be a safe procedure, though POPF rate remains high.

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Low Frequency of Microsatellite Instability Among European Patients with Pancreatic Ductal Adenocarcinoma

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Context Inherited and acquired defects of the mismatch repair (MMR) genes are responsible for gastrointestinal cancers with microsatellite instability (MSI), which account for 10-15% of the cases. however, the reported prevalence of the MSI phenotype among pancreatic tumors varies widely from 1% to 10%, and the contribution to the inherited burden of pancreatic tumors remains to be determined.

Objective To assess the prevalence of tumors with the MSI phenotype among pancreatic neoplasms in Caucasian patients. **Methods** We studied the prevalence of the MSI phenotype among 135 consecutive pancreatic tumor resections performed at an Italian and at a German referral center. Specimens from Italy comprised 10 ampullary cancers, 6 endocrine tumors and 57 pancreatic ductal adenocarcinoma (PDAC), and those from Germany

comprised 62 PDAC. MSI-status was determined by taking advantage of mononucleotide repeat markers (BAT25 and BAT26), which are almost monomorphic in Caucasians. **Results** Only one out 119 (0.8%) PDAC showed MSI, and was identified in a 77 years old Italian patient (1.7%), as compared to 1 out 10 ampullary cancers (10%, P=0.2), and 1 out of 6 endocrine tumors (17%; P=0.09; MSI in PDAC vs. other histotypes, P=0.04). **Conclusions** The prevalence of MSI was higher in pancreatic tumors other than PDAC in European patients. In PDAC MSI is a rare phenomenon, which likely does not contribute to the burden of pancreatic cancer, while it might be encountered in less frequent, susceptible to radical surgery, pancreatic neoplasms which might arise in the context of HNPCC.

Are Chronic Pancreatitis and Acute Recurrent Pancreatitis Two Different Faces of the Same Coin or Two Different Diseases?

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Context Clinical differences between chronic pancreatitis (CP) and acute recurrent pancreatitis (ARP) are controversial. **Objective** To investigate the clinical phenotype of ARP and CP patients as two distinct groups of patients. **Patients and methods** Eighty-one ARP and 162 CP patients were consecutively enrolled. We classified ARP patients on the basis of recurrence of acute pancreatitis in the absence of radiological findings of CP (ductal dilation/alteration and/or pancreatic calcifications). Clinical features analyzed were gender, age at diagnosis, alcohol intake, smoking habit, incidence of dyslipidemia, diabetes mellitus, cholelithiasis and pancreas divisum. **Results** ARP and CP are characterized by differences in clinical course and

associated factors. When compared to CP patients, ARP subjects had a significantly higher incidence of pancreas divisum (ARP 11.1%; CP 3.7%; P=0.02). With respect to mean alcohol intake, the percentage of drinkers in ARP was lower (ARP 27.1%; CP 40.1%; P=0.04). Smoking habit was significantly higher in CP patients (ARP 22.2%; CP 66%; P=0.006) even if the amount of cigarettes/day was similar (ARP 23.7±14.2; CP 23.6±12.1). Moreover, ARP patients had a minor incidence of type II diabetes (P<0.0001) and dyslipidemia (ARP 3.7%; CP 14.8%; P=0.008). **Conclusions** CP and ARP patients are characterized by distinct endogenous (incidence of pancreas divisum, pancreatic calcifications and/or ductal lesions, metabolic features) and exogenous factors (smoking

habit and alcohol intake). We do believe ARP may progress to CP as final epiphenomenon: chronic pancreatitis could be the final endpoint of different

pancreatic inflammatory diseases much as cirrhosis is the common late manifestation of a variety of chronic liver diseases.

POSTER SESSION

Very High Elevation of Carbohydrate Antigen 19-9 Serum Value in Benign Obstructive Jaundice

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Context Carbohydrate antigen (CA) 19-9 is frequently used as a gastrointestinal tumor marker, and shows a high positivity in pancreaticobiliary malignancies. Increases in its serum level have also been reported in benign disease of the liver, pancreas and biliary tract. However, there are very few reports of benign conditions with CA 19-9 value more than 10,000 U/mL. We report a case of obstructive jaundice due to an impacted stone in the common bile duct (CBD), where a CA 19-9 serum level higher than 20,000 U/mL prompted suspicion of a malignant cause. **Case report** A 78-year-old man was admitted to our department presenting with painless jaundice and dark urine for about 5 days. No fever was present. Laboratory exams revealed: total bilirubin: 13.8 mg/dL (normal values: 0.2-1.2 mg/dL), direct bilirubin: 9.1 mg/dL (normal values: 0-0.2 mg/dL), GGT: 505 UI/L (normal values: 5-50 UI/L), alkaline phosphatase: 178 U/L (normal values: 32-92 U/L), CA 19-9: >22,583 U/mL (normal values: 0-35 U/mL). AST, ALT and WBC were normal. Abdominal sonography revealed dilatation both of the CBD (maximum diameter: 1.2 cm) and intrahepatic biliary tree, but intestinal gas precluded

complete evaluation of pancreas and distal part of the CBD. In the gallbladder no stones were visualized, but biliary sludge was noted. An ERCP was done with evidence of impacted stone at the distal end of the CBD, extracted with Dormia basket after endoscopic sphincterotomy. Seven days post-ERCP, jaundice persisted elevated (total bilirubin: 14.5 mg/dL), but a MRCP showed normal pancreas and biliary tract. Slowly, conditions improved and eleven days post-ERCP total bilirubin decrease (4.9 mg/dL) and CA 19-9 fell to 226.2 U/mL, and returned to normal range (0-35 U/mL) after one month. Ten months later, CA 19-9 and total bilirubin are persistently normal and patient remains asymptomatic. **Conclusion** According to previous reports on jaundiced patients, even in our case high levels of CA 19-9 returned to normal after "successful drainage", in opposite to malignancies where persistently elevated CA 19-9 levels were seen despite treatment. This case emphasizes the need for caution in the interpretation of an elevated serum CA 19-9 as a marker for malignancy, especially in patients with obstructive jaundice.

Pancreatic Ascites Due to a Ruptured Pseudocyst Mimicking Peritoneal Carcinomatosis. A Case Report

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Context Pancreatic ascites is the accumulation of amylase-rich intraperitoneal fluid that can occur in association with a pancreatic duct disruption, or from a leaking or ruptured pseudocyst as a complication of chronic pancreatitis. Pancreatic ascites usually occurs in male (65-70% of cases), alcoholic (80-100%) patients. Initially patients with pancreatic ascites should be treated conservatively, but if the condition persists, surgery is often mandatory. **Case report** We

report the case of a 54-year-old woman, chronic alcoholic and heavy smoker, with a history of chronic pancreatitis and COPD. She was admitted to our department for pain and abdominal distension due to ascites of unknown origin. The patient underwent CT scan, EUS and MRCP showing the presence of multiple peritoneal nodules suspicious for carcinomatosis, with no evidence of a primary tumor in the abdominal organs (except for a thickness of the

rectal wall). A pseudocyst in the pancreatic tail was also noted, in the setting of a chronic pancreatitis. A proctoscopy and a transvaginal US were performed to rule out the presence of a primary lesion and resulted negative. The patient was initially treated conservatively with total parenteral nutrition and positioning of a percutaneous drainage. Peritoneal fluid analyses showed a high amylase level ($>170,000$ IU/L), and the absence of malignant tumor cells (MTC). For the persistence of ascites, and in order to assess the nature of the peritoneal nodules, the patient underwent an explorative laparotomy. Intraoperatively there were findings of severe peritonitis associated with multiple peritoneal nodules; two of them were biopsied and resulted inflammatory nodules, negative for MTC. A

rupture of the pancreatic pseudocyst was detected, confirming the diagnosis. A Roux-en-Y cystojejunostomy was fashioned. Postoperative recovery was characterized by mild initial respiratory insufficiency, treated conservatively. We then assisted to a progressive resolution of the symptoms and the patient was discharged on postoperative day 8. **Conclusion** The non-operative treatment of pancreatic ascites (TPN, endoscopic or percutaneous drainage) is effective in 50% of patients, and usually 2 to 3 weeks are required for the resolution of symptoms. In recurrent and persistent cases, or when the suspicion of malignancy has to be ruled out, the surgical approach is adequate, leading to a resolution of symptoms in a short time.

Pseudoaneurysm of Gastroduodenal Artery.

A Multiple Step Treatment

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Context Pseudoaneurysm of gastroduodenal artery (GDA) is the rarest splanchnic visceral aneurysm with a mortality rate due to gastrointestinal bleeding in 4-10% of cases. We present a case report of a giant GDA presenting with bleeding from the pancreatic duct and treated with a combined endovascular and surgical approach. **Case report** A 52-year-old man was admitted to Emergency because of melena and abdominal pain. No significant past medical history was reported. First investigations showed severe anemia and a bulging mass behind the duodenum with no active bleeding. A CT scan found a 5 cm GDA in calcific chronic pancreatitis. Patient underwent angiography with selective embolization of GDA. On day 16 a second digestive bleeding occurred. US

showed persistent arterial flow in GDA and embolization of residual GDA was done through direct percutaneous abdominal puncture. One week after the patient underwent laparotomy for persistent abdominal pain with suspicion of dissection: intraoperative findings ruled out dissection and Wirsung-jejunostomy was performed. Biopsy of Wirsung wall was negative for dysplasia confirming diagnosis of chronic pancreatitis. **Conclusion** GDA is a rare, potential life threatening disease often associated to pancreatic disease. In the case we reported, because of absence of clinical history and risk factors for chronic pancreatitis, GDA with its obstructive effect, may be the cause of pancreatitis itself.

Long-Term Survival After Pancreaticoduodenectomy for Pancreatic Ductal Adenocarcinoma. Case Report

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Context Pancreatic ductal adenocarcinoma is generally associated with a dismal prognosis even after curative pancreatic resection. Recently, some authors have reported cohort of patients with long survival. **Case report** A 60-year-old woman underwent pancreaticoduodenectomy (PD) for pancreatic head mass on May

1996. Pathological examination showed a well differentiated ductal adenocarcinoma of 2.5 cm in diameter, limited within the pancreatic gland (T2); loco-regional lymph node metastases (N1) were present and the resection margin was free from carcinoma (R0). The postoperative course was

uneventful and 5 weeks after surgery the patient began adjuvant therapy with gemcitabine plus CDDP for 6 cycles. The patient was clinically and CT followed every 3 months for the first year and every 6 months subsequently. Thirteen years later (December 2009), due to an impaired glucose tolerance, without other symptoms, a CT scan showed a cystic lesion with septa of 45 mm in diameter localized in the tail of the pancreas. A FDG-PET resulted positive and on January 2010, the patient underwent surgery. The operation consisted in an en-bloc resection of body-tail of the pancreas, spleen, left adrenal gland and a part of the gastric wall. Pathological examination showed moderately differentiated pancreatic adenocarcinoma, biliopancreatic and intestinal type, invading the peripancreatic fat tissue but without invasion of the

gastric wall and adrenal gland (T3); no lymph node metastases (N0) were present. Resections margin were also free from cancer cells (R0). The pathological characteristics of the mass suggest the hypothesis of a pancreatic adenocarcinoma arising from an intraductal papillary mucinous neoplasm (IPMN). The post-operative course was uneventful and at present the patient fourteen years after the first operation is in good general health and cancer free. **Conclusion** The long-term survival of our patient is probably due to a “non correct” pathological diagnosis at the first operation because IPMNs were not well known. This is also supported by the fact that the IPMN was pathologically diagnosed after the second surgical approach and it is possible that these lesions are slow-growing and may recur in other sites of the pancreatic gland.

Is Laparoscopic Pancreatectomy for Solid Pseudo-Papillary Tumors a Suitable Technique? A Retrospective Analysis of Our Experience with Long-Term Follow-up

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Context Only 17 cases of SPT laparoscopically treated have been published in literature, but long-term follow-up data are lacking. **Objective** To present our results with long-term follow-up after SPT laparoscopic resection. **Methods** Retrospective analysis of 10 patients (8 females, 2 males), mean age of 25.4 years, (DS: 12.1 years; range: 11-51 years) who underwent distal laparoscopic pancreatectomy with a definitive histological diagnosis of SPT. **Results** The average tumor size was 43.8 mm (range: 20- 65 mm). Five patients underwent distal splenopancreatectomy and 5 patients underwent spleen-preserving distal pancreatectomy, 3 with splenic vessel preservation and 2 with the Warshaw technique. The conversion rate

was nil. No case of perioperative mortality was recorded. The mean hospital stay was 7 days (DS: 2.7 days; range: 4-12 days). Six patients had an uneventful postoperative course. Four patients had postoperative complications. Two of them underwent re-operation, while the other 2 had nonsurgical complications. After a median follow-up of 47 months (range: 5-98 months) all patients are alive and disease free. **Conclusion** In patients affected by SPT laparoscopic pancreatic resection is a safe and feasible procedure, especially in young people, if possible with spleen-preserving technique. Laparoscopic or laparotomic biopsy, instead, in these patients, should not be performed.

Identification of Risk Factors Predicting Complications After Distal Pancreatectomy

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Context The rate of complications after distal pancreatectomy (DP) remains still high. **Objective** To evaluate the presence of risk factors related to postoperative morbidity in patients who underwent DP.

Methods From January 2006 to June 2010, data from 57 DP were collected. The main outcomes were overall postoperative complications rate, medical, postoperative pancreatic fistula (POPF) and postoperative

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pancreatic hemorrhage (PPH). The following parameters were evaluated: sex, age, co-morbidities, ASA score, type of resection, characteristics and management of pancreatic remnant, pathological diagnosis, and morbidity. These data were collected in a prospective database. Univariate analysis was carried out with appropriate test. **Results** Overall complication rate was 56.1%. Medical complications were in 22.8% of cases, POPF and PPH were both in 22.8% of patients. Postoperative mortality was 0%. At univariate analysis, ASA score, presence of co-morbidities and extended resections were related to overall complications rate ($P=0.023$, $P=0.033$, and $P=0.049$, respectively). Medical complications were significantly

more frequent for ASA score and co-morbidities ($P=0.019$ and $P=0.05$, respectively). POPF was significantly more frequent in patients who underwent extended resection ($P=0.020$). The treatment of the pancreas remnant did not affect the rate of POPF. No risk factors for patients with PPH were found. **Conclusion** Risk factors related to overall postoperative morbidity were ASA score, presence of co-morbidities and extended resection. Medical complications rate were high in patients with co-morbidities and ASA score III-IV. POPF was more frequent in patients who underwent extended resections.

Usefulness of Dindo-Clavien Classification in Evaluating the Postoperative Course of Distal Pancreatectomy

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Context There is a lack of a unified grading system for severity of complications after distal pancreatectomy (DP). **Objective** To evaluate the usefulness of Dindo-Clavien classification (DCC) in patients who underwent DP. **Methods** Fifty-seven DP were performed from January 2006 to June 2010. Data regarding sex, age, comorbidities, ASA score, type of resection, pathological diagnosis, morbidity and mortality were collected in a prospective database. All complicated patients were classified according to DCC. We compared in each grade of DCC the length of postoperative stay and the rate of most important complications after DP. Analysis was carried out with multi-way ANOVA test with polynomial, simple and repeat contrast. The linear-by-linear chi squared and the Spearman rank tests were used when appropriate. **Results** Mean age of patients was 59.4 ± 16.3 years. There were 33 (57.9%) females and 24 (42.1%) males. One or more comorbidities were present in 28 (50.9%)

patients; 24 (42.1%) patients were ASA II, 29 (50.9%) ASA III, and 4 (7%) ASA IV. DP was performed for malignant disease in 35 (61.4%) cases. Twenty-five (43.9%) patients were not complicated, 32 (56.1%) resulted complicated. Of these 9 (15.8%) had grade I, 16 (28.1%) grade II, 6 (10.5%) grade III, 1 (1.8%) grade IV. Postoperative mortality was 0% (grade V). POPF was found in 13 (22.8%) patients (38.5% grade A, 61.5% grade B). PPH was registered in 13 (22.8%) patients (30.8% grade A, 69.2% grade B). There was a significant progressive increase in length of postoperative stay from patients without complications to those with grade IV except in patients with grade I (grade I, II, and III: $P=0.203$, $P=0.011$, and $P<0.001$, respectively). The severity of POPF was related to DCC ($P=0.041$). **Conclusion** DCC appears a reproducible classification system in patients undergone DP. It is able to distinguish between no complicated and complicated patients.

Predicting Factors of Late Post-Pancreatectomy Hemorrhage After Distal Pancreatectomy

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Context Postoperative hemorrhage (PPH) is one of most severe complications after pancreatic surgery. **Objective** To evaluate the presence of risk factors

related to late PPH (IPPH) after distal pancreatectomy (DP). **Methods** From January 2006 to June 2010, 57 DP were performed. Data regarding sex, age,

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comorbidities, ASA score, type of resection, pathological diagnosis, morbidity and mortality were collected in a prospective database. We evaluated demographics, clinical, surgical and pathological factors related to the presence of IPPH. Univariate analysis was carried out by using the Fischer's exact test and the Pearson chi square test. The multivariate analysis was performed by using logistic regression. **Results** Mean age of patients was 59.4±16.3 years. There were 33 (57.9%) females and 24 (42.1%) males. One or more comorbidities were present in 28 (50.9%) patients; 24 (42.1%) patients were ASA II, 29 (50.9%) ASA III, and 4 (7%) ASA IV. Only 15 (26.3%) procedures resulted spleen-preserving; 12 (21.1%) patients underwent extended resection. Laparoscopic approach was used in 21 (33.3%) cases. The closure of pancreatic remnant was carried out with manual suture, stapler, and stapler plus manual suture in 25 (43.8%),

12 (21.1%), and 20 (35.1%) cases, respectively. DP was performed for malignant disease in 35 (61.4%) cases. The morbidity and mortality rates were 56.1% and 0%, respectively. POPF was found in 13 (22.8%) patients (38.5% grade A, 61.5% grade B). PPH was registered in 13 (22.8%) patients (30.8% grade A, 69.2% grade B). Seven out of 13 (53.8%) patients developed an early PPH and 6 (46.2%) a late PPH. The univariate analysis showed that the presence and the severity of POPF were the only factor related to IPPH (IPPH rate was 37.5%, 20%, and 4.5% in patients with POPF grade B, POPF grade A, and in patients without POPF, respectively; $P=0.020$). Logistic regression demonstrated the only factor related to IPPH was the severity of POPF, with a significantly increased risk in patients with POPF B (OR=20; 95% C.I.: 2-200; $P=0.010$). **Conclusion** In our experience the POPF grade B increased significantly the risk of IPPB.

Pancreatectomies Associated To Vascular Resection (PAVR). Post-Operative Outcome

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Context PAVR are considered high risk operations. **Objective** To analyze the postoperative outcome in a 231 succession of PAVR performed at our institution and the role of complications in the long-term outcome. **Patients and methods** From 1987 to 2010, 231 PAVR were performed at our institution. An isolated venous resection (IVR) was done in 167 cases, an isolated arterial resection (IAR) in 25 and a combined arterovenous (AVR) in 39. **Results** The total morbidity and mortality rates were 42.8% and 7.3%, respectively. The IVR, IAR, AVR morbidity and mortality rates were 38.9% and 6.5%, 52% and 4%, 53.8% and 12.8%, respectively (P NS). A meaning difference was found comparing mortality in patients undergoing pancreaticoduodenectomy, total pancreatectomy and distal pancreatectomy. (4.8% vs. 13.5% vs. 3.1%; $P=0.04$). The age of the patients, number of resected

vessels, T diameter, number of lymph nodes exsected, pre-operative CA 19-9 value, and pre-operative jaundice, were not risk factors for postoperative complications. A diagnosis of ductal adenocarcinoma (DA) seems to be joined with low risk of complications *versus* other kinds of tumor (38.1% vs. 56.9%; $P=0.01$). No statistically significant differences in 1-, 3- and 5-year survival rates were found comparing DA patients with or without post operative complications (29%, 4% and 9% vs. 61%, 4% and 5%; P NS). **Conclusion** Patients with diagnosis of DA seem to have less postoperative complications compared to other kinds of neoplasia. Total pancreatectomy is associated with an higher risk of mortality. The development of postoperative complications have not an impact on long-term survival.

Molecular Mechanisms Underlying the Synergistic Interaction of the Novel Anticancer Drug Ukrain with Gemcitabine in Preclinical Models of Pancreatic Cancer

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Context Ukrain increased median survival in combination with gemcitabine compared to

gemcitabine alone (10.4 vs. 5.2 months; $P<0.001$) in unresectable PDAC [1]. There is compelling evidence

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that gene transcripts of determinants of gemcitabine activity could be used to tailor PDAC chemotherapy [2]. **Objective** Therefore, the aim of present study was to evaluate modulation of expression of two pivotal genes (hENT1 and dCK) involved in gemcitabine activity. **Methods** Preclinical studies were performed in PL45 and MIA PaCa-2 cells and primary cell cultures obtained from PDAC patients who underwent resection at Pisa University-Hospital (PPTCC78 and PPTCC109). Cells were treated with ukrain at IC₅₀s for 48 h. PCR amplification data were normalized to the GAPDH housekeeping, and gene expression was quantified using standard curve and $\Delta\Delta CT$ method, in which the amount of target, normalized to the control and relative to the calibrator (untreated control cells) was calculated as $2^{-(\Delta\Delta CT)}$. **Results** Ukrain positively modulates hENT1 expression all PDAC cultures ($P<0.001$). The $2^{-(\Delta\Delta CT)}$ analysis revealed a 2.8-fold mean increase ($P=0.001$) with respect to controls. In

PL45 and MIA PaCa-2 cells ukrain positively affects dCK expression as well. **Conclusion** To date a few options are available for PDAC treatment. Most gemcitabine-based regimens resulted in a limited disease control, and studies attempting to widen the therapeutic armamentarium against PDAC are warranted. Based on previous clinical data the ukrain-gemcitabine combination appears a promising regimen and our results provide the experimental basis for further testing of the ukrain-gemcitabine schedule in PDAC patients.

References

1. Gansauge F, Ramadani M, Pressmar J, Gansauge S, Muehling B, Stecker K, et al. NSC-631570 (Ukrain) in the palliative treatment of pancreatic cancer. Results of a phase II trial. *Langenbecks Arch Surg* 2002; 386:570-4. [PMID 11914932]
2. Giovannetti E, Del Tacca M, Mey V, Funel N, Nannizzi S, Ricci S, et al. Transcription analysis of human equilibrative nucleoside transporter-1 predicts survival in pancreas cancer patients treated with gemcitabine. *Cancer Res* 2006; 66:3928-35. [PMID 16585222]

Different Uptake of Ukrain Can Explain the Selective Effect Against Pancreatic Adenocarcinoma Cell Cultures *in Vitro*

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Context Current therapy for PDAC is surgery followed by adjuvant chemotherapy for early-stage and palliative chemotherapy for advanced disease. Gemcitabine is the standard drug in both adjuvant and palliative treatment. The new drug ukrain in combination with gemcitabine significantly increased the median survival of advanced PDAC patients with respect to gemcitabine alone (10.4 vs. 5.2 months; $P<0.001$). Furthermore, preclinical studies showed that ukrain had selective cytotoxic effects in cancer cell lines derived from different tumor types, but not in normal cell lines. **Objective** To evaluate the cytotoxic effects of ukrain in 2 primary pancreatic cancer cell lines (PPTCCs), fibroblasts derived from PDAC specimens (F-PDAC) and an immortalized epithelial ductal pancreatic cell line (HPNE). **Methods** Cytotoxicity was assessed by the CellTiter 96 kit (Promega) based on the cellular metabolism of the

tetrazolium compound XTT, which is reduced by living cells to yield a soluble formazan product in the presence of the electron coupling agent phenazine methosulfate, while the modulation of ukrain uptake in the medium was studied using the fluorescence property of ukrain with the AlphaDigiDoc software by UV light excitation (ULA-DC test). **Results** Cytotoxic effects of ukrain in PPTCCs were significantly higher than those observed in F-PDAC and HPNE cells (20% vs. 80% alive cells, at 10 μM ukrain concentration). Furthermore, the ULA-DC test revealed that PPTCCs cells consumed more drug than F-PDAC and HPNE cells (paired Student's test, $n=4$, $P<0.001$). **Conclusion** These data demonstrated the selective effect of ukrain in PPTCCs, which may be related to a different transport system or higher metabolism of the drug in PDAC, and warrant further investigations in order to support the possible role of ukrain in PDAC treatment.

Wirsungocele. A Rare Cause of Severe Necrotic Acute Pancreatitis

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Context Cystic dilation of the terminal portion of dorsal pancreatic duct in patients with pancreas divisum, i.e. Santorinicele, has been documented among patients with recurrent acute pancreatitis. Cystic dilation of the distal portion of the duct of Wirsung (Wirsungocele) is a very rare abnormality of the main pancreatic duct (2 cases published) and has been described as an incidental finding (one case) and as a cause of recurrent acute pancreatitis (one case). We report here a case of Wirsungocele associated with recurrent attacks of severe acute pancreatitis (AP).

Case report A 48-year-old male was referred to our surgical department for evaluation after two attacks of acute pancreatitis during the previous year. No risk factors for acute pancreatitis were present (no familial history of pancreatic diseases, no gallbladder stones, no alcohol or cigarettes abuse). CT after the first AP showed four fluid collections in pancreatic gland, anteriorly to the stomach and in pelvic region. The patient improved with conservative treatment and was discharged after 3 weeks. A second episode of PA recurred after 6 months and this also subsided with conservative treatment. A MRCP with secretin stimulation performed 1 year after the first PA showed

a saccular cystic dilation of main pancreatic duct in the head of the pancreas, just upstream to the papilla, measuring 15x5 mm. After infusion of secretin i.v. the saccular dilation showed a relevant increase (15x7 mm) that persisted 10 minutes after secretin stimulation. No abnormalities of main pancreatic duct and secondary ducts upstream to the cystic dilation was observed during all phases of MRCP with secretin stimulation. A marked decrease of size of pseudocysts previously described was reported. During ERCP macroscopic aspect of the papilla was normal; opacification of Wirsung duct demonstrated a 2 cm cystic dilation of the terminal portion of the pancreatic duct. There was no opacification of bile duct (no choledochocoele) and upstream main pancreatic duct was perfectly normal. A selective pancreatic sphincterotomy was performed. At 6-month follow-up no further attacks of acute pancreatitis were reported. **Conclusion** To our knowledge this is the first case described of severe acute pancreatitis due to the presence of cystic dilation of distal main pancreatic duct (Wirsungocele). Endoscopic selective pancreatic sphincterotomy could be, like in Santorinicele, the therapy of first choice in these patients.

Incidental, Non-Functioning, Very Small Pancreatic Endocrine Tumors.

What Is the Best Management? A Lesson From a Single Case

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Context Even if non-functioning pancreatic endocrine tumors (PETs) are usually discovered when they are large and symptomatic, in recent years the frequency of incidental cases increased. The natural history of these PETs is not well known, and surgery remains the treatment of choice. In PETs non functioning and very small (<1 cm) there is no evidence of the proper management: resection or follow-up may be the two possible options. We report a case of an incidental, very small, non-functioning PET in whom this dilemma was discussed with a multi-disciplinary approach. **Case report** A 39-year-old asymptomatic female patient was admitted to our department because of the presence of small pancreatic lesion localized in the head of the pancreas. Two years before the admission to our hospital, an US detected a solid lesion

of 8x6 mm in diameter in the head of the pancreas, which was subsequently confirmed by EUS. At follow-up EUS study carried out one year later, this examination confirmed the presence of the pancreas head mass without increase in size. A FNA was performed and pathological features were suggestive of PET. Finally, a CT scan confirmed the pancreatic solid lesion in the pancreatic head. Considering the age of the patient, a surgical approach was suggested. An US examination was performed during the operation and it allowed to localize the solid, small (<1 cm) lesion on the posterior surface of the head of the pancreatic gland. Ultrasonographically guided enucleoresection was performed and the pathological features were compatible with a well-differentiated (G1) PET having benign biological behavior (size: <1 cm; Ki-67: <2%;

no angioinvasion). Postoperative course was characterized by the onset of acute pancreatitis requiring only conservative medical treatment; the patient developed also a grade B pancreatic fistula treated medically. **Conclusions** In our opinion, young patients affected by non-functioning, very small (<1 cm) PETs, surgical option is demanding because the

high risk of malignant progression of the tumor. Enucleoresection can be performed to avoid extended pancreatic resection and to preserve pancreatic parenchyma as much as possible. We should also underline that enucleoresection when carried out presents risk of complications such as the development of both acute pancreatitis and pancreatic fistula.

Risk Factors in Resected Pancreatic Cancer.

A Single Centre Experience

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Context The aim of the study was to determine risk factors of recurrence in resected pancreatic cancer.

Methods We retrospectively analyzed 43 patients who underwent pancreatic resection for ductal adenocarcinoma, from January 2006 to December 2009. Demographic (age, sex), surgical (type of resection), pathological data (grading, TNM stage, lymph node ratio, R status, perineural and vascular invasion) and type of therapy (surgery alone *versus* surgery plus different adjuvant treatment) were evaluated. Adjuvant chemotherapy was performed in 24 patients with R0 status: 19 received gemcitabine alone (GEM) (1,000 mg/m² days 1, 8, 15 every 28) and 5 GEM plus cisplatin (CDDP) (75 mg/m² day 1 every 28). Radiotherapy was performed in 9 patients with R1 status: 6 associated with GEM alone and 3 with GEM plus CDDP. **Results** Overall survival (OS) and disease free survival (DFS) were (mean±SD) 23.3±3.8 and 12.8±1.2 months, respectively. Recurrence of disease

occurred in 31 out of 43 patients (72.1%) with local relapse in 11 (35.5%) and distant metastases in 20 patients (65.5%). Among the prognostic factors evaluated, lymph node ratio and grading were significantly related to recurrence (lymph node ratio P=0.010; G1 *vs.* G2-G3, P=0.012). Regarding to postoperative treatment there were no significant differences between surgery alone *versus* surgery plus adjuvant therapy (median DFS: 16.8 *versus* 11 months; P=0.103). Risk of recurrence was increased in patients treated with chemo-radiotherapy compared those who received chemotherapy or surgery alone (P=0.042 and P=0.09, respectively). **Conclusions** The risk of recurrence was higher in patients treated with surgery plus chemoradiotherapy if compared to the others, probably because the combination treatment with additional radiotherapy was performed in R1 status patients.

Variable Number Tandem Repeat (VNTR) Gene Polymorphism of CYP2E1 in Patients with Pancreatic Adenocarcinoma (PA)

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Context The genetic polymorphism is considered a major source of variability, influencing the levels of gene expression. Cytochrome P450 2E1 (CYP2E1) is a mixed-function oxidase involved in the metabolism of many endogenous and exogenous substances (ethanol, chemical carcinogens) in the hepatic and pancreatic tissue. CYP2E1 gene polymorphisms can cause various

abilities of metabolize xenobiotic substances within a population with consequent increased susceptibility to various diseases, including cancer. One of the polymorphisms of the CYP2E1 gene is a variable number tandem repeat (VNTR) of some sequences in its 5' flanking region. **Method** VNTR genotype CYP2E1 was determined by RFLP-PCR performed on

DNA extracted from peripheral blood lymphocytes and paraffin embedded tissue of Central-Western Sicilia population with PA, to confirm or exclude a correlation between certain genotypes and specific disease. A population of university students, without specific overt disease, was used as control. **Results** CYP2E1 VNTR A2/A2 was the modal genotype found in all subjects, while CYP2E1 VNTR A2/A4 was the least represented in both populations. The A2/A3 genotype was different between patients with pancreatic cancer and healthy subjects, suggesting a correlation between this genotype and pancreatic cancer. Recent studies

indicated A2 allele might be associated with a negative regulation of the gene and nothing about it has been reported for the allele A3. **Conclusion** Our preliminary data indicate an association between genotype A2/A3 and PA and they allow us to hypothesize that the A3 allele is associated with low activity of the CYP2E1 gene. Consequently, individuals with this allelic association may have inadequate ability to metabolize toxic xenobiotic substances: a condition that might increase susceptibility to develop neoplasms, including PA.

Exacerbating Effect of Protease-Activated Receptor 2 in Macrophage-Monocyte During the Progression of Acute Pancreatitis. Hints for Systemic Complications in Clinics?

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Context Proteinase-activated receptor-2 (PAR-2) belongs to a family of G protein-coupled receptors activated by tethered ligand sequences within the N-terminal. It is known that one of the pancreatic enzymes, trypsin, modulates many biological processes by acting on specific PAR-2. PAR-2 is distributed throughout the gastrointestinal system including the pancreas and may be involved in the inflammatory process of acute pancreatitis (AP). It is uncertain whether pancreatic PAR-2 plays a protective or an injurious role in acute pancreatitis. **Objective** The aim of this study is to attempt further insights into the role of PAR-2 in acute pancreatitis in two different experimental AP rat model. **Methods** We induced mild pancreatitis by using cerulein to induce acute edematous pancreatitis (AEP) and severe pancreatitis by using DL-ethionine and a protein-deficient meal to induce acute necrotizing pancreatitis (ANP). Gabexate mesylate (GM) (10 or 30 mg/kg) was injected intraperitoneally to the AEP rats every 12 hours to investigate the effects of protease inhibitor on pancreatitis and PAR-2 activation. Camostat mesylate (CM) (200 mg/kg) was orally administered to ANP rats

every 24 hours. **Results** Immunoreactive PAR-2 was most prominent in ED1-positive macrophages/monocytes in ANP and infiltration of PAR-2-positive macrophages was significantly inhibited by CM. PAR-2-positive macrophages/monocytes were observed in AEP. Plasma IL-8 levels increased in ANP and were inhibited by CM. Amylase secretion from acinar cells was elicited in a dose-dependant manner by SLIGRL-NH₂, an amino-terminal residue of PAR-2-tethered ligand, indicating that PAR-2 may exist in acinar cells and may mediate amylase secretion. **Conclusion** Contrary to very recent findings in PAR-2 knockout mice [1], our present studies *in vivo* would suggest that the PAR-2 system of macrophages/monocytes is indeed activated and involved in the exacerbation of acute pancreatitis, presumably via release of cytokines such as IL-8.

References

1. Namkung W, Yoon JS, Kim KH, Lee MG. PAR2 exerts local protection against acute pancreatitis via modulation of MAP kinase and MAP kinase phosphatase signaling. *Am J Physiol Gastrointest Liver Physiol* 2008; 295:G886-94. [PMID 18755806]

Intensive EPA/DHA and Selenium Supplementation in Alcohol-Induced Chronic Pancreatitis. A Safe and Rationale Approach

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Context Patients with chronic pancreatitis (CP) suffer from malabsorption and complex while subtle

nutritional deficiencies. Few years ago, it has been shown that docosa-hexaenoic-acid (22:6(n-3)) (DHA)

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may be significantly decreased in the CP with associated diabetes mellitus. This abnormality has been advocated for by the effects of diabetes mellitus and by selenium deficiency. We have also recently shown that patients with alcohol-induced chronic pancreatitis (AICP) without overt diabetes would show a DHA deficiency associated with impaired essential fatty acids index (16:1(n7)/18:2(n6)). **Objective** The aim of the present investigation was to study the effect of EPA/DHA and selenium supplementation in patients with AICP. **Methods** Sixteen clinically-stable patients with proven AICP, abstinent for at least 5 years and without major associated diseases or malnourishment were recruited. A dietary questionnaire was used at the entry and re-assessed at the end of the study using the web-based version of the National Institutes of Health Diet History Questionnaire to assess diet history over the past 3 months and along the study period. Subjects were advised not to use any multivitamin supplement, fortified food or fish oil supplement while maintaining their usual diet. A 3-week wash-out period from such use was observed when present. Patients were given a 8-weeks supplementation with high quality 2 cp/day of eicosapentaenoic acid-EPA/DHA (Mega EPA/DHA®: EPA 720 mg/DHA 480 mg, LEF, Ft. Lauderdale,

USA) during meals and 2 tab/day of a high-bioavailability selenium (SuperSelenium Complex®: Se-methylselenocysteine, SelenoPure™, L-selenomethionine, sodium selenate, selenodiglutathione 200 mg and d-alpha tocopheryl succinate 30 IU, LEF, Ft. Lauderdale, USA). **Results** Plasma DHA and selenium were significantly low in all patients and normalized after supplementation (P<0.01). Plasma Se was inversely correlated with RBC omega6 polyunsaturated FA (PUFAs) and positively with omega3 PUFAs. Plasma Se, RBC omega3 PUFAs, and EPA increased with supplementation (P<0.05). Plasma and 24 h urinary F2-isoprostanes were within normal limits in CP patients and did not change after supplementation. **Conclusion** Given the multifactoriality of the disease and the subtle and progressing clinical deterioration, such dietary intervention seems an effective integrative therapeutic tool within the complex fatty acid profile abnormalities occurring in these subjects. Moreover, this supplementation seems safe and, probably due also to the selenium-combined schedule, does not increase lipid peroxidation markers despite the likely concomitant ongoing oxidative stress abnormalities, as we have already shown in prior studies.

Pancreatic Cystic Lesions. Increasing Diagnosis in an Italian Surgical Department of Middle-High Volume for Pancreatic Resections

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Context Pancreatic cystic lesions are increasingly recognized due to expanding use of cross-sectional imaging. High-volume pancreatic centers reported an increase of endoscopic ultrasound procedures and surgical operations for these lesions **Objective** To assess the incidence and the management of pancreatic cystic lesions in an Italian department of general surgery of middle-high volume for pancreatic resections. **Methods** From January 2004 to June 2010 all patients who underwent endoscopic ultrasound for pancreatic cystic lesions were identified and analyzed. **Results** In the study period 73 patients were evaluated. Patients' mean age was 67 years and 65% were women. The identification of pancreatic lesions was incidental in most of the cases. The number of endoscopic ultrasound procedures was 1 in 2004 and, respectively, 2, 5, 12, 20, 18 and 15 in the following

years until 2010. Sixteen patients underwent surgical resection (10 pancreaticoduodenectomies, 6 distal pancreatectomies). Histopathological analysis showed intraductal papillary mucinous neoplasm in 5 cases, mucinous cystic neoplasm in 3, serous cystic neoplasm in 3, cystic ductal adenocarcinoma in 3, solid pseudopapillary neoplasm in 1, hemorrhagic pseudocyst in 1. **Conclusions** The increasing incidence of pancreatic cystic lesions has been reported in dedicated high-volume pancreatic centers. This study demonstrates an increase in recognition, endoscopic ultrasound procedures and surgical resections for these lesions also in a general surgery department of middle-high volume for pancreatic resections like ours. The evaluation of cystic lesions of the pancreas is challenging and international consensus guidelines are needed.

Aggressive Surgical Approach in a Locally Advanced Pancreatic Endocrine Tumor. Case Report

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Context Non-functioning pancreatic endocrine tumors (PETs) are often diagnosed at an advanced stage when they are large in size, locally advanced or metastatic. However, the long-term course of the disease justifies in selected cases an aggressive surgical approach in order to improve the survival. We report a case of locally advanced, non-functioning PET in whom this approach was justified. **Case report** A 65-year-old, obese woman, with the recent onset of impaired glucose tolerance, but without other symptoms was admitted at the Department of Internal Medicine of our hospital. An US of abdomen revealed the presence of a poorly vascularized, very large, round lesion of the pancreatic tail, probably invading adjacent organs as well as the left kidney and the adrenal gland. These findings were confirmed by CEUS and CT scan. A percutaneous US-guided FNAB showed the presence of a well differentiated endocrine carcinoma with Ki-67 of 2.8%. A preoperative PET with 68-Ga-DOTANOC was also performed to evaluate the presence of somatostatin receptors and the extension of the disease. The patient underwent surgery for a locally advanced, non-functioning PET (T4). An en-bloc left pancreatectomy (with resection of the pancreas to the

right side of the portal-mesenteric trunk) with splenectomy, left nephrectomy and left adrenalectomy was performed. The histological examination showed the presence of a well differentiated endocrine carcinoma of the pancreas with invasion of peripancreatic fat tissue, left kidney and left adrenal gland (T4). Nodal metastasis was found in 6 of 31 lymph nodes (N1). Resection margins were free from carcinoma (R0). The pTNM stage was IIb and Ki-67 was 6.1%. The postoperative course was complicated by a grade B pancreatic fistula with a fluid abdominal collection successfully treated with CT-guided percutaneous drainage (grade IIIa according the Clavien-Dindo classification for surgical complications). The patient was discharged 18 days after surgery. Four months from the surgery the patient is good general health and free of disease recurrence. **Conclusion** In patients with non-functioning, well-differentiated PETs invading adjacent organs as well as left kidney and adrenal gland, with positivity to somatostatin receptor and with Ki-67 <10%, an aggressive surgical approach is justified, in high volume center, to improve long-term survival.

GemOx and Ovarian Pancreatic Cancer Metastasis (PC)

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Context We report a case of clinical benefit and RP with GemOx in patient with cystadenocarcinoma of pancreas with ovarian metastasis. **Case report** In July 2008 a 42-year-old woman complained of abdominal pain and constipation. The CT scan and the MR showed the presence of two bilateral ovarian mass with pancreatic extension. The patient arrived then to our hospital and ECOG PS was 2. She underwent bilateral ovarian and womb resection. During surgery peritoneal carcinosis, a pancreatic mass and multiple abdominal lesions were found. Multiple biopsies of pancreatic lesion and other abdominal lesions documented mucinous cystadenocarcinoma of pancreas, with ovarian and peritoneal metastases. In December 2008 the patient started chemotherapy (CHT) with gemcitabine 1000 mg/m²/dL and oxaliplatin 100

mg/m²/d2 every 2 weeks (GemOx). After 6 cycles of CHT a CT scan showed a stable disease. Clinical conditions were good (ECOG 0) so we decided to continue the medical treatment with other 6 cycles of CHT. In August 2009 a CT scan showed a reduction of the abdominal mass, and a surgical resection was then possible. The patient underwent distal pancreatic resection, regional lymphadenectomy and splenectomy. Pathologic examination documented biliopancreatic well differentiated adenocarcinoma. Surgical margins presented malignant cells and mucoid areas without cells. After surgery we decided to continue CHT with gemcitabine as "adjuvant treatment" for other 3 cycles, CT scan showed no disease, clinical conditions were good and the patient stopped the treatment. Actually there is no evidence of relapse. **Conclusion** As

reported in literature, GemOx is associated with improvement in PFS and clinical benefit in patient with advanced pancreatic cancer. This is an interesting case

where GemOx leaded inoperable pancreatic cancer to a operable cancer.

Pancreatic Secondary Lesions from Renal Cell Carcinoma

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Context Metastatic lesions to the pancreas are rare: less than 5% of pancreatic cancers are metastatic. The most frequent metastases are from renal cell carcinoma (RCC). They typically occur long time after nephrectomy. Their behavior is considered indolent and if the lesion is single, the main option is surgical resection. **Objective** The aim of this study was to analyze the clinical features of patients affected by pancreatic metastases of RCC observed in our department. **Methods** We collected clinical data of patients with pancreatic metastasis from RCC, observed in our department from January 2004 to December 2009. Follow-up to June 1st, 2010. We analyzed also: type of surgery, complications, follow-up and disease free survival. **Results** We observed 13 patients (8 males, 5 females) averaging 66 years. All patients had a previous nephrectomy before the diagnosis of the pancreatic lesion (range: 0.5-22 years; median: 6 years; mean: 8.5 years). In only one case the pancreatic lesions were synchronous with the renal cancer, but in 2 cases within 1 year, the pancreatic lesion was detected by CT imaging. In 3 additional

cases, where abdominal CT scans were available, we reviewed the scans and we found that the pancreatic lesion was present 2, 3 and 6 years before the diagnosis of recurrent disease, respectively. Nine patients were resected (2 pancreaticoduodenectomy, 1 duodenum-preserving pancreatic head resection, 5 left pancreatectomy and 1 central pancreatectomy). In these patients we had five complications: 3 pancreatic fistula, 1 lethal pulmonary embolism, 1 splenic infarct. The mean follow-up was 27.2 months. Four patients died (1 pulmonary embolism, 2 for progression of disease, 1 for a non-related cause). Among the other 7 resected patients, 4 are alive without disease, one patient has pulmonary metastases since diagnosis, one developed hepatic metastases, and one thyroid secondary lesions. The mean disease free survival was 26.7 months. **Conclusion** Pancreatic metastases from RCC are surgically curable with a good survival. They are often asymptomatic and occasionally overlooked despite follow-up with serial CT-scan. We are not able to predict in which patients they will have an aggressive behavior with early relapse.

Enucleation of Benign Tumors of the Pancreas. Thirty-Five Year Experience in a Single Center

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Context Tumor enucleation is a surgical procedure traditionally reserved to treat small benign tumors of the pancreas. Complication rate of this operation in small series of patients is reported to be high. **Objective** To evaluate complications of pancreatic tumor enucleation in a series of patients collected in 35 years in a single center. **Methods** From 08/1975 to 12/2009, 60 patients underwent enucleation for benign or uncertain behavior tumors of the pancreas. Five patients were excluded from the study because of an associated procedure of pancreatic resection. In 55 patients we retrospectively evaluated: age, sex, histotype, site, size, operative ultrasound, morbidity, mortality, length of hospital stay and postoperative complications. **Results** Fifty-five patients (24 males

and 33 females) averaging 53 years (range: 0.2-86 years) were included in the study. Three cases had two surgical enucleations due to the onset of a new lesion 4 to 11 years after the first operation. Overall 6 cases had a previous pancreatic operation; in three cases an additional surgical procedure on the GI tract was performed. Finally, the operative procedures were 58, one of which with a double enucleation. Mean size of the lesion was 2.0 cm (range: 0.5-15 cm), 53.4% in the head of the pancreas. Fifty-two out of 59 (88.1%) were endocrine tumors; insulinomas were 36/59 (61.0%). Operative ultrasound was performed in 37 cases (63.7%). Mean hospital stay was 15.1 days (range: 6-54 days); in the last 10 years (2000-2009) median hospital stay was 9 days. Main surgical complications

were found in 20/58 cases (34.5%): 11 pancreatic fistulas (18.9%), 3 acute pancreatitis (5.2%), one of these lethal (overall mortality 1.7%) and 4 abdominal fluid collections (6.9%) and 2 cases (3.5%) with other complications (1 duodenal fistula and 1 abdominal wall

dehiscence). **Conclusions** Enucleation of benign tumors of the pancreas is a simple pancreas sparing operation but a complicated course in 1/3 of patients is still to be expected.

Solid-Pseudopapillary Tumor of the Pancreas in Males.

Report of Two Cases

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Context Frantz's tumor is a rare neoplasm of young females (averaging 25 years; female/male ratio: 10/1) of the body/tail of the pancreas. About 1,300 cases are described in the literature. They usually have low malignant potential and mostly behave benign.

Objective We report two cases of solid pseudopapillary tumor of the pancreas occurring in two adult men. **Methods** We respectively review the clinical data of two patients observed in January 2007 and March 2010. **Patients** Case#1: A 58-year-old male. In December 2006, due to dyspepsia and palpable mass in left hypochondrium the patient underwent abdominal ultrasound that showed a cystic neoplasm with irregular wall and unhomogeneous liquid content and septa of 12.3 cm size, close to the pancreatic tail. A CT scan confirmed a 12 cm cyst of tail of the pancreas, with thin wall and few solid parietal nodules and dense septa. CEA and CA 19-9 were in the reference range. A FDG-PET scan showed uptake of the tracer in an area of 2 cm around the cyst with a high SUV (3.4; reference range: 0-2). The clinical diagnosis suggested a mucinous cystadenocarcinoma. On January 2007 the patient underwent left pancreatectomy. Pathologic examination showed a solid-pseudopapillary tumor of the tail of the pancreas 11.5 cm in size with hematic content and two solid nodules (max size: 2.5 cm).

Mitotic index was 3 x10 HPF and Ki-67 was 4.5%. Margin was free. Patient was discharged in the 10th postoperative day. The patient developed later a fluid collection and then a symptomatic pseudocyst of 6.3 cm so underwent in December 2007 a cyst-jejunostomy. Since then the patient is alive and well without disease at a follow-up of 41 months after resection. Case#2: A 75-year-old male. In February 2010, incidental finding at ultrasound of oval solid lesion close to spleen hilum. CT scan showed a solid, hypodense lesion with septa 4.5 cm in the tail of the pancreas. At MRI intensity was partially cystic with peripheral enhancement and with septa within the cyst. FDG-PET was negative. CA 19-9 was negative. The clinical diagnosis suggested a serous cystadenoma and indication for surgery was location close to the splenic hilum and the large size of the lesion. In May 2010 the patient underwent a left pancreatectomy. Pathology showed a 4.5 cm solid-pseudopapillary tumor with central hemorrhagic area, completely resected. Mitosis were absent, and immunocytochemistry was positive to B-catenin. The course was uneventful and the patient was discharged in 8th postoperative day. **Conclusion** Frantz's tumor is an uncommon pancreatic neoplasm. Advanced age and male sex do not exclude the occurrence of this tumor, although rare.

Successful Percutaneous Drainage of Post-Acute Pancreatitis Pseudocyst. How Did It Turn Out?

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Context Last year, at the XXXIII National Congress of AISP, we reported a case of severe AP due to hypertriglyceridemia, complicated by a large pseudocyst treated with percutaneous drainage. **Case report** Six months later the pseudocyst percutaneous drainage, the patient become symptomatic for gastric outlet

(satiety, nausea and vomiting, pain). Abdominal CT demonstrated an uncomplicated mature pseudocyst of 16 cm diameter of the body and tail of the pancreas, with bulging into the posterior gastric wall. The patient underwent a cystogastrostomy without complication. After 3 weeks, the patient was readmitted due to

abdominal pain and fever. Blood tests and imaging techniques (US and CT scan) showed a sepsis of the cystic cavity. The patient was treated with ceftriaxone and ciprofloxacin for two weeks with complete remission of the fever. However, fever recurred within

one week. At this, the patient was advised to change decubitus frequently in order to maximize the complete drainage of the cystic cavity. This procedure, even if anecdotal and not evidence-based, appeared successful and the patient is now in good healthy condition.

Pancreaticoduodenal Fistula Associated with Severe Pancreatitis. Should We Operate?

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Context Antibiotic therapy, guided percutaneous drainage, nasojejunal tube for enteral feeding and markedly delayed surgical “rescue” have been reported for severe pancreatitis, but few reports are available on the management of pancreaticoduodenal fistula associated with the acute pancreatitis. **Methods** We reported our experience of two cases with spontaneous pancreaticoduodenal fistula associated with severe pancreatitis and we focused on the diagnosis and treatment of this complication. **Results** The two cases presented an acute necrotizing pancreatitis and the CT scans revealed air bubbles making the impression of pancreatic abscesses. As reported by some authors we started a conservative management of the infected necrosis complicating the severe acute pancreatitis and we placed guided percutaneous drainages of the

necrotic areas. Abdominal radiography with gastrograffin through the percutaneous drainage showed the presence of a pancreaticoduodenal fistula. We continued to treat conservatively the patients without surgery: antibiotic therapy was applied according to the antimicrobial activity found in the collection, a nasojejunal tube for enteral feeding was placed after the duodenal fistula and the percutaneous drainages were controlled to be functioning. After two months of conservative treatment, the two patients were discharged with oral diet and without any drainage. **Conclusion** The correct diagnosis of pancreaticoduodenal fistulae vs. pancreatic abscesses is an important pitfall to decide the correct management of these patients, who may survive with conservative treatment.

Predicting Factors of Late Post-Pancreatectomy Hemorrhage After Pancreaticoduodenectomy

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Context Postoperative hemorrhage (PPH) is one of most severe complications after pancreaticoduodenectomy (PD). **Objective** To evaluate the presence of risk factors related to late PPH (LPPH) after PD. **Methods** From January 2006 to June 2010, 85 PD were performed. Data regarding sex, age, co-morbidities, ASA score, type of resection, characteristics and management of pancreatic stump, pathological diagnosis, morbidity and mortality were collected in a prospective database. These data were evaluated as potential risk factors related to the presence of LPPH. Univariate analysis was carried out with Fischer's exact test and Pearson Chi square test.

The multivariate analysis was performed using logistic regression. **Results** Mean age of patients was 66.3±10.2 years. There were 34 (40%) female and 51 (60%) male. One or more co-morbidities were present in 58 (68.2%) patients; 19 (22.4%) patients were ASA II, 58 (67.1%) ASA III and 9 (10.6%) ASA IV. We performed 70 (82.4%) PD pylorus preserving and 15 (17.6%) PD according to the Child operation. An extended resection was carried out only in 8 (9.4%) cases. The main pancreatic duct was dilated only in 35 (41.2%) cases. The texture of pancreatic stump was hard in 36 (42.4%) cases. A pancreaticojejunostomy was performed in 58 (68.2%) patients. At pathological

examination a malignant disease was present in 74 (87.1%) cases. The morbidity, mortality, and reoperation rate were 67.1%, 4.7%, and 5.9% respectively. Twenty-six patients (30.6%) had POPF (11.5% grade A, 80.8% grade B, and 7.7% grade C). The PPH was detected in 31 (36.5%) patients (9.7% grade A, 28.2% grade B, and 4.7% grade C). PPH were early in 5 (16.1%) and late in 26 (83.6%). The univariate analysis showed that the presence of POPF

was the only factor related to LPPH rate (53.8%, and 46.2% in patients with and without POPF, respectively; $P=0.004$). Logistic regression demonstrated the only factor related to LPPH was the presence of POPF, with a significantly increased risk in patients with POPF B (OR: 12; 95% CI: 3-155; $P=0.002$). **Conclusion** The POPF grade B increased significantly the risk of LPPH after PD.

Pancreaticoduodenectomy for Infiltrative Duodenal Gastrointestinal Stromal Tumor Mimicking Pancreatic Head Neoplasm

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Context The origin of gastrointestinal stromal tumor (GIST) has been recognized to Cajal's cells and more recently to multipotent stem cells. Only 3-5% of GIST occurs in the duodenum and up to now very few cases of primary pancreatic GIST have been described. Due to this peculiar anatomical proximity, it is difficult to differentiate the organ from which the GIST lesion originates. **Case report** A 79-years-old female presented with anemia. Upper endoscopy showed an intraluminal and erosive mass in the second duodenal portion close to papilla of Vater. Endoscopic biopsy revealed aspecific signs of inflammation. Abdominal CT scan demonstrated a 4x5 cm mass of the pancreatic head dishomogeneously enhanced on contrast-enhanced images. On the basis of these findings, the diagnosis of pancreatic tumor with infiltrative signs to duodenal wall was strongly suspected. No jaundice or signs of biliary dilatation were observed. The patient underwent to pancreaticoduodenectomy. Intraoperatively, the tumor showed transmural growth towards the pancreas, without vascular involvement

and lymph node abnormalities. Immunohistochemical findings with positivity for CD 117/c-kit antigen confirmed the GIST diagnosis. Microscopically the lesion revealed a duodenal origin with pancreatic infiltrative aspects. Histologically, the tumor presented spindle cells with high mitotic rate, more than 5 per 50 high power fields. The patient was recovered without complications and subsequently referred to oncologist. No radiological signs of recurrences were observed after 6 months of clinical follow-up. **Conclusion** Here we report our first case of duodenal GIST which was assessed as a pancreatic head tumor, successfully treated with pancreaticoduodenectomy. Endoscopy may be diagnostic in duodenal GIST, especially for well-defined tumor with centrally ulcerated umbilication. This was not our case. Unfortunately, the lesion did not show the typical radiological and endoscopic pattern. The presented case underlines the difficulties of a correct preoperative diagnosis in such uncommon clinical condition where infiltrative duodenal GIST might mimic a pancreatic head tumor.

Intraoperative Ultrasound with Contrast Medium in Resective Pancreatic Surgery. A Pilot Study

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Context The introduction of contrast-enhanced ultrasound has been a major innovation in liver and pancreatic imaging. Previous studies validated its intraoperative use during liver surgery, while there is a lack of data regarding its use during pancreatic surgery. **Objective** To prospectively evaluate the possible role

of contrast-enhanced intraoperative ultrasound (CEIOUS) during resective pancreatic surgery for primary lesion characterization and intraoperative staging. **Methods** Thirty-four patients (70% males, mean age 72.4 years) were candidate to pancreatic surgery between October 2006 and July 2009. All

patients underwent intraoperative ultrasound with intravenous injection of 4.8 mL sulphur-hexafluoride microbubbles. Location of primary tumor, relation to the main vessels, contrast medium uptake modalities, presence of liver metastases and multifocal pancreatic involvement were evaluated. The majority of operations were pancreaticoduodenectomies (70.6%) performed for pancreatic ductal adenocarcinoma (64.7%). **Results** In 6 patients (17.6%) intraoperative ultrasound provided additional data and impacted on surgical decision-making, by detecting unknown liver metastases (4 patients), unknown liver lesion (characterized as hemangioma by CEIOUS, in 1 patient) and a second pancreatic lesion (1 patient). Intraoperative findings regarding location of primary

tumor, relation to the main vessels and lesion characterization did not differ from preoperative imaging. **Conclusions** In our preliminary experience CEIOUS seems to represent a valuable tool: in patients with pancreatic adenocarcinoma for optimizing detection and characterization of liver metastases in spite of accurate preoperative imaging, thus possibly avoiding unnecessary resections; in patients with neuroendocrine neoplasms, for detecting possible further pancreatic and hepatic lesions, increasing radicality. If confirmed in larger series, CEIOUS could be useful for establishing a more accurate operative decision-making in patients undergoing pancreatic surgery for tumors.
