

ORAL COMMUNICATIONS

Spectrum of MRCP Findings in Patients with Asymptomatic Hyperamylasemia and/or Hyperlipasemia

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Context The spreading of the serum pancreatic enzymes dosage in clinical practice results in a ever-increasing number of patients with elevated amylase and/or lipase serum levels, without clinical evidence of pancreatic disease. A recent study shows that MRCP yielded pancreatic findings in more than 50% of patients with asymptomatic pancreatic hyperenzymemia [1]. **Objective** Aim of this study was to assess the spectrum of MRCP findings in patients with asymptomatic hyperamylasemia and/or hyperlipasemia. **Patients and Methods** From April 2004 to March 2007, we prospectively enrolled 48 asymptomatic patients (32 males and 16 females, mean age 46±12 years) with a documented (at least in three occasions) increase of serum amylase (16 patients), serum lipase (4 patients) or both (28 patients) over the upper normal limit. Patients who drank more than 40 g/day of alcohol were excluded. All patients underwent MRCP before and after secretin stimulation. Radiological images were individually analyzed by two radiologists without knowledge of the results of the standards of reference or the final diagnosis. Discordant interpretation were settled by consensus.

Results Fourteen out of 48 patients (29%) had a normal pancreatic ductal tree. In the remaining 34 patients (71%), 2 patients (4%) showed santorinicele after secretin stimulation, 7 patients (15%) pancreatic changes compatible with IPMN, 6 patients (12%) ductal changes consistent with chronic pancreatitis, 2 patients (4%) had a focal stenosis with a final diagnosis of endocrine tumor and 17 patients showed an altered MRCP after secretin stimulation consistent with sphincter of Oddi dysfunction. Anatomic abnormalities were observed in 12 patients (25%) (11 pancreas divisum and 1 annular pancreas), 4 of whom showed a dilated main pancreatic duct. **Conclusion** Patients with asymptomatic hyperamylasemia and/or hyperlipasemia showed abnormal MRCP in more than 70% of cases. A long term follow-up is necessary to set up the clinical meaning of MRCP alterations.

Reference

1. Mortelé KJ, Wiesner W, Zou KH, Ros PR, Silverman SG. Asymptomatic nonspecific serum hyperamylasemia and hyperlipasemia: spectrum of MRCP findings and clinical implications. *Abdom Imaging* 2004; 29:109-14. [PMID 15160763]

Pancreatic Duct Stents in the Prophylaxis of Post-ERCP Pancreatic Damage: A Systematic Analysis of Benefits and Associated Risks

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Context The prophylactic use of pancreatic stent placement is becoming standard practice, although several shortcomings are present in the available literature. **Methods** Efficacy of pancreatic stenting for prevention of post-ERCP pancreatitis (PEP) was evaluated by a meta-analysis of 6 controlled studies; 12 additional, uncontrolled studies were searched for rates of associated risk. **Results** The overall quality of these studies was unsatisfactory, as two studies scored 0, and the remaining 4 studies had a mean score of 3.25. PEP developed in 16.5% of controls, and in 5.1% or 9.6% in the stent group at the per-protocol (PP) or intention-to-treat (ITT) analyses, respectively. By analyzing only the four randomized trials, PEP developed in 24.1% of controls, and in 6.1% or 12.0% of stented patients at the PP or ITT analyses. The risk was significantly lower in the stent group as compared with controls: OR=0.44 (CI: 0.24-0.81). The absolute risk reduction is 12.0 (CI: 3.0-21.0), the number needed to treat 8

(CI: 5-34), and the publication bias 2. Odds ratio for mild to moderate PEP were reduced in the stent group (OR=0.537, CI: 0.283-1.021), as where those for severe PEP (OR=0.123, CI: 0.021-0.726). Non-pancreatic complications were 4.2%, and included early stent migration (1.4%), perforations (0.4%), bleeding (1.4%), and infections (1.0%). In the 12 retrospective, uncontrolled reports PEP was reported in 408 of 3,264 (12.5%) patients who had a pancreatic duct stent placed, and non-pancreatic complications in 4.2% of patients and included early stent migration (13 events in 943 patients, 1.4%), perforations (12 events in 3,205 patients, 0.4%), bleeding (16 events in 1106 patients, 1.4%), and 9 infections in 859 patients (1.0%). Overall, the rate of non-pancreatic complications was 4.2%. **Conclusion.** Available trials show benefit for pancreatic stenting in the prophylaxis of PEP, but more randomized studies are needed before endorsing a routine use of this endoscopic procedure.

Sclerosing Cholangitis, Autoimmune Chronic Pancreatitis and *Situs Viscerum Inversus Totalis*: An Incidental Association?

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Context Autoimmune pancreatitis is a rare case of pancreatitis which is becoming increasingly recognized. It has been described as a single disease or as a part of the spectrum of autoimmune gastrointestinal or systemic syndrome. The association between autoimmune pancreatitis and *situs viscerum inversus totalis* has never been described before in literature, only few cases of pancreatic ductal adenocarcinoma and *situs viscerum inversus totalis* are reported. **Case report** A 76-year-old man with *situs viscerum inversus totalis* previously diagnosed, was

admitted in our Institute with jaundice, fever and abdominal pain. Laboratory findings were normal except for a marked increase in total and conjugated serum bilirubin levels (7.72 mg/dL and 5.75 mg/dL, respectively), alkaline phosphatase and GGT. Serum levels of CA 19-9 and CEA were respectively 198 U/mL (reference range: 0-37 U/mL) and 2 ng/mL (reference range: 0-6.5 ng/mL). US, CT scan and ERCP showed a stenosis of distal common bile duct with marked intra- and extra-pancreatic duct dilatation. A common bile duct cancer was suspected.

Surgical approach was planned and pylorus-preserving pancreaticoduodenectomy was performed. The postoperative course was uneventful. Pathological examination of the resected specimen showed sclerosing cholangitis of the common bile duct with mild-moderate dysplasia, eosinophilic enteritis, lymphocito-eosinophilic chronic pancreatitis with PanIN 1-2-3. **Conclusion** To our knowledge this is the first case of

association of sclerosing cholangitis, autoimmune chronic pancreatitis and *situs viscerum inversus totalis* reported in literature. Differential diagnosis between sclerosing cholangitis and bile duct cancer is sometimes difficult. The association between sclerosing cholangitis and autoimmune chronic pancreatitis is a well known entity while we believe that *situs viscerum inversus totalis* is an incidental association.

Multiple Drains after Pancreaticoduodenectomy: An Old-Fashioned Choice?

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Context Pancreatic fistula after pancreaticoduodenectomy (PD), especially in hard risk pancreatic stump, is the most severe complication after PD and leads to a prolonged hospital stay, increase in per-patient costs and it still remains a challenge for the pancreatic surgeon. **Objective** To find an effective way of drainage of the pancreatic stump in order to reduce pancreatic fistula incidence and its sequelae. **Methods** Since January 2005 until May 2007 we performed 43 PD (Group A) with hard risk pancreatic remnant (tender stump and/or Wirsung duct less than 2 mm). In these patients pancreatic stump was drained by two surgical drainages put forward and under pancreatic anastomosis respectively. This group of patients was compared to a group of 39 consecutive patients (Group B) in which only one drainage was put under pancreatic stump. Postoperative morbidity, additional radiological procedures of percutaneous drainage and hospital stay were registered. Pancreatic fistula was defined according to ISGPF classification [1]. **Results** Overall postoperative complications rate was 77% in both groups; (30/39 patients in Group A and 33/43 patients in Group B). Four patients (9%) underwent re-operation in Group A versus 6 patients (15%) in Group B (P=0.6)

with a mortality rate of 4% and 7%, respectively (P=0.9). Pancreatic fistula incidence was similar in both groups (63% in Group A versus 64% in Group B) but after stratification according to ISGPF classification, we have registered an incidence of A fistulas of 23% in Group A versus 10% in Group B (P=0.2). Incidence of B fistulas was 30% in Group A versus 28% in Group B (P=0.9) and C fistulas occurred in 9% and 26% in groups A and B, respectively (P=0.08). Additional radiological percutaneous drainage rate was 4% in Group A and 36% in Group B (P=0.07). Mean length of hospital stay was 16 days in Group A versus 19 days in Group B (P=0.2). **Conclusions** Double pancreatic drainage does not reduce incidence of pancreatic fistula but seems to be effective in reducing weight of pancreatic fistula's management (less re-operations, less radiological procedures) leading to a faster recovery for the patient when compared to classic drainage. However, this trend must be confirmed by further studies with more numerous and powerful samples.

Reference

1. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; 138:8-13. [PMID 16003309]

Survival and Prognostic Factors at Diagnosis in Non-Functioning Pancreatic Endocrine Tumors: Analysis of 180 Patients

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Context Non-functioning pancreatic endocrine tumors (NF-PET) belong to the heterogeneous group of endocrine neoplasm, whose natural history is not well known.

Objective The aims were: a) to assess survival; b) to test the prognostic role of selected pathological or clinical parameters; c) to test WHO classification.

Methods Between 1990 and 2004, 180 patients were treated at our Department, and were entered in a prospective database according to WHO criteria classification. Survival analysis was performed by Kaplan-Meier survival function with log rank test. Relevant clinico-pathological data were tested as predictors of prognosis in both uni- and multivariate models. **Results** Twenty-five benign neoplasms (WDET-B, 13.9%), 38 uncertain behavior neoplasms (WDET-U, 21.1%), 100 well differentiated carcinomas (WDEC, 55.6%), and 17 poorly differentiated carcinomas (PDEC, 9.4%) entered in the study; 148 patients (82.2%) underwent surgery. Radical resection was possible in 93 patients (51.6%) and a debulking procedure was performed in 19 (10.5%). The overall 5, 10 and 15 year-survival rates were 67%,

49.3% and 32.8%, respectively, while for radically resected patients were 93%, 80.8% and 65.2% (P<0.001). No differences were seen between unresected patients and those who underwent palliative resection (median: 30.4 vs. 57.8 months; P=0.81). Upon multivariate analysis, poor differentiation (HR=7.3; P<0.001), liver metastases (HR=3.29; P=0.003), nodal metastases (HR=3.05; P=0.020), Ki-67 greater than 5% (HR=2.5; P=0.012), and weight loss (HR=3.06; P=0.001) were significantly associated with disease-related mortality.

Conclusions This study confirms: a) the relatively good long-term survival of patients with NF-PETs; b) the role of radical resection as the most favorable treatment option. However, resection by itself cannot be considered a long-term cure for all patients with NF-PETs, and other parameters (nodal or liver metastases, Ki67 greater than 5%, poor differentiation, and weight loss at diagnosis) play a prognostic role. The WHO classification provides a good estimation of prognosis and is mandatory in a clinical setting.

Urokinase Plasminogen Activator Receptor Could Be a New Useful Marker in Pancreatic Cancer and Appears to Be Related to Survival

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Context Urokinase plasminogen activator receptor (uPAR) has been recently reported as highly expressed in various types of human cancer and above all in pancreatic ductal

carcinoma. **Objective** In order to verify this hypothesis and to assess whether it could represent a potential diagnostic and prognostic indicator in pancreatic cancer we

evaluated uPAR levels both in healthy controls and in patients suffering from pancreatic disease. **Methods** We collected plasma and urine in 61 patients (28 males, 33 females; mean age 52.8 years, range 18-77 years) suffering from: pancreatic cancer (PDC), 36 patients, 59%; chronic pancreatitis (CP), 12 patients, 20%; cystic tumors (CT), 9 patients, 15%; endocrine tumors (PET), 4 patients, 6%. In the same manner we collected as control group plasma and urine from a similar population as regards age and gender. Then uPAR was measured both in plasma and urine after correlating with creatinine levels. **Results** After correction with creatinine, correspondence between plasma and urine uPAR levels reached to 60%. Mean values in patients affected by pancreatic disease were respectively: 50.8 pmol/L and 321.6 pmol/L in the whole series, 58.9 pmol/L and 357.3

pmol/L in PDC. uPAR levels in healthy controls resulted significantly less. Matching both plasma and urine levels led to a significant difference among PDC and other disease (*vs.* CP $P < 0.007$; *vs.* CT $P < 0.001$, *vs.* PET $P < 0.01$). As regards the survival in 36 patients (15 males, 21 females; mean age 56.8 years) affected by PDC, only one is still alive after 51.9 months while the other patients died with a mean follow-up of 13.2 months. We found significantly higher ($P < 0.02$) levels of uPAR in short (less than 6 months) *vs.* long (greater than 18 months) survivors. **Conclusion** These data suggest a possible usefulness of uPAR as a new marker for diagnosis and follow-up in PDC. However, in order to confirm these preliminary results and stress a likely relationship with survival, further evaluation on a wider series is strongly required.

Induction Irinotecan/Gemcitabine Followed by Twice-Weekly Gemcitabine and Radiation in Locally Advanced Pancreatic Cancer

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Context Early clinical studies combining irinotecan (CPT11) and gemcitabine (GEM) have reported encouraging results. GEM administered via a twice-weekly schedule results in an enhanced radiation-sensitizing effect. **Objective** To improve systemic control of disease and to impact on overall survival, investigators from many institutions are currently testing neoadjuvant chemotherapy strategies. This is a phase II study of induction CPT11 and GEM followed by twice-weekly GEM and radiotherapy (RT). **Patients and Methods** Forty-one patients with cytological and/or histological evidence of unresectable pancreatic adenocarcinoma entered the study. Median age was 58 years (range: 37-75 years) and median Karnofsky score was 90 (range: 80-100). Patients received two cycles of induction CPT11(100

mg/sm) and GEM (1,000 mg/sm) on days 1 and 8 of each 3-week cycle. Three weeks later, they received RT at daily doses of 180 cGy, to a total dose of 54 Gy combined with bi-weekly GEM on Tuesday and Friday, at a daily dose of 40 mg/sm. Dose reduction or treatment delay was required with toxicity of grade II. **Results** All patients completed the neoadjuvant chemotherapy (CT)-RT treatment as scheduled whereas the concurrent RT-GEM treatment was completed by 2 patients only; the median number of GEM cycles was 8 (range: 3-12). Median follow-up time was 12 months (range: 4-33 months) and median survival time was 13 months. Radiological confirmed response was: PR in 20 patients and NC in 15; 6 patients had progression of disease during treatment. Twenty-eight patients had a subjective PR.

Hematological toxicity of grade III was reported in one patient and grade II in 11 patients. Gastrointestinal toxicity was: grade III in 1 patient and grade II in 11 patients. **Conclusions** Induction CPT11/GEM followed by twice weekly GEM and RT is feasible in patients with locally advanced pancreatic cancer, but with modest activity on local control and overall survival. The results

of the study indicate that neoadjuvant CPT11/GEM followed by twice weekly GEM is a feasible treatment. However, from a review of the literature, it appears that the impact on overall survival of the combination is not superior to GEM alone. In an attempt to improve on these results, additional therapies should be considered, including targeted therapy agents.

Exocrine Pancreatic Function Assessed by Secretin Cholangio-Wirsung Magnetic Resonance

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Context It has been reported that MRCP is useful to assess the exocrine pancreatic function by combining rapid imaging acquisition and the administration of secretin, a gastrointestinal hormone able to stimulate the secretion of bile and pancreatic juice; however, there are no extensive data in this respect. **Objective** To evaluate if MRCP with secretin administration is able to detect simultaneously both the possible presence of alterations of the pancreatic ducts and the exocrine pancreatic function. **Methods** All subjects with age greater than 18-year-old who underwent to MR and CWMR for the suspicion of benign or malignant pancreatic diseases from January 2006 to December 2006 were enrolled in the study. MR and CWMR were carried out using a dedicated apparatus (Signa GE Medical Systems 1,5 T, Milwaukee, Wisconsin, USA). **Results** Eighty-seven patients (46 males, 41 females; mean age 59.7±14.6 years, range 27-87 years) were enrolled. Of the 87 patients studied, 20 (23.0%) had an intra-papillary mucinous tumor (IPMT) (4 main duct type, 12 branch duct type, and 4 mixed type), 3 (3.4%) had mucinous cystadenomas, 6 (6.9%) had serous cystadenomas, 7 (8.0%) had chronic pancreatitis, 5 (5.7%) had a previous attack of biliary acute pancreatitis, 5 (5.7%) had ductal congenital abnormalities, one (1.1%) was previously operated of pancreatic head

resection for autoimmune pancreatitis, one had a cholangiocarcinoma (1.1%), and the remaining 39 subjects (44.8%) had a normal pancreatic gland at imaging. From a morphological point of view, we found two pseudocysts (2.3%) (one of the 7 patient with chronic pancreatitis and one of the 5 patients studied after an attack of acute pancreatitis; this last pseudocyst communicated with the main pancreatic duct). The presence of calcifications were found in 3 of the 7 patients (42.9%) with chronic pancreatitis. In all patients with IPMT and mucinous cystadenoma, and in 3 patients with serous cystadenoma, the diagnoses were histologically confirmed. In the remaining patients we had an adequate follow-up to confirm the diagnosis obtained at imaging. According to the Matos criteria, we found that 73 patients (83.9%) had grade 3, 8 had grade 2 (9.2%), 4 had grade 1 (4.6%) and the remaining 2 had grade 0 (2.3%). The pancreatic diseases able to impair the exocrine pancreatic secretion stimulated by secretin were only the chronic pancreatitis (57.1% of the patients had grade 0-1) and the IPMT mixed type in whom 2 of the 4 patients (50%) had Matos grade 1. **Conclusion** Secretin MRCP is a useful technique to detect simultaneously both the possible presence of alterations of the pancreatic ducts and the exocrine pancreatic function.

Incidence at Diagnosis of Exo-Endocrine Insufficiency in Advanced Pancreatic Cancer Patients: Results of a Prospective Study

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Context The real incidence of exo-endocrine pancreatic insufficiency in patients with advanced pancreatic cancer (APC) has never been completely assessed. **Objective** To estimate prospectively the incidence of exocrine and/or endocrine pancreatic insufficiency at the diagnosis in a consecutive series of patients with APC. **Methods** Between October 2006 and May 2007, all the patients with unresectable, cyto- and/or histologically proven APC diagnosed at our institution were prospectively enrolled. Blood tests, OGTT and fecal elastase 1 (F-EL1) dosage were evaluated in all the patients. The presence of diabetes was defined according to the American Diabetic Association guidelines and exocrine insufficiency when F-EL1 less than 200 µg/g. **Results** Eighty-six patients (44 males, 42 females) with median age of 64 years (range: 41-83 years), were staged as IVA in 54 (62.8%) cases, and IVB in 32 (37.2%), respectively. The median BMI was 23.5 kg/m² (range: 16.4-35.9 kg/m²). The tumor was in the head of the pancreas in 68 patients (79%) and in the body-tail in 18, respectively. Weight-loss in the previous 6 months was present in 79% of the patients

(median loss 5 kg; range: 0-30 kg). Forty-five (52%) patients had diabetes, with a new onset in 23 cases (51%). Considering F-EL1, 40 patients (47%) had a normal value (greater than 200 µg/g), 8 (9%) presented a mild-moderate insufficiency (between 100 and 200 µg/g), and 38 (44%) had a value less than 100 µg/g (severe insufficiency). The Table summarizes the relationship among different F-EL1 values, diabetes and clinical steatorrhea. **Conclusions** At diagnosis clinical steatorrhea is present in only 10% of APC patients with a BMI which remains in the normal range. However, more than 50% and 79% of patients present an exocrine insufficiency and weight loss, respectively. Moreover 50% of the patients are diabetic and this seems to be strictly related to the degree of exocrine insufficiency. It remains unclear whether pancreatic insufficiency might impact both antitumoral therapies tolerability and survival.

Fecal elastase 1 (µg/E1/g)	Patients (n=86)	Diabetes (n=45)	Steatorrhea (n=9)
Less than 100	38 (44%)	24 (53%)	8 (17%)
100-200	8 (9%)	2 (5%)	1 (2%)
Greater than 200	40 (47%)	19 (42%)	0

Risk Factors for Pancreatic Endocrine Tumors: A Multicenter Case-Control Study

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Context Pancreatic endocrine tumors (PETs) are rare neoplasms with an incidence of some 0.1/100,000. Apart from genetic disorders, risk factors for the occurrence of PETs have never been specifically investigated. Smoking, drinking, and BMI have been found

to be risk factors both for GI carcinoids and pancreatic ductal adenocarcinoma (PDAC). The possible role of family history has not been evaluated in GI endocrine tumors before. **Objective** We aimed at determining risk factors for the occurrence of PETs. **Methods**

Multicenter case-control study. Patients with either new diagnosis of sporadic PET or in follow-up seen at the Rome or Verona Units were administered a specific questionnaire registering data on possible risk factors (smoking, alcohol intake, BMI, medical history one year before PET diagnosis) and family history of cancer. Sex and age-matched controls were patients with non-neoplastic, non-chronic disorders seen at the same Units. Anamnesis and follow-up data on diagnosis of secondary cancers were also recorded. Fisher test, t-test and related odds ratios were calculated through a dedicated software. **Results** One-hundred and 15 patients and 115 matched controls were enrolled. Mean age at diagnosis was 52 years. Amongst PETs, there were 89 NF and 26 F; 22 WDET, 80 WDEC, 13 PDEC; TNM stage was IV in 37 cases. 39.8% of PETs and 42.6% of controls smoked more than 5 cigarettes/day ($P=0.68$). Heavy smoking (equal to, or greater than 20 cigarettes/day) was more frequent amongst PETs (12% vs. 5%; $P=0.09$; $OR=2.48$; $95\%CI: 0.9-6.7$). Drinking (more than 3 units/week) was equally frequent in PETs (37.2%) and controls (35.6%) ($P=0.88$), heavy drinking was also non significant. The mean BMI was 24.8 in PETs and 24.9 in controls ($P=0.93$), and obesity was also similarly distributed (11.2% PETs vs. 10.4% controls). History of diabetes and pancreatitis were also not significant risk factors. 56.1% of PETs had at least one first degree family member with a neoplasm vs. 48.6% of controls ($P=0.29$).

14.9% of PETs had more than one first degree family member with a neoplasm vs. 7.8% of controls ($P=0.09$; $OR=2.95$; $95\%CI: 0.8-4.8$). 29.8% of PETs and 20% of controls had both first and second degree cancer family history ($P=0.09$). PDAC first degree family history was found in 7 PETs (6.1%) and 2 (1.7%) controls ($P=0.1$; $OR=3.6$; $95\%CI: 0.7-18.1$). Second degree family history of PDAC was also seen in 4 PETs and 2 controls, with one PET patient's kindred meeting criteria for familial pancreatic adenocarcinoma. All 7 PETs with PDAC first degree family history were NF (7/89, 7.8%) with a significant difference vs. controls ($P=0.043$). No other site specific neoplasm family history was significantly associated with PET diagnosis. Nine patients had a secondary cancer diagnosed before or after PET (mean follow-up 38.6 months). **Conclusions** In this case-control study no factors were significantly associated with PET risk. However, heavy smoking and family history of cancer, particularly of PDAC, show a trend toward significance. This last finding is interesting as PETs occur relatively often in families with familial pancreatic cancer. Notably, PDAC family history is associated with NF PETs only. We are in the process of extending cases and controls recruitment to a ratio of 1:4, to achieve a better statistical power and highlight significances missed at this preliminary analysis. Comparison of secondary cancer incidence with SIR is also ongoing.

Endoscopic Ultrasound-Guided Application of a Cryotherm[®] Probe in the Pancreas: Results in an Animal Model

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Context The development of linear array therapeutic probes with a large working

channel (3.8 mm) has made endoscopic ultrasound (EUS) more operative. **Objective**

The aims of the study were to evaluate feasibility, efficacy, and safety of EUS-guided transgastric application of a new cryotherm probe (CTP) in the pancreas of an animal model, as well as to objectify risks, complications and histological changes. **Methods** A new hybrid ablative device that combines radiofrequency (RF)-ablation with cryotechnology has been developed by ERBE. The cryotechnology has been used to support and increase the killing effect of the RF-technology. A Hitachi ultrasonographic system and a linear array Pentax EG3830UT echoendoscope were used. The CTP was applied under EUS guidance in 19 domestic pigs. The animals were killed immediately (n=1), one week (n=10), two weeks (n=7) and 4 weeks (n=1) after ablation. Pathologic examination was performed. **Results** All pigs tolerated the procedure well. Correlation

between EUS and gross pathology showed a correlation coefficient of 0.69. Excluding an animal with severe pancreatitis, the correlation coefficient was 0.87. The ablation area was correlated to the application time and measured by means of the robust regression: it showed a fitted ratio of 2.294 (P<0.001), in the pancreases of the animals killed after one week, 2.709 in the pig immediately killed (P<0.001) and 0.209 in the animals killed after 2 weeks (P<0.001). Three animals presented a burning of the gastric wall, one developed a fistula between the cystic lesion and the gut, two had acute pancreatitis. **Conclusion** This is the first device which combines radiofrequency and cryotechnology to create selective necrosis. We demonstrated the feasibility, efficacy and safety of its EUS-guided application in the pancreas in a porcine model.

“Bull’s Eye Calculi” in Diagnosis of Gene Mutation Associated Chronic Pancreatitis: The Role of MDCT

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Context In patients with chronic pancreatitis “bull’s eye calculi” is highly associated with gene mutation associated pancreatitis (GMAP). **Objective** To evaluate MDCT findings of ductal calculi useful allow to detect GMAP from obstructive pancreatitis. **Materials and methods** From May 2006 to June 2007, 20 patients affected by chronic pancreatitis with ductal calculi were prospectively enrolled in this study (14 males, 6 females). Inclusion criteria were: clinical, laboratory and imaging (US, ERCP, RM) findings of pancreatitis, presence of ductal calculi, genetics test, and MDCT study examination. Exclusion criteria were: Patients with autoimmune pancreatitis, with intraductal papillary mucinous tumors, who underwent ERCP and surgery treatment. Clinical symptoms at presentation included, abdominal pain, diabetes, steatorrhea and jaundice. Images analysis was performed by

two independent radiologists. Qualitative criteria were: structure of the endoductal calculi (homogeneous/heterogeneous: non-calcified central core “bull’s eye”), pancreatic parenchyma contrast-enhancement in pancreatic phase compared to renal cortex (hypo-/iso-/hyper-vascular). Quantitative criteria were: number and diameter of endoductal calculi, size of pancreatic parenchyma (head, body, tail), size of main pancreatic duct (MPD). **Results** Qualitative analysis: heterogeneous calculi with non-calcified central core (“bull’s eye”) in 7/20 and homogeneous calculi in 13/20; pancreatic parenchyma was hypovascular in 13/20, isovascular in 7/20. Quantitative analysis: mean number of calculi was 19 (range: 5-40), mean diameter of calculi was 13 mm (range: 3-40), median thickness of the pancreatic parenchyma in head, body and tail was 15 mm (range: 2-40), 12 mm (range: 2-40) and

12 mm (range: 2-40), respectively; mean size of MPD was 11 mm (range: 3-20). Gene mutations were: CFTR 4/20, SPINK1 3/20 and 1/20 both CFTR and SPINK mutation. Five out of 8 patients with GMAP (63%) and 2 out of 13 patients with chronic pancreatitis

(15%) had “bull’s eye” calculi; in particular one of these two had an idiopathic pancreatitis and the other had alcoholic pancreatitis. **Conclusions** In this initial phase of our study MDCT can identify “bull’s eye” and have a good correlation with GMAP.

Mucinous Cystic Neoplasm of the Pancreas Is not an Aggressive Disease. Lessons from 163 Resected Patients

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Context Mucinous cystic neoplasms (MCNs) of the pancreas have often been confused with intraductal papillary mucinous neoplasms.

Objective We sought to evaluate the clinicopathological characteristics, prevalence of cancer, and prognosis of a large series of well-characterized MCNs in two tertiary centers. **Methods** Analysis of 163 patients with resected MCNs, defined by the presence of ovarian stroma and lack of communication with the main pancreatic duct. **Results** MCNs were seen mostly in women (95%) and in the distal pancreas (97%); 25% were incidentally-discovered. Symptomatic patients typically had mild abdominal pain, but 9% presented with acute pancreatitis. 118 patients (72%) had adenoma, 17 (10.5%) borderline tumors, 9 (5.5%) in-situ carcinoma and 19 (12%) invasive carcinoma. Patients with invasive carcinoma were significantly older than those with non-invasive neoplasms (55 vs. 44 years,

$P=0.01$). Findings associated with malignancy were presence of nodules ($P<0.001$) and diameter equal to or greater than 60 mm ($P<0.001$). All neoplasms with cancer were either equal to or greater than 40 mm in size or had nodules. There was no operative mortality and postoperative morbidity was 49%. Median follow-up was 57 months (range: 4-233 months); only patients with invasive carcinoma had recurrence. The 5-year disease-specific survival for non-invasive MCNs was 100%, and for those with invasive cancer 57%. **Conclusions** This series, the largest with MCNs defined by ovarian stroma, shows a prevalence of cancer of only 17.5%. Patients with invasive carcinoma are older, suggesting progression from adenoma to carcinoma. While resection should be considered for all cases, in low-risk MCNs (equal to or less than 4 cm, no nodules), non-radical resections are appropriate.

A Retrospective Analysis of 248 Consecutive Distal Pancreatectomies

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Context Complications occurring after distal pancreatectomy (DP), though seldom fatal, carry significant morbidity. **Objective** To analyze the outcomes of a consecutive series of DPs. **Methods** Between November 1987 and August 2005 we performed 248 DPs; data

were retrospectively analyzed. There were 112 (45.2%) males and 136 (54.8%) females; the mean age was 60.6 years (range: 15-86 years); 216 patients (87.1%) underwent splenopancreatectomy (SDP) and 32 (12.9%) spleen preserving distal pancreatectomy

(SPDP); in 24 cases the procedure was carried-out laparoscopically (0.9%). **Results** The median operative time was 357 minutes (range: 140-720 min); the median number of blood transfusions was 0.4 (range: 0-12). Perioperative morbidity and mortality rates were 24.6% (61/248) and 3.6% (9/248), respectively; stump related morbidity rate was 13.3% (33 cases); relaparotomy rate was 4.8% (12 cases). Final pathologic diagnosis included 88 (35.5%) pancreatic carcinomas, 42 (16.9%) endocrine tumors, 44 (17.7%) cystic neoplasms, 49 (19.7%) other tumor types and 25 (10.1%) other benign diseases. The median postoperative stay was 15.9 days (range: 4-101 days). Patients undergoing SDP and SPDP showed similar postoperative morbidity rates (59/216, 27.3% vs. 5/32, 15.6%, respectively; P NS); no overwhelming post-splenectomy infection was recorded following SDP after a mean follow-up period of 51.4 months (range: 5-222 months) in the

absence of a systematic policy of vaccination. Eighty-three patients (33.5%) underwent extended distal pancreatectomy (EDP), including en-bloc resection of additional viscera and/or non-splenic peripancreatic vessels. When compared to conventional DP, EDPs did not show significantly different morbidity (24.7%) or mortality (1.3%) nor 1-3- and 5-year survival rates (60.9%, 27.1%, and 6.5% vs. 65.2%, 29.4%, and 19.6%, respectively; P NS). One-, 3- and 5-year survival of patients diagnosed with ductal adenocarcinoma was 60.1%, 27.8%, and 22.3%, respectively. **Conclusions** Nowadays, DP is a safe procedure; spleen preservation should be performed in selected candidates, since splenectomy does not entail an increased rate of infectious events. Pancreatic stump complications remain the leading cause of morbidity and the main technical challenge of this procedure.

Ectopic Spleens in the Tail of the Pancreas Mimicking Multifocal Neuroendocrine Tumors in a Patient with History of Endocrine Neoplasia. A Case Report

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Context Accessory spleens are found in more than 30% of unselected autopsies, 20% being located within the tail of the pancreas. Usually, accessory intrapancreatic spleens are discovered incidentally and, since they appear as hypervascular solid nodules, are often misdiagnosed as neuroendocrine tumors (NT). **Case report** A 29-year-old woman with acromegaly due to pituitary GH-secreting adenoma and previous bronchial carcinoid was referred to our Hospital for further evaluation and follow-up. She had been diagnosed with acromegaly 6 years earlier. The bronchial carcinoid, with lymph nodes metastases, had been resected 2 years later and, since then, the patient had been treated

with somatostatin analogues. Genetic analysis of Menin was negative. Whole body scan with ¹¹¹I octreotide revealed an area of increased uptake in the pituitary gland, corresponding to an adenoma, and in the mediastinum, where additional investigations did not find further evidence of disease. Incidentally, abdominal CT scan revealed two small hypervascular pancreatic lesions (less than 1 cm) and two tiny liver nodules with superimposable features. Serum neuroendocrine tumor markers were below cut-off levels. Based on past medical history and CT findings, the patient was scheduled for surgery with a presumed diagnosis of multifocal pancreatic NT possibly associated

with liver metastasis. At laparoscopy no gross liver lesions could be observed and contact ultrasonography only showed a small nodule, located deep in segment V, measuring approximately 2 mm in its largest diameter. No lesions could be observed in the pancreatic tail but, based on contact ultrasonography, the two nodules identified at preoperative CT were located in the very distal part of the pancreatic tail. The pancreatic tail was then resected while preserving the spleen and the pancreatic vessels. Pathology showed that the pancreatic nodules were ectopic spleens deeply embedded in the normal pancreatic parenchyma. The post-operative course was uneventful and the patient was discharged

from the hospital in the 4th post-operative day. The endocrine and exocrine function of the pancreas are normal at the longest follow-up. **Conclusion** Ectopic location of accessory spleens in the pancreas is uncommon but not rare. At imaging, ectopic spleens show many diagnostic features of NT (i.e., solid hypervascular mass). The only specific diagnostic test is ^{99m}technetium heat damaged red blood cell SPECT. In the present case the diagnosis of ectopic intrapancreatic spleen was not considered due to patient's medical history. We suggest however, that in the absence of findings diagnostic for NT, the presence of ectopic spleen(s) should be ruled out by means of ^{99m}technetium heat damaged red blood cell SPECT.

Correlation with Different Motility and Metastatic Potential in Pancreas Cancer Cell Lines

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Objective The aims of this study were to gain insights on the molecular features of pancreatic cancer metastatic phenotype using a cell model derived from SUIT-2 pancreatic adenocarcinoma cell line: S2m (motile, non metastatic) and S2CP9 (motile, highly metastatic). We focused on the signaling that regulate cell motility and migration using functional interference approaches based on cell permeable inhibitory peptides of RhoA and ζ PKC enzymes. **Methods** SUIT-2 subclone S2m has been established in our laboratory [1] while S2-CP9 are described by Kitamura *et al.* [2]. We used RhoA and ζ PKC inhibitory peptides in *in vitro* experiments (adhesion plate, wound-healing assay and transwell assay) to evaluate the role of these enzymes. **Results** In both cell lines the combination of RhoA and ζ PKC inhibitory peptides inhibited cell adhesion, although this effect was more evident in S2-CP9 cell line. In wound healing assay, we noticed that S2m was unable to migrate toward both ends of the wound even if its motility score was overlapping with that of S2-CP9. We then studied how both clones behaved in an

experimental setting used to study chemotaxis, where migration of the cells occurs through a 8 μ m pores membrane. In this case the spontaneous migration occurs, although at different extent, in both clones and was almost completely abolished by the individual treatments with RhoA and ζ PKC inhibitory peptides. **Conclusions** The invasive and metastatic capability of malignancies is associated with the acquisition of anomalous motile behavior by cancer cells. Our experiments demonstrate that RhoA and ζ PKC enzymes are involved in different aspects related to cell adhesion, motility on a surface or through 8 μ m pores in non metastatic or metastatic S2m and S2-CP9 clones. Altogether these results indicate that motility and metastatic attitude activate overlapping, yet distinct pathways and that metastatic clones appear to be more sensitive to the disruption of cytoskeleton dynamics than highly motile but non metastatic clones.

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Serum Adhesion Molecules in Acute Pancreatitis:

Time Course and Early Assessment of the Severity of the Disease

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Context Adhesion molecules determine microcirculatory derangement in acute pancreatitis. **Objective** To evaluate the adhesion molecule time course in the early phases of acute pancreatitis and to explore the usefulness of these proteins in assessing the severity of the disease. **Subjects** Fifteen consecutive acute pancreatitis patients (7 males, 8 females; age 63.1±14.5 years; ten patients with the mild form and five with the severe form) admitted to the Emergency Room within 6 hours after the onset of pain, and fifteen age- and sex-matched healthy subjects. **Methods** Blood samples of the patients were taken on hospital admission and for the following two days. VCAM-1, ICAM-1, E-selectin, P-selectin, and L-selectin were quantified by a biochip array analyzer. (Evidence®, Randox Laboratories Ltd., Crumlin, UK). Using this procedure, all five molecule assays were performed simultaneously. **Results** Acute pancreatitis patients had VCAM-1 and P-selectin concentrations significantly lower, and L-selectin concentrations significantly higher than the healthy subjects. Only E-selectin was significantly higher in the severe forms of the disease (P=0.029); a value of E-selectin ranging from 3.83 to 3.92 ng/mL was the best cut-off value for differentiating severe from

mild acute pancreatitis (sensitivity: 60.0%, specificity: 90.0%, cases correctly classified: 80%). At multivariate logistic regression, performed by taking into account the five adhesion molecules as independent variables, both E-selectin (P=0.003) and P-selectin (P=0.013) entered the procedure showing a significant additional contribution of P-selectin to that of E-selectin in differentiating the severe from the mild form of acute pancreatitis. By combining the coefficients computed by the logistic analysis with the serum concentrations of the adhesion molecules, the following score was computed: score = -2.022 + 2.202 * E-selectin - 0.215 * P-selectin. This score showed an accuracy (AUC±SE) in differentiating severe from mild acute pancreatitis of 0.951±0.032 with a sensitivity of 93.3%, a specificity of 86.7%, and a frequency of 88.9% of cases correctly classified. It should be noted that, while a good value of specificity had already been obtained by E-selectin alone, the addition of P-selectin into the score contributed to an increase in the specificity. **Conclusion** The score computed by using the circulating levels of both E-selectin and P-selectin seems to be useful for the early assessment of the severity of acute pancreatitis.

Activation of Liver X Receptors Suppresses Proliferation Induces Apoptosis and Reduces Invasiveness in Pancreatic Cancer Cells

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Context Therapeutic challenges in the treatment of pancreatic cancer remain. Liver X receptor (LXR) is a nuclear hormone receptor implicated in lipid metabolism and cellular inflammation. Drugs that target nuclear receptors are potential antineoplastic candidates. **Objective** To investigate the effects of a LXR agonist (T0901317) on cell proliferation, apoptosis and invasiveness in a human pancreatic cancer cell line, PANC-1. **Methods** PANC-1 cells were cultured with 10 to 50 μ M LXR agonist (T0901317) for 6 to 72 hours. Western blot was performed to confirm the presence of LXR in PANC-1 cells and to determine caspase 3 precursor, p27, p21, phospho-Rb and p73 levels. Time course and dose proliferation assays were performed. Flow cytometric analysis examined cell cycle progression with treatment, while apoptosis rate was determined with an Annexin assay. Caspase 3/7 activation was measured by a luminescent assay. Matrigel invasion assay was used to evaluate the ability of Panc-1 cells to invade the extracellular matrix. **Results** LXR is present in PANC-1 cells; treatment with T0901317 did not modulate its expression. T0901317 significantly inhibited PANC-1 proliferation in a dose and time-

dependent fashion (at 6 h, 24 h, 48 h: 10 μ M 84%, 58%, 37%; 50 μ M 53%, 4%, 3%). Flow cytometry analysis of cell cycle progression showed that T0901317 arrested PANC-1 cells in G0/G1 phase, preventing cell progression to S phase. Expression of p73 (a tumor suppressor protein), p27 and p21 (two cyclin-dependent kinase inhibitors) was elevated by T0901317, while phosphorylation of pRb, a key-event for G0/G1-S progression, was inhibited. Apoptosis rate was significantly increased after 6 h treatment with T0901317 (untreated cells 1.8%, 50 μ M T0901317 20.4%). Significantly increased caspase 3 and 7 activation and decreased caspase 3 precursor concentration was demonstrated in cells treated with T0901317. As assessed by Matrigel invasion assay, T0901317 significantly decreased the ability of PANC-1 cells to invade extracellular matrix in a dose-dependent manner. **Conclusion** The LXR agonist T0901317 inhibits cell cycle progression, induces apoptosis and reduces invasiveness in Panc-1 cells. These data indicate that LXR agonists may be novel antitumor agent in treatment of pancreatic cancer.

Homozygosis Mutation in K-ras Oncogene in Primary Cell Culture from Pancreatic Ductal Adenocarcinoma. Characteristic of the Tumor or Adaptation *in Vitro*?

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Context The K-ras oncogene mutations are a frequent event in pancreatic ductal adenocarcinoma (PDAC). These alterations

have also been reported in pre-neoplastic pancreatic lesions (PanINs) and in cell lines derived from PDAC. The majority part of

these mutations are at codons 12, 13 and 61. In pancreatic tumor cell lines heterozygosis *K-ras* mutations have been documented. One of primary cell culture (PP117), obtained in our laboratory has had an homozygosis mutation in *K-ras* gene. This cell culture had two different morphological features, most of them were having a small and round shapes (S) and the other were larger and astrocyte-like (L). **Objective** The purpose of this study was to analyze the phenotype respect to genotype in S and L cells. **Methods** Primary cell culture PP117 was seeded on a new support with a poly-ethylene tereftalate membrane, specifically designed for the laser microdissection (LMD) instrument (Leica LMD6000). S and L cells, where microdissected using differential contrast microscopy and directly transferred into the cap to perform DNA extraction. *K-ras* mutational analysis at codons 12, 13 (exon 1),

and 61 (exon 2) was carried out on primitive tumor and primary cell cultures by PCR and automated sequencing. **Results** The original tumor had a *K-ras* mutational codon 12 in heterozygosis and the same pattern of mutation was found in early phases of PP117. After about 40 passages revealed S and L morphology and they were submitted to another *K-ras* profiling using laser microdissection. Surprisingly, the S and L cells gained a homozygosis mutation on *K-ras* gene at codon 12. **Conclusion** Until now, it is not clear if acquired homozygosis *K-ras* mutation is due to *in vitro* adaptation or due to expansion of colony, having homozygosis mutation, present in the primary tumor. The two different cells are under examination to detect differences in aggressiveness, invasiveness and drug-resistance by gene and proteins analyses.

Cellular Transfection Evidence in Pancreatic Tumor Primary Cell Cultures Through Electroporation of Green Fluorescent Protein (GFP)

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Context Pancreatic ductal adenocarcinoma (PDAC) is an incurable disease, but monochemotherapy with gemcitabine has shown to improve overall survival in PDAC patients. Recently, some authors have illustrated the effectiveness of this drug in combination with silencing of some important genes in PDAC progression using pancreatic tumor cell lines (MiaPaca2, Panc-1). Silencing of target genes occurs through cellular transfection using a virus or other molecules such as oligofectamines. The electroporation technique can deliver nucleic acids alone or carried by vectors in cell cultures. **Objective** The purpose of this study was to introduce a DNA plasmidic vector

expressing a green fluorescent protein GFP in PDAC primary cell culture using electroporation system. **Methods** From 81 primary tumors selected to set up primary cell cultures, we obtained 9 primary cultures (PP78, PP109, PP117, PP147, PP161, PP103, PP111, PP391 and PP437), which were grown in RPMI 1640 (supplemented with 10% FCS, 1% L-Glu and 1% streptomycin) at 37°C, in 5% CO₂. To perform the transfection technique the cell culture PP78 was randomly chosen. Electroporation was obtained using 10 different protocols of different intensity and number of electric impulses. **Results** Cellular transfection with good cellular vitality has been documented in four

protocols. The totality of the cells showed marked expressions of GFP. Negative controls excluded the presence of autofluorescence in the cells. **Conclusion** This method is rapid, efficient, cost-effective and highly reproducible to be used for gene-induced silencing through electroporation of

siRNA in the cells. In the next future a series of four pancreatic tumor primary cell cultures obtained in our laboratory (PP78, PP109, PP161 and PP391) will be tested for gemcitabine toxicity by silencing genes involved in gemcitabine metabolism.

Multidetector Computed Tomography (MDCT), Endoscopic Ultrasonography (EUS) and Color-Doppler Ultrasonography (CDU) in Periapillary Tumors: Evaluation of Vascular Involvement of Major Peripancreatic Vessels

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Context In patients affected by periapillary tumors, preoperative evaluation of vascular involvement is necessary to avoid surgical treatment, not amenable to curative resection.

Objective To assess the usefulness of MDCT, EUS and CDU in the evaluation of vascular involvement of major peripancreatic vessels in periapillary tumors. **Methods** In two years, 66 patients affected by periapillary tumors underwent MDCT, EUS and CDU examination to determine vascular involvement of the following peripancreatic vessels: portal vein, superior mesenteric artery and vein, hepatic artery, celiac trunk. Surgical evaluation was considered gold standard and the intraoperative vascular involvement was assessed by this pattern: grade 0 (no touch between tumor and vessel), grade 1 (touch between tumor and vessel, bloodless surgical excision), grade 2 (vascular infiltration, bloody surgical excision or vascular resection). **Results** 54/66 (82%) patients underwent curative (n=48) or palliative (n=6) surgical treatment; 12 patients were excluded because of clear vessel

infiltration and underwent radio/chemotherapeutic treatment. We analyzed 270 major peripancreatic vessels. Surgical grade 0, grade 1 and grade 2 were respectively in 224, 18, 28 vessels. MDCT sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) in grade 2 were 71%, 100%, 95%, and 97%, respectively. EUS sensitivity, specificity, PPV and NPV were 68%, 99%, 90%, and 96%, respectively. CDU sensitivity, specificity, PPV and NPV in grade 2 were 46%, 98%, 76%, and 94%, respectively. Accuracy of MDCT, EUS, CDU was 94%, 89%, 88% in grade 0, 93%, 91%, 88% in grade 1, and 97%, 96%, 93% in grade 2, respectively. Overall accuracy of MDCT, EUS, CDU was 95%, 92%, and 90%, respectively. **Conclusion** MDCT demonstrated to be the best imaging technique in the evaluation of vascular involvement of major peripancreatic vessels in periapillary tumors; MDCT can better evaluate grade 2 pattern, and this can avoid non curative resections.

Concomitant Intraductal Papillary Mucinous Neoplasm of the Pancreas and Pancreatic Endocrine Neoplasm: Report of Two Cases

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Context It has been suggested that the occurrence of intraductal papillary mucinous neoplasms (IPMN) in association with pancreatic endocrine neoplasms (PEN) is more frequent than expected. Up to now, 10 cases of concomitant IPMN and PEN have been reported. In most cases the synchronous existence of both tumors is fortuitously discovered after examination of the surgical specimen. We report two additional patients with both IPMN and PEN. **Case reports** First Case: A 59-year-old female with who was discovered to have an one cm cystic lesion in the pancreatic isthmus on a CT performed to evaluate a few month history of lower abdominal pain. A secretin-stimulated MRCP subsequently performed showed the presence of multiple sub-centimetric cysts throughout the pancreas that were in communication with the MPD. Few months later, she underwent an endoscopic ultrasound (EUS) that confirmed the presence of multiple pancreatic cysts, but also disclosed a 7.8 mm well-delimited, hypoechoic, rounded lesion in the pancreatic tail. Fine needle aspiration was performed and was diagnostic for a non-functional PEN. Because of this finding, patient underwent distal pancreatectomy, and the histopathological analysis of the resected specimen confirmed the presence of multiple benign

branch type IPMNs and of PEN with low malignant potential. Second Case: A 55-year-old asymptomatic male with a previous history of alcohol abuse and pseudocyst-jejunostomy who was discovered to have a 2 cm cystic lesion in the uncinete process of the pancreas at an abdominal US performed as a routine follow up after his surgery. A CT and MRI confirmed the presence of the uncinete cyst, but also disclosed the presence of multiple smaller cystic lesions throughout the pancreas consistent with a multifocal IPMN. The main pancreatic duct appeared of normal caliber and course, while small diffuse calcifications were observed throughout the pancreatic parenchyma consistent with chronic pancreatitis. Patient underwent total pancreatectomy which confirmed the presence of multifocal side branch IPMN with a borderline histology. Moreover, a 3 mm well differentiated PEN with low malignant potential was found in the pancreatic head. **Conclusion** IPMN and PEN can occur concomitantly. We showed that in one of our patient the diagnosis of PEN affected the long-term management of IPMN. Further studies to determine the true incidence of concomitant IPMN and PEN are needed to establish if this association is more than just fortuitous.

Necrotizing Acute Pancreatitis:

Long-Term Follow-up of a Primarily Nonsurgical Treated Patients

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Context The late outcome after acute pancreatitis (AP) is not clearly defined. Many

studies showed that patients who survive an episode of severe AP may develop

impairment of endocrine (mean 45%, range 7-90%) and exocrine (mean 23%, range 0-86%) pancreatic functions. However, great part of these reported patients underwent pancreatic surgery at the moment of the acute episode. **Objective** We herein report the results of a long-term follow up of primarily nonsurgical treated patients. **Patients and Methods** Starting from January 1994 till December 2006 (156 months), a group of patients who experienced an acute episode of necrotizing AP were prospectively followed up. Clinical characteristics of the initial group of patients, recruited during a 10-year period, were previously published [1]. The study group included 132 patients all treated conservatively during the index hospital admission. Follow up schedule comprised two yearly controls for the first two years after AP and then one control/year and it consisted of: a) outpatient clinical observation; b) routine laboratory test; c) abdominal ultrasound; d) fecal elastase; e) oral glucose tolerance test (in patients with fasting glycemia ranging 120-140 mg/dL). During the follow up period we observed 15 deaths (all unrelated to pancreatic diseases) and 36 patients (27.2%) were considered drop-out (mean number of lost patients per year: 3.9; range: 2-8). So, data of 81 patients (61.3%) were analyzed. Male/female ratio was 35/46 and the mean age at end of follow up was 64.7±16.3 years. **Results** Endocrine function. Two patients

were already diabetic before the AP episode; 12 out of the remaining 79 patients (15.1%) developed overt diabetes. The disease appeared within the 3rd year from the AP episode in five patients, between the 3rd and the 4th year in three patients, between the 6th and 7th in three patients and after the 10th year in one patient. All patients required treatment: oral hypoglycemic drugs in seven patients and insulin in five. Exocrine function. Sixteen patients (19.7%) showed fecal elastase impairment (nine patients at the first control after AP - six months - and seven at one year); in all these patients ultrasound were normal and fecal elastase level returned above the normal range during the follow up (in eight patients at 2nd year, in six at the 3rd year and in two at the 4th year). Pancreatic calcifications and exocrine insufficiency developed in two additional patients (2.4%) with initial 'idiopathic' AP (in both the final diagnosis was celiac disease). **Conclusions** In the vast majority of patients suffering from an episode of necrotizing AP treated without surgery the endocrine and exocrine pancreatic function is not impaired in the long term follow up. Complete recovery is achieved in almost all patients.

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Specific Inhibition of Glycogen Synthase Kinase 3beta Ameliorates Cerulein-Induced Acute Pancreatitis in the Mouse

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Context An area of current interest in acute pancreatitis (AP) research is on identification of intracellular signal transduction pathways that regulate the nature, magnitude and

duration of the inflammatory response. Glycogen synthase kinase-3beta (GSK-3beta) is an ubiquitous serine-threonine kinase that participates in several intracellular processes.

In particular, GSK-3 beta influences the activity of the transcription factor NF-kB and, thus, may play a key role in the pathogenesis of AP. **Objective** To assess the effects of TDZD-8, a selective GSK-3beta inhibitor, in a murine model of AP induced by cerulein (CER). **Methods** AP was induced by intraperitoneal injection of CER (hourly x 5, 50 µg/kg) in mice (n=20). TDZD-8 was administered (10 mg/kg) at one and 6 hours after first CER injection; control groups received vehicle treatment. Mice were sacrificed at 24 h after the induction of AP. We analyzed histological and biochemical features of AP, expression of pro-inflammatory cytokines, VEGF and adhesion molecules, neutrophil infiltration (myeloperoxidase activity), the formation of oxygen and nitrogen-derived radicals, and lipid peroxidation. Furthermore, the levels of Ikb-alpha, phospho-NF-kB (as indicators of NF-kB activity) and phospho-GSK-3beta (as an indicator of GSK-3beta inactivation) were measured by Western blot. In another set of

experiments, mice were randomized to receive identical treatment regimens to the ones listed above (n=20), but were monitored for 12-day mortality. **Results** Treatment with TDZD-8 significantly reduced histologic degree of AP, pancreas edema, amylase, lipase, TNF-alpha and IL-1 plasma levels, immunostaining for TGF-beta, VEGF and ICAM-1, and neutrophil accumulation (P<0.01). Similarly, immunostaining for iNOS and nitrotyrosine, as well as plasma nitrite/nitrate levels and tissue malondialdehyde levels, were significantly reduced after the administration of TDZD-8 (P<0.01). Western blot analysis showed significant GSK-3beta and NF-kB inactivation (P<0.01). All of these findings ultimately led to a reduced mortality rate at 12 days (P<0.01). **Conclusion** GSK-3beta specific inhibition ameliorates cerulein-induced AP and improves survival. Blocking protein-kinases may be a novel approach for the therapy of this inflammatory condition.

Red Palm Oil Supplementation in Patients with Chronic Pancreatitis: Is There Any Beneficial Effect on Serum Fatty Acid Profile and Inflammatory-Oxidative Status?

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Context We had previously shown that patients with chronic pancreatitis (CP) have an impaired monocyte burst ability which is unrelated to flare-up of the disease and to the weight loss *per se*. Unlike other oils, red palm oil (RPO) is the richest food source of carotenoids and it is endowed by a good oxidative stability due to its peculiar abundance of tocopherols, tocotrienols and the virtual lack of linoleic acid. **Objective** To investigate the status of the reticulo-endothelial system, as assessed by superoxide anion generation of blood monocytes, the erythrocyte oxidability and to analyze serum fatty acids and cytokines in patients with CP.

We considered 24 patients with CP. **Methods** A dietary questionnaire was used at the entry and re-assessed at the end of the study using the model of seven-day diet history. Patients were instructed not to consume any fish oil supplement and refrain from olive oil dietary consumption, being put on a 2-week wash out period from such use when present. Patients were then given a sample containing a specific highly-purified, non-OGM RPO, (kindly provided by Malaysian Palm Oil Board, Pasir Gudang, Selangor, Malaysia) with the aim of using 40 mL daily for 2 weeks without any frying or heating processing. **Results** Twenty-two patients fully complied

with the supplementation protocol reporting good palatability of RPO and no side effect. BMI and WHR and routine biochemistry remained stable throughout the study period, being comparable to age-matched controls. As compared to baseline values, CP patients fed-RPO showed a significant improvement of the peak value of generated superoxide anion ($P<0.05$) and a reduced erythrocytes oxidability ($P<0.01$). These data were paralleled by a significant normalization of serum vitamin E concentration ($P<0.001$) and the previously observed reduced level of linoleic acid and of docosa-hexenoic-acid

($P<0.05$). RPO brought about also a significant decrease of TNF-alpha and IL-6 ($P<0.05$) which in these patients was constantly higher than in healthy controls ($P<0.05$). **Conclusion** Taken overall, these data suggest that a dietary enrichment with RPO is able to significantly improve the oxidative-inflammatory profile in CP patients while also beneficially correcting their fundamental deficiencies in essential fatty acids. Given the multifactoriality of the disease and the subtle and progressing clinical worsening, such dietary intervention seems an amenable integrative therapeutic tool.

Role of Scores in Evolution of Severe Acute Pancreatitis Complicated by Multiple Organ Dysfunction and Infection

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Context In acute severe pancreatitis organ dysfunctions or infection of pancreatic necrosis are associate conditions with high mortality rate. Many scores have been proposed in order to assess severity. **Patients and Methods** Clinical course of twenty-one patients with severe acute pancreatitis complicated by infected necrosis was evaluated. Severity of disease was estimated by criteria of Atlanta and the amount of necrosis was measured in accordance with Balthazar indications. APACHE II, SAPS II and SOFA scores were computed daily or every other day; two particular phases were studied: the day of ICU admission and the day of surgical treatment. All patients were operated, and undermitted to open packing always after identification of positive pancreatic cultures. Moreover SOFA score was used in order to identify the presence of organ dysfunction. Mann-Whitney, Student t test and chi-squared were calculated. **Results** The mean age of patients was 60.8 years (female/male ratio: 12:9); mean Ranson and APACHE II scores were 6.2 (range: 3-8) and 14.9 (range: 4-28) at the onset of the disease,

respectively. The extent of necrosis was more than 50% in all cases. At the ICU admission 9 out of 21 patients (43%) presented an organ dysfunction. At the day of identification of infected pancreatic necrosis and the contemporaneous surgery 17 out of 21 patients (81%) had organ dysfunction (admission vs. treatment: $P<0.05$). Incidence of failure at the admission was: respiratory 52%, hepatic 33%, renal 28%, cardiovascular 0%; while incidence of failure at the operative treatment was: 62%, 38%, 9.5%, and 43%, respectively. Open packing was performed 2-6 weeks after the onset of the acute pancreatitis. The mean time of open treatment was 26 days and the ICU length of stay was 52.4 days. Six patients died. Six-hundred and 78 scores were calculated; all scores were higher in patients who die. In particular a difference was found between SOFA score at admission and at operative treatment of patients 5 ± 3.2 vs. 8.5 ± 3 (mean \pm SD), $P<0.05$. **Conclusions** In our opinion a persistent high SOFA score could contribute to indicate a surgical treatment even without identification of pancreatic infection.

Patient-Reported Outcomes in Subjects Who Underwent Pancreatic Head Resection for Benign and Malignant Diseases.

The Interim Report of a Multicenter Study

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Context There are few studies regarding patient-reported outcomes in subjects who underwent pancreatic head resection for benign and malignant diseases. **Objective** A one-year follow-up study to evaluate the quality of life in subjects who underwent pancreatic head resection. **Patients** One hundred and seventy-six (99 males, 77 females; mean age 62.1 years, range 20-84 years) consecutive patients who underwent pancreatic head resection for benign and malignant diseases from February 2006 to February 2007. **Methods** The patients were asked to fill out an EORTC QLQ-C30 questionnaire immediately before surgery as well as 6 and 12 months following surgery. Presently, 115 out of the 176 patients (65.3%) filled-out the questionnaire at 6 months and 45 (25.6%) completed the study. The stratified mean±SD values of the various domains and symptom scales referring to 176 sex- and age-matched Swedish subjects were used as a normative group. The ANOVA was applied to analyze EORTC and VAS data. **Results** The final diagnoses, as assessed by histology, were: pancreatic neoplasia (128 patients, 72.7%; 83 ductal carcinomas, 33 IPMT, 7 endocrine tumors, 5 serous cystadenomas); ampullary neoplasia (31, 17.6%); chronic pancreatitis (6, 3.4%), other neoplasia (11, 6.3%; 5 duodenal, 3 common bile duct, and 3 other neoplasia). Abdominal pain was present in 53/157 patients (33.8%) before surgery: 40/114 (35.1%) pancreatic neoplasia; 4/28 (14.3%) ampullary neoplasia; 5/5 (100%) chronic pancreatitis; 4/10 (40.0%) other neoplasia; P=0.002. Eight patients died (4.6%): one patient in the post-operative

period (ampullary neoplasia); 4 (2 ductal adenocarcinomas, 1 ampullary neoplasia, 1 with another neoplasia) and 3 patients (1 ductal adenocarcinomas, 1 ampullary neoplasia, 1 with serous cystadenoma) died before the first and second visit, respectively. In patients with abdominal pain, the 0-10 VAS score (4.7±2.9, mean±SD) was not significantly different (P=0.201) among the four groups of patients. At the baseline study, the following EORTC domains were significantly lower (P<0.05) in the study population as compared to the normative population: global health, role functioning, emotional functioning, and social functioning; on the other hand, the symptom scales such as fatigue, nausea-vomiting, insomnia, loss of appetite, constipation and diarrhea were significantly higher (P<0.05) in resected patients as compared to the normative population; finally, the symptom scale dyspnea was significantly lower (P<0.05) in the study population as compared to the normative population. Furthermore, at the baseline study, no differences in the various domains and symptoms scale of the EORTC questionnaire were found among patients with pancreatic neoplasia, ampullary neoplasia, chronic pancreatitis, and other neoplasia. Within the group of patients with pancreatic neoplasia, no significant differences in the various domains and symptoms scale of the EORTC questionnaire were found among patients with ductal carcinoma, IPMT, endocrine tumors, and serous cystadenoma. In the 45 patients who completed the study, there was a significant progressive improvement (P<0.05) of the global health,

emotional functioning, and cognitive functioning as well as an improvement of symptom scores ($P<0.05$) such as fatigue, pain, insomnia, loss of appetite, constipation. In addition, the improvement of global health and fatigue was significantly higher ($P<0.05$) in ampullary neoplasia ($n=9$) than in pancreatic tumors ($n=34$). **Conclusion** The patient reported outcome shows that before

pancreatic head resection there is an impairment of the quality of life as compared to the reference population. Most important, this impairment is not related to the disease responsible for the surgery. The quality of life significantly improves in the 12 months following surgery particularly in patients with ampullary neoplasia.

Pancreatic Head Mass. Is always Malignant Tumor?

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Context Pancreatic adenocarcinoma is one of the most aggressive of human malignancy. Because of its silent course, late clinical manifestation and rapid growth, it has been considered as a silent killer. For this reason malignant tumor is the most important differential diagnosis when you find a pancreatic head mass. Others differential diagnosis include ampullary carcinomas, neuroendocrine tumors, acute and chronic pancreatitis and at least autoimmune pancreatitis (AIP). We report a case of pancreatic head mass in which differential diagnosis has led to resolve some questions about diagnostic and therapeutic choice.

Case report C.G: male 52-year-old, was admitted in our department due to abdominal pain. Laboratory bloody test showed acute pancreatitis. Medical therapy was administered to the patient. An abdominal ultrasonography identified a pancreatic head mass. The abdomen CT was then performed, confirming the mass that involved the superior mesenteric vessels. Bloody tumoral markers levels were normal. Suspecting a malignant neoplasm, an EUS with FNA was performed, but it revealed a chronic pancreatitis. The patient was discharged with a EUS follow-up at 2 months, but after 2 weeks he came back due

to abdominal pain and jaundice. The CT scan performed, did not show any modification comparing with the previous one. An explorative laparotomy was planned and an intraoperative ultrasound identified vessel invasion. An intraoperative incisional biopsy was suspected for neoplasm but not confirmed the malignancy. Due to the unresectability of the mass a choledocojejunal anastomosis was performed in order to resolve the jaundice and the patient was led to the oncologist for adjuvant chemotherapy. The definitive histological result of the incisional biopsy revealed a chronic pancreatitis. After 3 months of chemotherapy the pancreatic mass disappeared, and a AIP was suspected in this patient, but until now not confirmed. **Conclusion** Not all pancreatic head mass are malignant tumor; the 9.2% of Whipple resection are performed for benign but clinically suspected for malignant mass of the pancreas. The most common benign etiology in this case is the AIP. Preoperative diagnosis of this disease is very rare but in patients responders to risk factor for AIP, serum level of IgG4 should be performed. This screening may avoid unnecessary surgery and chemotherapy in future case.

Morphological and Functional Study Using Magnetic Resonance Cholangiopancreatography (MRCP) with Secretin Stimulation in Patients Affected by Pancreatitis

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Context The morphological and functional study of the pancreas with magnetic resonance (MRI) has assumed a fundamental role in the diagnosis and follow up of subjects affected by chronic pancreatitis. After the administration of secretin, the duodenal filling indirectly indicates the presence of exocrine pancreatic insufficiency. The secretin stimulates the secretion of pancreatic fluids and bicarbonates in the exocrine cells and augments the tone of Oddi's sphincter. After stimulation, the main and secondary ducts are better defined and visualized, favoring the detection of ductal abnormalities. **Objective** In our study we have correlated the morphological and functional data obtained by secretin-MRCP and with clinical biochemical data from the patients affected by chronic pancreatitis and acute reoccurring pancreatitis. **Methods** Nine subjects with chronic pancreatitis have been studied (5 males; 4 females), 3 with genetic etiology, 4 alcoholics and 2 idiopathic, as well as 6 subjects with acute recurring pancreatitis (2

males; 4 females). The following evaluations have been done: amylase, lipase, hepatic cytolysis and cholestasis, fecal elastase, blood glucose concentration, age at onset, and clinical history. The patients were studied with a 1.5 Tesla scanner using a T2 weighted single shot fast spin echo sequence. Size of the main pancreatic duct (head, body and tail) and duodenal filling before and after secretin stimulation were measured quantitatively. Image analysis included also anatomical variants, visualization of side branches, endoluminal filling defect and acinar filling. **Results** We have found a good correlation between ductal variations, number of secondary ducts, pancreatography, pre- and post-secretin stimulation, duodenal filling and biochemical indexes of exocrine functionality. We have also found significant differences among each form of pancreatitis. **Conclusion** The MRCP with secretin stimulation is fundamental in the morphological and functional evaluation in patients affected by pancreatitis.

Endocrine Pancreatic Tumors: Usefulness of Mangafodipir Trisodium-Enhanced MR Imaging

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Context Development of faster MRI systems with improved contrast and temporal resolution, and tissue-specific contrast agents such as mangafodipir trisodium, have significantly enhanced the role of magnetic resonance in imaging of pancreatic

neoplasms, especially of endocrine pancreatic tumors. **Objective** To determine whether mangafodipir trisodium-enhanced MRI could improve the characterization of endocrine pancreatic tumors. **Methods** Our study group included fifteen patients with proven

diagnosis of endocrine pancreatic tumors, that underwent MRI at 1.5 T unit (Signa Infinity[®], GE Healthcare, Milan, Italy). After acquisition of axial/coronal, thin/thick-slab, single-shot T2w sequences, MR protocol included axial T1w fat-suppressed breath-hold SPGR images obtained before and 30-40 minutes after intravenous infusion of mangafodipir trisodium (Mn-DPDP, Teslascan[®]; GE Healthcare, Milan, Italy). The detection of a focal pancreatic lesion and its signal intensity (SI), compared with that of normal parenchyma, were evaluated in consensus by two observers for pre- and post-contrast T1w images. SI measures were calculated at the level of pancreatic parenchyma and focal lesion before and after Mn-DPDP administration. Imaging results

were correlated with those of surgery, biopsy, and/or imaging follow-up. **Results** A total of 20 pancreatic endocrine tumors were correctly identified by the observers; two of them were malignant. On Mn-DPDP-enhanced MRI the signal intensity pattern of 10/20 lesions was isointense or hyperintense, whereas the other 10 lesions appeared as well-circumscribed hypointense areas. In 3/20 lesions a cystic component was also identified. A significant increase of the contrast-to-noise ratio was found in the post-contrast images ($P < 0.05$). Furthermore, all the lesions showed the uptake, even slight, of Mn-DPDP. **Conclusion** Our preliminary data suggest that contrast-enhanced MRI with Mn-DPDP helps to improve the detection and characterization of endocrine pancreatic tumors.

A Case of Adult Cystic Fibrosis Due to Extremely Rare Compound Heterozygous Mutation: Phenotype and Possible Association with Gastrointestinal Damage

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Context Cystic fibrosis (CF) is the most common life-threatening inherited disorder in Caucasian population. More than 1,300 mutations have been described. Most of the mutations have a low frequency. It is difficult to correlate the phenotype of CF disease with the genotype especially in rare compound heterozygous (CH) mutations. **Case report** We report the case of a 31-year-old man with diagnosis of CF due to CH mutations. The patient had a history of respiratory disorders since 8 (asthma, recurrent bronchitis and sino-nasal disease). At age 25 he received surgery for an intestinal obstruction diagnosed as a colonic Crohn's disease (CD), he had no gastrointestinal symptoms since then; he came to our attention for a suspect of CF. We demonstrated pancreatic insufficiency by the evidence of steatorrhea (fecal fat 9.7 g/day) and decreased duodenal filling at secretin-enhanced MRCP, also showing pancreas

divisum and complete pancreatic fatty atrophy confirmed by h-CT. He had no diabetes. He had liver steatosis with mildly increased AST and ALT, gastro-esophageal reflux disease with histological esophagitis and malnutrition signs with BMI equal to 19.5 kg/m². The pulmonary function was normal, but h-CT showed diffuse bronchiectasis. He had the sweat test positive and azoospermia too. A colonoscopy (CS) revealed a normal colon and neo-terminal ileum both macroscopically and histologically, challenging the previous CD diagnosis. A genetic test demonstrated a CH with mutations 2183AA>G and 2789+5>A. We started pancreatic enzymes with normalization of fecal fat levels. Genetic analysis of the patient's family is ongoing. **Discussion** This is the first case of this CH mutation reported in our country. Frameshift mutation (class I) at 2183AA>G and splicing mutation (class V) at 2789+5>A are both rare

mutations accounting respectively for 0.36% and less than 0.1% of cases in Europe. CH for these two mutations is extremely rare with only four cases reported until now to our best knowledge. Notably, the 2183AA>G mutation which is associated with a severe phenotype, is relatively frequent in North-East Italy (9.3%) where the patient's mother family originated. The 2789+5>A mutation has only been described in Greece and Bulgaria in European databases and is associated with a mild phenotype with late onset and no PI. There are no data available

on the severity of this CH nor on the possible association with gastrointestinal involvement. The diagnosis of CD is in our opinion unlikely given the following normal findings at CS, but the possibility of a fibrosing colonopathy in the absence of any pancreatic enzyme replacement also seems unlikely. **Conclusions** This report highlights the importance of careful testing for multiple mutations in patients with a suspect of CF and of multicenter databases to help identifying genotype/phenotype associations.

Multidisciplinary Approach for Severe Acute Pancreatitis in Children: Our Experience in a Pediatric Surgery Unit

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Context Acute pancreatitis is rare in children (5-10 cases/year at major children's hospitals). Severe acute pancreatitis (SAP) is usually treated in Pediatric Surgery Units. SAP is a complex disease requiring different and specific management depending on its course. **Objective** To evaluate SAP etiologies, outcome, management and complications and the importance of a multidisciplinary approach. **Methods** From 1992 to 2006 the hospital records of 22 consecutive patients treated for SAP in our Pediatric Surgery Unit (S. Bortolo Hospital, Vicenza, Italy) were reviewed. The children were divided into three groups: group 1, congenital abnormalities; group 2, trauma; group 3, other causes. In all patients, serum amylase was greater than 3 clinical and ultrasound or CT scan showed evidence of pancreatitis. Patients were selected on the basis of a calculated Glasgow equal to or greater than 3. MRI, hepatobiliary scintigraphy scan and ERCP were also used. Patients underwent medical, surgical, endoscopic or radiological procedures. Range follow-up: 6 months to 10 years. **Results** A total of 13 males and 9 females (median age:

7 years, range: 3-17 years) were studied: 5 cases in the group 1; 12 cases in the group 2; 5 cases in the group 3. Eleven patients with SAP benefited from a non-operative management (50%). Three traumatic SAP required ultrasound or CT guided pancreatic pseudocyst external drainage (13.6%); one child required endoscopic papillotomy and biliary stones extraction (4.5%); 7 cases (31.8%) were resolved by surgical procedures: 3 surgical papillotomies (in one case followed by a hepatic-bowel-anastomosis), 1 bowel-cyst -anastomosis (for an large pancreatic pseudocyst), 1 hepatic-bowel-anastomosis, 2 external pancreatic surgical drainage. Complications: 4 recurrent pancreatitis, 2 cases in each group 1 and 3; 6 pancreatic pseudocysts (one of which spontaneously resolved), 1 pancreatic fistula treated with a caudal pancreatectomy, in the group 2; no mortality reported. **Conclusions** In our experience, abdominal trauma was the most important cause of hospitalization for SAP (54.5%). An urgent and multidisciplinary approach is associated with low morbidity rate and no mortality (in the literature a mortality of 2-10% is reported). In

the pediatric patient, an initial suspicion of pancreatic disease is important in preventing complications. Close collaboration between pediatricians, pediatric surgeons, gastro-

enterologists, infectivologists, radiologists and nuclear medicine specialists is recommended in the treatment of SAP.

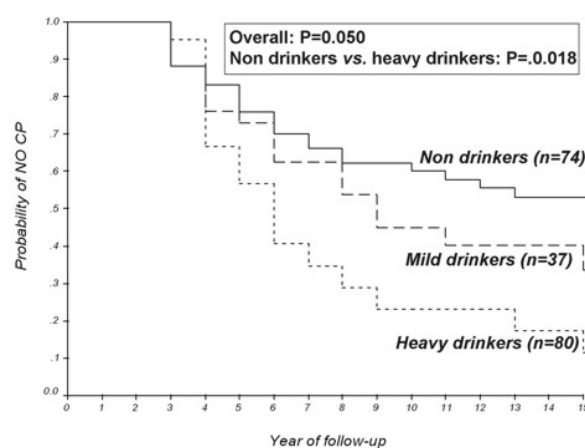
Recurrent Pancreatitis: Effect of Alcohol on the Progression To Chronic Stage

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Context In Western countries, alcohol is epidemiologically associated to chronic pancreatitis (CP). However, its role on the pathogenesis of the disease is still unclear. Experimentally, alcohol may activate pancreatic stellate cells and, therefore, induce pancreatic fibrosis. Alcohol abuse may be a factor involved on the evolution from acute to CP. **Objective** Aim of this study was to investigate if alcohol is a key factor in the onset and progression toward CP. **Patients and methods** One-hundred and 33 patients (68 males and 65 females, mean age 50±14 years) suffering from recurrent pancreatitis (RP) (at least two episodes of pancreatitis) without instrumental findings (CT, MR and RMCP, ERCP, EUS) of chronic disease, were retrospectively enrolled from January 1997 to December 2003. The patients were then followed up to June 2006. For each patients, we collected clinical, instrumental and biochemical data, as well as information about alcohol and smoking habits. The mean follow up time from the onset of the disease (first episode of acute pancreatitis) was 10±8 years. Seventy-four patients (56%) were non drinkers, 37 (28%) drank less than 80 g/day of alcohol and 22 (16%) 80 g/day or more of

alcohol. **Results** A final diagnosis of CP was made on 77 patients (60%), 46% in non drinker group, 62% in mild drinkers and 91% in heavy drinkers (P=0.001). The Figure shows the survival curve for the diagnosis of chronic pancreatitis in the three groups. In addition, there was a strong association between alcohol intake and cigarette smoking (r=0.41; P<0.001). Other risk factors for CP were male sex and the diagnosis of cystic dystrophy of the duodenal wall, both strictly associated with alcohol and smoking habits. **Conclusions** In patients with recurrent pancreatitis, alcohol intake and cigarette smoking influence the progression toward chronic pancreatitis.



Endotherapy of Recurrent Pancreatitis Following Scarring of the Pancreatic Orifice after Biliary Sphincterotomy

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Context Recurrent acute non-biliary pancreatitis (ANBP) can occur as a clinical

manifestation of many pancreatic diseases. Endoscopic or surgical biliary precut/

sphincterotomy can lead to a scar of the pancreatic orifice with subsequent obstruction of the pancreatic duct and development of ANBP. **Objective** Aim of the study is to review the results of endoscopic treatment of 'iatrogenic' pancreatic duct obstruction secondary to biliary precut/sphincterotomy. **Methods** During a 22-year period, 9 patients (6 females, 3 males; mean age 60 years, range 11-78 years) underwent ERCP because of a history of recurrent ANBP occurring after endoscopic (n=7) or surgical (n=2) biliary precut/sphincterotomy for common bile duct stones. CT scan or MRCP with secretin stimulation showed in all cases a dilation (equal to or greater than 5 mm) of the main pancreatic duct (MPD) with a papillary obstruction. All patients had been cholecystectomized and precut/sphincterotomy had always been performed in other institutions. Endoscopic treatment consisted in pancreatic sphincterotomy (PS) or sphincter dilation. If pancreaticoduodenal outflow of contrast medium was not satisfactory after PS or dilation, one or two pancreatic plastic stents were inserted and then removed within 6 months. **Results** Previous treatment consisted in biliary precut (n=6), surgical sphincterotomy (n=2) and standard biliary sphincterotomy (n=1). The first episode of ANBP occurred after a mean of 18 months and 27 years after endoscopic

and surgical precut/sphincterotomy, respectively. The mean number of ANBP before endoscopic treatment was 6 (range 2-14). A tight stricture of the pancreatic orifice was detected in all cases. MPD cannulation failed at the first attempt in 3 cases (33%) due to the tightness of the papillary stricture, but it succeeded at the second (n=2) or third (n=1) attempt. In 4 cases (45%) PS alone allowed a satisfactory drainage; in 3 cases (33%) one or two pancreatic plastic stents were inserted without sphincterotomy; the last 2 patients (22%) underwent both PS and stenting. No specific complications were recorded. After a mean follow-up of 3.7 years (range: 0.4-10.9 years) 8 patients (89%) did not experience additional ANBP. One patient had an ANBP 6.8 years after endoscopic treatment (stricture of the pancreatic sphincterotomy) and underwent re-sphincterotomy; the patient is asymptomatic after a further 18 months. **Conclusions** Endoscopic treatment of 'iatrogenic' obstructive pancreatitis following endoscopic or surgical precut/sphincterotomy is safe and effective. These cases are characterized by a tight fibrotic stricture of the pancreatic orifice and their incidence is higher after precut techniques. Endoscopic pancreatic drainage is difficult in this setting as shown from the high failure rate at the first attempt in our experience.

Persistent Elevation of Serum CA 19-9 without Any Evidence of Malignant Disease

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Context Serum CA 19-9 is the mainstay marker for the diagnosis of biliopancreatic malignancies, but a slight elevation of its levels can also be observed in various benign diseases. **Case report** In this study a marked and persistent increase of serum CA 19-9 was reported in 9 patients, who had no evidence of malignant disease. Eight women and one man

were studied and initial diagnoses were lung fibrosis in 2, diabetes in 2, non ulcer dyspepsia in 2, obesity in 1, acute diarrhea in 1, and colon diverticula in 1. Their past medical history included, endoscopic resection of colon adenoma in 2, papillo-sphincterotomy due to cholelithiasis in 1 and mastectomy due to breast cancer in 1. At

admission, routine blood tests were normal except for leukocytosis in 3 patients, anemia in 2, hypoalbuminemia in 2, elevation of gamma-glutamyl transpeptidase (GGT) in 3 and high C-reactive protein levels in 2. Serum CA 19-9 levels ranged from 112 to 1,118 IU/mL (mean 298 IU/mL). The other tumor markers were normal, except for CEA elevated in 3, CA 15-3 in 2, CA 125 in one. Abdominal ultrasonography, CT-scan, upper X-ray gastrointestinal series and gastrointestinal endoscopies were negative for malignancies. Follow-up period ranged from 2 to 6 years: during this lapse of time serum CA 19-9 values were persistently elevated in all patients. Leukocytosis and anemia disappeared and GGT levels normalized in 1 of the 3 patients. Diabetes was diagnosed in one patient. Magnetic resonance cholangio-

pancreatography (RMCP), endoscopic ultrasound (EUS) and 18F-FDG Positron emission tomography (PET), performed in 3 patients because of a further increase of serum CA 19-9 did not reveal any malignancies. At present, 8 patients are alive: 6 are in an apparently healthy conditions, and 2 suffer from chronic respiratory insufficiency. One patient died due to end stage renal disease secondary to amyloidosis. **Conclusion** Our study confirms that persistent and significant elevation of serum CA 19-9 are not infrequent in non malignant-non cholestatic disease. The reason for this finding is not univocal: a disorder of immune response can be suggested in conditions such as interstitial lung disease, while in the other cases it remains unclear.

Incidental Cystic Lesion of the Pancreas: What Kind of Management?

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Context Incidental pancreatic lesions are seen more frequently in relation to the improving of diagnostic accuracy of the imaging techniques. Cystic lesions of the pancreas are several and different is its natural history. Thus it is mandatory to recognize the different type of cystic lesion to plan the proper management. **Methods** From January 2004 to June 2007 we enrolled all the cases of incidental cystic pancreatic lesions in our prospective database. For every patient, surgery was suggested in presence of the following features: size greater than 3 cm, dilation of main pancreatic duct, intramural nodal. The other patients were followed-up according the size of the cystic lesion: less than 1 cm, every year; 1-2 cm, every six months; 2-3 cm, every 3 months. CA 19-9, US and spiral multislice CT were performed in the follow-up. MRCP was performed every year. **Results** We observed 39 patients; they

were asymptomatic, 18 were males and 21 were females, mean age was 70.3 years (range: 43-80 years). Nine patients underwent surgery at diagnosis (23.1%). Thirty were followed-up (76.9%). Four out of the nine operated patients were borderline-IPMN, 2 were oligocystic serous tumors, 1 benign IPMN, 1 cystic neuroendocrine carcinoma and 1 solitary cyst. Among followed-up patients 12 were observed every 3 months, 12 every 6 months and 6 every year. No one had a change in the clinical and morphological characteristics at a mean follow-up of 14 months. **Conclusions** Every incidental cystic lesion is to be considered for surgical treatment. It is important to recognize the morphological characteristic at diagnosis to plan a proper management. Follow-up is mandatory because some of these lesions could develop malignancy.

POSTER SESSION

Autoimmune Pancreatitis Associated with Anisakis Infection

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Context Anisakidosis is a parasitic disease of the human gastrointestinal tract caused by ingestion of larvae of marine nematodes such as *Anisakis spp.* or, rarely, *Pseudoterranova spp.*, present in raw or undercooked fish. This infection may determine diagnostic problems.

Case report A 67-year-old man with type 2 diabetes mellitus of seven years duration was observed because of persistent epigastric pain of mild intensity, deterioration of the diabetes and diarrhea of seven months duration. At physical examination, the epigastric pain increase at palpation. Laboratory values were normal except for hyperglycemia, eosinophilia (leucocytes $6.74 \times 10^3/\mu\text{L}$, eosinophils 8.6%) and a total IgE count of 206 kU/L (reference limit: less than 100 kU/L). Fecal fat excretion was clearly abnormal (12 g/24 h). Computed tomography scan revealed a small mass in the head of the pancreas; endoscopic ultrasonography confirmed a hypoechogenic pancreatic mass of 23x12 mm in diameter. The common bile duct and the main pancreatic duct were normal; cytologic examination revealed only

rare leucocytes. A surgical exploration was planned due to the suspicious of pancreatic cancer. During the operation a small mass in the gastric antrum was also found and a pancreaticoduodenectomy with distal gastrectomy was performed. The histological examination of the pancreatic specimen shows a picture similar to autoimmune pancreatitis (presence of small lymphocytes together with duct destructive pancreatitis). Grossly the gastric specimen showed the presence of a granuloma of the gastric wall and the histological examination showed the presence of an eosinophilic granuloma with peripheral vasculitis reaction and containing *Anisakis*. After this finding the patient was interrogated again and he reported to had eaten sushi about 8 months before. The patient had an uneventful recovery and he was discharged of postoperative day 10. **Conclusion** The possibility of a casual association between autoimmune pancreatitis and worm infection should be kept in mind after a carefully taken medical history and when an unexplained eosinophilia is found.

Bilio-Pancreatic Mini-Invasive Oncologic Surgery in Elderly

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Context More minimally invasive techniques are currently available for the surgical oncologist in the optimal staging of bilio-pancreatic cancer. Age is not a limitation for oncological surgery; tumor stage and co-

morbidity define the surgical treatment. The increased age of population is accompanied by an increase of age-related diseases, such a cardiovascular disease, hypertension, arthritis and other malignancies. With the

development of endoscopy, laparoscopy, ultrasonography and biopsy equipment, more minimally invasive techniques are currently available for the surgical oncologist to provide a better optimal diagnosis and staging strategy, followed by an appropriate surgical treatment of biliopancreatic cancer. **Objective** Improvement in the diagnostic and surgical care of elderly cancer patients will have a final impact on disease and overall survival rates of the different types of cancer treatment. **Methods** We retrospectively reviewed the records of patients between January 2001 and December 2006 who had either a mass in the biliopancreatic area classified as clinically resectable. Tumors were considered to be resectable when there was no evidence of distant extra pancreatic disease or involvement of lymphnodes outside the classic margins of resections. Occlusion or encasement of the superior mesenteric artery or vein, celiac artery or portal vein were used as a criteria for unresectability.

Twenty-one patients over 65 and under 75 years (middle age 69) with primary biliopancreatic cancer were submitted to operations for potentially operative resection. In all cases staging laparoscopy was performed just prior to planned open exploration and resection. **Results** Fifteen patients underwent exploratory celiotomy for potential resection. Two of five patients (40%) with distal cholangiocarcinoma survived at 5 years. Six patients (28.6%) had unresectable disease identified at laparoscopy and were spared an unnecessary laparotomy. **Conclusions** Laparoscopy may have a role in the staging of patients with biliopancreatic malignancies. Staging laparoscopy should be performed to identify patients with metastasis in whom short term endoscopic palliation is satisfactory. Also in elderly pancreaticoduodenectomy for pancreatic and biliary has been associated with the falling post-operative morbidity and mortality rates and long term survival.

Intestinal Autotransplantation for Locally Advanced Pancreatic Cancer

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Context Pancreatic cancer (PC) involving the superior mesenteric artery (SMA) and vein (SMV) is usually associated to deep spread into the mesenteric root (MR) and for this reason deemed unresectable. However, the efficacy of new chemotherapeutic drugs can allow in selected cases the surgical treatment of such lesions. **Objective** To assess the preliminary outcomes of en-bloc resection of superior mesenteric vessels and MR for locally advanced PC. **Methods** On a total number of 163 pancreatectomies associated to vascular resection we carried out in 7 cases (4.3%) simultaneous resection of SMV and SMA en-bloc with the MR, followed by intestinal autotransplantation. This paper focuses on 6 of these patients (5 women and 1 man) who were diagnosed with ductal adenocarcinoma. In the first period of our experience (1987-1998; group 1) the

indication to surgery was based only on technical grounds (n=3), while subsequently (1999-2006; group 2) we selected only those patients (n=3) who responded to neoadjuvant treatments. **Results** There were 5 (83.3%) total splenopancreatectomies and 1 (16.7%) pancreaticoduodenectomy. In 4 (66.7%) cases, besides superior mesenteric vessels, celiac trunk and/or hepatic artery were resected, for a total number of 16 vascular segments. Two patients (33.3%) developed post-operative complications (upper digestive bleeding and laminar portal thrombosis, respectively) and there were no perioperative deaths. SMV was histologically proven to be infiltrated in 2 patients (all from group 2) and SMA in 2 cases (all from group 1). Overall 1-year survival was 75% (65% in group 1 vs. 100% in group 2; P NS). All patients from group 1 died due to liver metastases after a

mean survival of 25.3 months; in the group 2 one patient died due to tumor recurrence at multiple distant sites 16 months after resection and the remaining 2 patients are still alive. **Conclusions** En-bloc resection of superior mesenteric vessels followed by intestinal autotransplantation for locally

advanced PC is doable with an acceptable operative risk in appropriate candidates, furthermore at the light of the sometimes striking efficacy of new neoadjuvant treatments. This pilot experience, although encouraging, need to be verified in a larger and standardized study.

Arterial vs. Pancreatic Phase: Which is the Best Choice in the Evaluation of Pancreatic Endocrine Tumors with Multidetector Computed Tomography (MDCT)?

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Content In literature there is no clear consensus in acquisition technique in pancreatic endocrine tumors. **Objective** To assess whether pancreatic phase may replace the arterial one in the evaluation of endocrine pancreatic tumors. **Methods** Twenty-nine endocrine pancreatic lesions, with definitive morphological and immunohistochemical characterization, after surgical treatment (n=24) or endoscopic-ultrasonography guided fine-needle-aspiration cytology (n=5), were retrospectively evaluated. All lesions were studied with MDCT (16 rows technology) triple-phase technique from December 2004 to August 2006. Images obtained during each phase were separately interpreted by two senior radiologists, experienced in pancreatic pathology, blinded to surgical results. The attenuation of the endocrine tumors and of normal pancreas and the mean absolute tumor-to-gland attenuation difference, were

measured in each phase and these data were analyzed with the Student-t test. Furthermore the detection of arterial vascular abnormalities and of hypervascular liver metastases, in arterial and pancreatic phase, and diagnostic contribution of these two phases were compared. **Results** For both radiologists the mean absolute tumor-to-gland attenuation difference in pancreatic phase (40±53 HU and 34±56 HU) resulted significantly higher (P<0.05) than the one in arterial phase (31±38 HU and 26±43 HU). There were no differences in detection of arterial vascular abnormalities and hypervascular liver metastases in both phases. Diagnostic contribution was higher in pancreatic phase. **Conclusion** In our experience, we observed that pancreatic phase can replace arterial one in the evaluation of pancreatic endocrine tumors.

Overgrowing Mucinous Cystic Neoplasm of Pancreas in Pregnancy: Case Report

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Case report We describe a case of a 36-year-old pregnant woman who, for the onset of abdominal not specific pain, at 16th week

performed abdominal US and MRI demonstrating a 70x40x30 mm cystic mass arising from the body-tail of the pancreas.

The mass was well delimited, multiloculated for the presence of several septa and caused compression of splenic artery and the occlusion of the splenic vein, with the presence of collateral circoli. A MRI and EUS performed at 20th week showed a rapid increase of volume mass (150x90x110 mm); considering the symptoms and the risk related to uterus compression and fetal intra-uterine growth restriction by the voluminous mass, a surgical resection was indicated. The patient underwent a laparotomic distal pancreatectomy: intraoperatively a large mass originating from the pancreas without signs of infiltration was found; because its size it was necessary to drain the cyst; the fluid was analyzed for cytology and tumor markers and there was no evidence of malignancy. The operation time was 300 minutes and blood loss was 450 mL. Post-operative course was

regular and she was discharged on 9th post-operative day. Histological examination demonstrated a benign mucinous cystic tumor of the pancreas; microscopic examination showed a well differentiated mucin secreting epithelium associated with ovarian-like stroma. Immunohistochemical studies revealed diffuse positive staining for progesterone and estrogens receptor and these features may justify the rapid increase of volume mass during pregnancy because of the hormone-dependent epithelium. The patient had a healthy full term infant. **Conclusion** Our experience demonstrates that, in the rare case of a symptomatic fast growing pancreatic cystic mass during pregnancy, there is an indication to surgery to prevent complication to the fetal growth, with good results and an acceptable risk for the fetus, if surgery is performed between 20th and 26th week.

Chronic Pancreatitis: Problems in Diagnosis and Treatment. Two Different Cases

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Context Chronic pancreatitis is a disease resulted in a progressive inflammatory process that causes an eventual endocrine and exocrine insufficiency of the pancreatic gland and a substitution of the normal tissue with fibrotic one. The most frequent cause is alcohol intake, because of this, the pathology is very frequent in Northern Italy and very less common in Southern. Other causes are tobacco, drugs, idiopathic form, genetic one and groove pancreatitis which represent a cystic dystrophy of the duodenal wall. The predominant symptom is the pain. The diagnosis is performed by instrumental exams as CT scan, MR and more of all EUS. The treatment is based on the removal of the cause, when it is possible, but there are other situations that need an urgent management such as intractable pain. The treatment can be pharmacological, endoscopic and surgical. We report two cases, with two different kind

of pancreatitis **Case report #1** A 76-year-old male, admitted to our department with abdominal pain and vomit. Laboratory exams did not show anything important. CT scan, abdominal MR, and EUS showed a pronounced dilatation of the Wirsung. He underwent to ERCP and discharged 3 days later. After 6 months he is in good clinical situation and does not need treatment. **Case report #2** A 37-year-old alcoholic male admitted to our department with diffuse abdominal pain. Laboratory tests demonstrated increase of amylase and lipase. CT scan and abdominal MR showed a Wirsung duct dilatation and pseudocyst, EUS showed an alteration of the duodenum wall suggesting a typical paraduodenal type of chronic pancreatitis. He underwent to ERCP. Actually he stopped alcohol intake and he is in good clinical situation. A surgical approach was planned but the patient refused it.

Conclusion The choice of treatment is decided on the basis of the kind of the pancreatitis, when possible in alcoholics the abstinence is the first choice. Endoscopic approach, less invasive than surgical one, must be pursued. The surgical treatment generally follows endoscopy but sometimes it represent the only choice. The kind of

surgical operation varies in relation to the morphologic aspect, and if there is suspicion of neoplasia. The type of chronic pancreatitis and also the clinical differences of the patients are important factors influencing the decisions concerning the treatment.

Safety and Efficacy of Bioglue® in Preventing Pancreatic Fistula after Major Pancreatic Resections

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Context Pancreatic fistula (PF) represents the main complication (10-29%) after pancreatic surgery and it is the consequence of pancreatic-enteric anastomosis leakage or parenchymal leak not related to an intestinal anastomosis. Soft pancreatic texture with a not dilated pancreatic duct represent the major risk factors for PF. Mortality after pancreaticoduodenectomy (PD) is reported in several large series to be less than 5%. PF and local sepsis are the main causes of delayed arterial hemorrhage with a high mortality rate (14-38%). Therefore, any effort should be implemented in order to reduce the incidence of PF. The biological adhesive Bioglue® has not been described previously as a pancreatic or pancreaticojejunostomy sealant after major pancreatic resections. **Objective** We describe our experience with using Bioglue® to coat pancreatic resection surface after distal pancreatectomy (DP) and pancreaticojejunostomy after PD. **Methods** From June 2006 to May 2007 an overall of 17 patients affected by periampullary or distal pancreatic

neoplasms have been operated on by a major pancreatic resection: 13 PD and 4 DP. Two mL of Bioglue® have been applied on the anastomotic or pancreatic stump surfaces. PF was defined as the collection on 5th postoperative (PO) day, from the abdominal drains, of any volume of amylases rich fluid containing more than x3 amylases serum values. **Results** No PO mortality has been observed. PF has been documented in 3/13 (23%) after PD and none after DP. In 2 cases PF has been successfully treated conservatively by NPO and octreotide. One patient, required surgical drainage of multiple intra-abdominal collections and radiological PTBD. This latter patient has been discharged on 82nd PO day after PTC documentation of PF closure. **Conclusion** Bioglue® can be safely utilized to coat pancreatic surface after DP and pancreaticojejunostomy after DP. This experience warrants further larger controlled studies of the potential value of Bioglue® in reducing the incidence of PF after major pancreatic surgery.

HIPK2 Gene Plays a Relevant Role in Human Pancreatic Tumors

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Context Pancreatic carcinoma is one of the leading causes of cancer-related death in

virtually all industrialized countries and is characterized by aggressive tumor growth and

by high metastatic propensity, which are responsible for treatment failure. Major genetic alterations have been reported in this type of cancer, affecting the proto-oncogene *K-ras* and a subset of tumor suppressor genes such as p53, p16, Rb and DPC4/SMAD4. Recent studies suggest that HIPK2 gene is an upstream regulator of p53 activity, functions as a co-repressor for homeodomain transcription factors, and it regulates transforming growth factors (TGF). **Objective** Aim of our study was to analyze the role of HIPK2 in human pancreatic tumor tissue samples by analyzing its expression levels and the DNA alterations at its specific chromosomal locus. **Methods** HIPK2 mRNA and protein expression levels were evaluated in 11 pancreatic cases by RT-PCR and western blot, respectively. **Results** Our results show that HIPK2 mRNA level decreased in tumoral tissues compared to matched extratumoral tissues in 63% of the cases. Similarly, HIPK2 protein expression levels were reduced in 72% of the cases. In addition, we performed LOH analysis using two microsatellites mapping at 7q33-35, one of which (D7S6440) was located inside the HIPK2 gene. The analysis was performed on both laser capture microdissected epithelial and stromal cells in 84 pancreatic lesions,

including 27 pancreatic tumors and 6 pancreatitis. We found a high frequency of LOH for the microsatellite D7S6440 in tumor tissue (36%), while the highest LOH frequency in samples with pancreatitis was found at D7S1779 (29%). Surprisingly, LOH at D7S6440 was observed at high frequency in stromal tissue too (69%). The high LOH frequency observed for the microsatellite located inside the HIPK2 gene in both epithelial and stromal cells suggest that the HIPK2 gene is involved in the pancreatic tumorigenesis. To investigate the possible biological role of HIPK2, we manipulated HIPK2 gene expression in two cellular lines, characterized by different p53 status and HIPK2 expression levels, namely HPAC (p53^{wt} /HIPK2⁻) and PANC-1 (p53^{mut} /HIPK2⁺). Overexpression of HIPK2 gene in HPAC cells, by transfecting the pCMV-2B-HIPK2 vector increased cell death by cell count while RNA interference of HIPK2 gene in PANC-1, obtained by transfecting the pSUPER-Retro-HIPK2 vector reduced the number of cell that undergo to cell death. **Conclusion** Our results indicate that HIPK2 gene can be considered as a new oncosuppressor gene and that the HIPK2/p53 pathway can be relevant in the pancreatic tumorigenetic process.

Pancreatic Leakage in Pancreatic Surgery for Cancer: Our Experience

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Context We present an analysis of the role of pancreatic leakage in rising of complications linked to pancreatic surgery at our Centre. **Case report** From January 2000 to April 2007, 38 consecutive patients underwent surgical procedure for pancreatic cancer. We performed 7 pancreaticoduodenectomy (PD) and 26 distal pancreatectomy (DP); we recorded results of only 25 patients who

underwent PD or DP, actually also in follow-up. The surgical reconstruction after PD was as follows: 1 manual non-absorbable stitches closure of the main duct, 3 closure of the main duct with linear stapler, 3 temporary occlusion of the main duct with neoprene glue and 24 duct-to-mucosa anastomoses. **Conclusion** Morbidity rate was 60%, caused by: pancreatic leakage (48%) hemorrhagic

complication (10%) and infectious complication (15%). At the multivariate analysis complications were linked to: age 70 years (p 0.0139), T3 (p 0.031) and N2 (P=0.000001), surgical procedure (PD, P=0.0018) and pancreatic residual treatment (duct-to-mucosa anastomosis P=0.003, and stapler closure P=0.002). Hemorrhagic

complication, biliary anastomosis leakage and infectious complication were consequences of pancreatic leakage (all P=0.025). On the ground of our data we believe that manual non-absorbable stitches closure of the main duct and temporary occlusion of the main duct with neoprene glue should be avoided in the reconstructive phase.

Solid Masses of the Head/Body of the Pancreas: Role of Multidetector Computed Tomography (MDCT) in the Evaluation of Superior Mesenteric Vein (SMV) involvement to Assess Surgical Strategy

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Context SMV involvement is not an absolute criterion of non resectability of a solid mass in head/body of pancreas. MDCT is an useful imaging modality to evaluate vascular involvement. **Objective** To evaluate impact of MDCT with 2D/3D reconstructions to assess SMV involvement and surgical resection. **Materials and methods** From May 2006 to June 2007, 27 patients affected by solid mass of head/body of pancreas were prospectively enrolled in the study (15 male, 12 female). All patients underwent triphasic MDCT study with 2D/3D reconstructions, surgery and pathologic examination of resected specimen or biopsy. Exclusion criteria: cystic lesions, non neoplastic solid lesions, arterial involvement, hepatic metastasis. Images analysis was performed by two radiologists. Qualitative criteria was: neoplastic adhesion to SMV in axial images, multiplanar reconstructions (MPR) and maximum intensity projections (MIP) orthogonal to vasal axis (Grade 0: no contact; Grade 1: adhesion 0-90°; Grade 2: 90-180°; Grade 3: 180-270°; Grade 4: 270-360°). Quantitative criteria was: craniocaudal extensions of neoplastic adhesion to SMV lumen in MPR and MIP parallel to vasal axis.

Final MDCT assessment was: resectability (without venous infiltration), non resectability (venous infiltration greater than 20 mm), resectability with venous resection (venous infiltration less than 20 mm). **Results** Qualitative analysis: neoplastic adhesion to SMV circumference in axial images (Grade 0: 18/27, Grade 1: 2/27, Grade 2: 2/27, Grade 3: 3/27, Grade 4: 2/27), in MPR and MIP orthogonal to vasal axis (Grade 0: 17/27, Grade 1: 3/27, Grade 2: 2/27, Grade 3: 4/27, Grade 4: 1/27). Quantitative analysis: craniocaudal extensions of neoplastic adhesion to SMV lumen in MPR and MIP parallel to vasal axis (3/27 greater than 20 mm; 3/27 less than 20 mm). Final MDCT assessment was: resectability without venous resection in 21/27, non resectability in 3/27, resectability with venous resection in 3/27. In 25/27 patients there was correspondence between MDCT and pathologic/surgical examination, 2 SMV assessed infiltrated were not infiltrated. **Conclusions** MDCT is highly reliable in assessing venous infiltration of solid masses of head/body of pancreas and can significantly contribute to preoperative planning.

Idiopathic Fibrosing Pancreatitis in a Child Mimicking a Head Tumor of the Pancreas

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Context Idiopathic fibrosing pancreatitis (IFP) is a rare cause of abdominal pain and obstructive jaundice in childhood characterized by replacement of exocrine and/or endocrine tissue by fibrosis which determines compression of common bile duct (CBD) within pancreatic head. In our knowledge, only 50 cases are reported in literature. **Objective** To establish correct indications to surgical treatment **Case report** The authors reported the case of a 11-year-old jaundiced Caucasian child who was admitted to our surgical department because of progressive obstructive jaundice with episodic upper abdominal pain. The patient was submitted to abdominal ultrasounds (US), endoscopic ultrasonography (EUS) and MRI cholangio-pancreatography which demonstrated a distended alithiasic gallbladder and a dilatation of the intrahepatic, extrahepatic bile ducts and Wirsung duct. The pancreatic head was normal. **Results** After the work up, the young patient underwent surgery. At laparotomy a fibrotic, hard in consistence pancreas was found. The common bile duct was dilated. Biopsies were done on the head, body and tail of pancreas showing fibrosis, no epithelial dysplasia was found. A resection of common bile duct (CBD) from the

convergence to the intrapancreatic choledochus was done with hepatico-jejunosotomy on Roux en Y jejunal loop. **Conclusions** Actually an accurate diagnosis of idiopathic fibrosing pancreatitis is very difficult at preoperative imaging in fact, most patients, as in our case, underwent surgical exploration because of a suspicion of malignant pancreatic neoplasm. However, diagnosis would be improved if physicians will be aware of this rare disease. Unfortunately there is not a specific laboratory test. Several imaging procedures (CT, MRI, MRCP, EUS, endoscopic retrograde cholangiopancreatography (ERCP)) can be useful for preoperative diagnosis but we think that only EUS guided FNA might play a significant role to rule out neoplasm. As regard treatment, ERCP with temporary stenting of common bile duct (CBD) is the gold standard in case of transient biliary obstruction. Surgical treatment is recommended if obstruction of biliary tree is persistent and if diagnosis of IFB is uncertain. Moreover, IFP carries a very high risk of long term pancreatic exocrine and/or endocrine insufficiency, so long-term follow up is mandatory.

Diagnosis And Follow-up of Cystic Pancreatic Lesions: Possibilities of Contrast-Enhanced Ultrasonography in Comparison with Magnetic Resonance Imaging and Pathology

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Objective To compare the accuracy of contrast-enhanced ultrasonography (CEUS) and Magnetic Resonance Imaging (MRI) with pathology in the diagnosis of cystic pancreatic

lesions. **Methods** CEUS and MRI examinations of 33 resected cystic pancreatic lesions were retrospectively reviewed. The lesions were 13 mucinous cystadenomas, 4

endocrine tumors, 4 intraductal papillary mucinous tumors, 3 mucinous cystadenocarcinomas, 3 pseudopapillary tumors, 3 serous cystadenomas, 3 pseudocysts. The presence of parietal nodules, septa and the parietal wall thickness were evaluated. Sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values and diagnostic accuracy (Acc) were calculated. CEUS and MRI results were compared by McNemar test. Interobserver variability was determined. **Results** All the lesions were well visible at basal ultrasound. CEUS correctly detected intralesional septa in 14/15 lesions with sensitivity, specificity, PPV, NPV and accuracy of 87.5%, 94.1%, 93.3%, 88.9%, and 90.9%, and nodules in 6/8 lesions with sensitivity, specificity, PPV, NPV and accuracy of 85.7%, 92.3%, 75%, 96%, and 90.9%. MRI correctly detected

intralesional septa in 14/15 lesions with sensitivity, specificity, PPV, NPV and accuracy of 66.7%, 91.7%, 93.3%, 61.1% and 75.8% and nodules in 7/8 lesions with sensitivity, specificity, PPV, NPV and accuracy of 58.3%, 95.2%, 87.5%, 80% and 81.8%. CEUS characterized 25/27 (92.5%) malignant and 5/6 (83.3%) benign lesions. MRI characterized 26/27 (96.2%) malignant and 5/6 (83.3%) benign lesions. Difference in diagnostic accuracy between CEUS and MRI were not significant ($P=0.05$) in the identification of septa and nodules. Interobserver agreement was good for both readers (overall, $k=0.86-0.94$). **Conclusions** CEUS is accurate in the detection of septa and nodules, improving the characterization of cystic pancreatic lesions and could be included in the follow-up of border-line lesions.

Role of Fistulography in Postoperative Pancreatic Fistulas

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Objective To describe the radiological features of post-operative pancreatic fistula (PF) after pancreaticoduodenectomy (PD) and their correlation with the clinical impact. **Materials and methods** A retrospective study was performed on the fistulogram carried out for clinical suspicion to PF after PD. Out of a total of 80 PDs performed from 2001 to 2005, 56 fistulogram were found. PF was clinically defined according to the international study group (ISGPF) as Grade A, B and C. Fistulograms were performed only on patients with important clinical impact of PF (Grade B and C) or with suspect of drain migration into an intestinal loop. We correlated the results of fistulography (incidence and site of PF, occurrence of fluid collection, communication with main pancreatic duct, biliary tree and jejunal loop

and presence of drain into the jejunal loop or stomach) with the clinical suspicion of PF. **Results** Forty-two out of 56 patients (75%) had PF confirmed by fistulogram. We visualized 29 communications with the jejunal loop, 8 with the jejunal loop and the biliary tree, 12 with the main pancreatic duct and 9 with the stomach. In 14 patients (25%) the drain was abnormally placed inside the jejunal loop or stomach: in all these cases, once the drain was mobilized, the complication resolved within 72 hours. **Conclusions** Fistulogram helps in the confirmation of clinical suspected of PF decreasing post-operative morbidity and re-operation rate. Fistulogram is crucial in distinguishing cases of gastro-intestinal fistula due to the migration of the drain into an intestinal loop was determined.

Heat Shock Responsive Elements (HSEs) Magnify Heat Shock Response of HSP70B' Inducible Promoter.

A Promise For Pancreatic Cancer Gene Therapy

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Context Gene therapy with bacterial toxins might be an effective approach for pancreatic cancer (PC) treatment. It needs a very strict control of expression. **Objective** To verify the efficiency of heat inducible promoters in PC lines. **Methods** We purchased (Stressgen) the promoter of Hsp70B' protein, which was inserted into a eGFP reporter vector (V1). We engineered V1 with a 104 bp sequence including repeats of HSEs (V2). A third promoter made of the 104 bp only was used (V3). The PC lines MIAPaCa2, PANC1, BxPC3, PSN1 were transfected with all vectors. Control cultures were maintained at 37°C and experimental cultures were heat shocked (42.5°C for 1.5 h). eGFP protein was evaluated by western blotting (WB) and FACS analysis. eGFP transcription was measured by Q-RT-PCR. **Results** eGFP was detected by WB only in heat shocked

transfected cell. The Table shows FACS fluorescence intensity (mean±SE) and statistical analysis (Student's t test for paired data). After heat shock, 8, 35 and 7 fold increase in eGFP transcription was found in V1, V2 and V3 transfected cells, respectively. All lines studied were transfected with a vector expressing *Dyphtheria toxin A* (DTA) under the control of V1. Control and heat shocked transfected cells were equally killed. **Conclusions** Heat inducible promoters are a good system to control protein expression in PC cells; Hsp70B' response to heat shock was significantly magnified by the 104 bp sequence designed by us. These promoters are extremely promising for future applications in vivo, even if they cannot be used to control the expression of toxins as DTA characterized by a lethal effects at very low concentration.

	MIAPaCa 2			PANC1			BxPC3			PSN1		
	37°C	42.5°C	Statistics	37°C	42.5°C	Statistics	37°C	42.5°C	Statistics	37°C	42.5°C	Statistics
V1	4±0.8	19±3.2	t=5.9 P<0.005	18±2.0	49±4.6	t=7.6 P<0.005	7±0.9	52±1.6	t=27.0 P<0.005	3±0.4	38±6.5	t=5.7 P<0.05
V2	3±0.5	47±1.5	t=28.4 P<0.001	22±3.6	102±4.9	t=11.7 P<0.005	8±0.7	100±2.2	t=32.0 P<0.05	5±0.8	97±2.9	t=25.2 P<0.05
V3	4±1.0	32±0.7	t=19.2 P<0.005	19±1.1	85±10.9	t=6.0 P<0.05	7±0.5	52±4.5	t=9.0 P NS	7±1.2	64±5.3	t=14.1 P<0.05

Easy Access to the Pancreatic Duct Via the Minor Papilla: The Pancreatic Rendez-Vous Technique

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Context Minor papilla cannulation and sphincterotomy is usually required for patients with pancreas divisum and chronic

pancreatitis. Moreover, it can be useful in patients with fused ducts and a difficult drainage of the main pancreatic duct (MPD)

via the major papilla. Direct cannulation of the minor papilla is a challenging procedure also for expert endoscopists. Major-minor papilla pancreatic rendez-vous (PRV) can allow an easier access to the minor papilla. **Objective** Aim of the study is to evaluate technical results of PRV in a large retrospective series of patients. **Patients and methods** From 1994 to May 2007, PRV was attempted by expert endoscopists in 36 patients with chronic pancreatitis (23 males, 13 females; median age 44 years, range 11-79 years) due to a difficult drainage of the MPD through the major papilla. PRV was performed as follows: a dorsal and ventral duct connection was identified at pancreatography from the major papilla; an angled-tip hydrophilic guidewire (0.035"/0.018"), inserted from the major papilla, was maneuvered to pass through the accessory duct and minor papilla into the duodenum; the tip of the wire was grasped with a foreign-body forceps and retracted from the accessory channel; minor papilla was cannulated over-the-wire. Other operative procedures were performed as clinically requested. **Results.** Indications to drain the

MPD through the minor papilla were: incomplete pancreas divisum (n=18); easier access to the MPD through the minor papilla due to a tortuous ventral duct (ansa pancreatica and "H-configuration") (n=9); normal anatomy with strictures or stones hindering drainage from the major papilla (n=9). The PRV was successfully performed in 32 (89%) patients; in 4 cases (13%) only after a second attempt. No specific complications after PRV occurred. PRV failed in 4 patients. Direct minor papilla cannulation was unsuccessfully attempted in all 4 patients. Minor papilla precut was performed in 2 of these patients. MPD drainage was achieved in one case only. In the other 3 patients MPD drainage was completed from the major papilla after several attempts. **Conclusions** The PRV is a feasible, reliable and safe procedure. It can allow a quick cannulation of the minor papilla when the drainage of the MPD through the major papilla is difficult. The PRV can theoretically reduce the risk of complications due to traumatic maneuvers on the minor papilla or precut.

High Frequency Mutations of K-ras Gene at Codon 61 in Pancreatic Ductal Adenocarcinoma Tissues and Primary Cell Cultures

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Context Mutations in the K-ras gene have been found in many human tumors. In pancreatic ductal adenocarcinoma (PDAC) this gene results changed frequently at codons 12 and 13 and rarely at codon 61. For this reason many genetic epidemiological and clinical studies often neglect the analysis of this codon that has the same functional importance as codons 12 and 13. Some authors have investigated only the presence of point mutations at codon 12. However, it is also true that the totality of PDAC cellular

lines change at codon 12, and only one mutated K-ras at codon 13. **Objective** To check the mutations of K-ras gene in PDAC tissues and primary cell cultures. **Methods** Fresh sections from 56 selected tumors were laser micro-dissected (Leica LMD6000) and DNA extractions were performed. Cell cultures from 52 tumor samples were also carried out. Eight primary cultures (PP:78, 109, 117, 147, 161, 244, 391 and 437) were established. K-ras mutational analysis at codons 12, 13 (exon 1), and 61 (exon 2) was

realized on primitive tumor and primary cell cultures by PCR and automated sequencing. **Results** Mutational analysis of codon 12 and 13 showed mutations in 45/56 tumors (80.4%). Five out of 11 primitive tumors unaltered at codons 12 and 13 were mutated at codon 61 (8.9%). In the set of samples examined *K-ras* mutation frequency was 89.3%. Six primary cultures were mutated at codon 12 (75%) and two were mutated at codon 61 (25%). The cell culture mutational

profile was identical to the one evidenced in respective original primitive tumor. **Conclusion** A ratio of *K-ras* mutations is attributable to codon 61, it is 8.9% for tissues and 25% for the cell cultures respectively. These results show that the rare frequency can be attributed to codon 13 in our casistic (only one case changed at this codon), while codon 61 contributed to increasing the frequency of mutations in PDAC patients.

Treatment and Outcome of Pancretico-Jejunal Anastomosis Leakage after Pancreaticoduodenectomy

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Context Postoperative pancreatic fistula (POPF) is still regarded as the major complication after pancreatic resection and is a potentially serious, life-threatening event. A clinical grading system of POPF was developed by an international study group (ISGPF) [1], defining as grade C fistula requiring re-intervention. **Objective** To assess in a high-volume center of pancreatic surgery the treatment and outcome of grade C pancreatic fistula. **Methods** We retrospectively collected data from patients operated for pancreaticoduodenectomy (PD) from 1981 to 2007 in our surgical department. We realized 933 PD, 272 (29%) with duct occlusion and 661 (71%) with pancreaticojejunostomy: 112 out of these 661 patients (16.9%) developed a pancreatic fistula, 28 of them (4.2%) underwent re-operation and represented the object of our study. **Results** They were 22 men and 6 female, median age 66 years (range: 20-81 years). Indications to re-operation were: bleeding in 20 patients (18 because of intra-abdominal bleeding and 2 for gastrointestinal hemorrhage) and peritonitis and/or sepsis in 8 patients. The median day of re-intervention was 11.5 (range: 2-45 days). Re-exploration implicated an attempt to repair

site of leakage with: conversion of anastomosis to duct occlusion in 17 patients, positioning of a wide peripancreatic drainage in 5, total pancreatectomy in 4 and stump suture in 2. Ten patients died (mortality rate: 35.7%): 5 in the group of duct occlusion (29.4%), 1 in that of drainage (20%), 3 in that of total pancreatectomy (75%) and one in the group of stump suture (50%). The cause of death were: sepsis (n=4), respiratory insufficiency (n=4), MOF (n=1) and acute myocardial infarction (n=1). Post-operation hospital stay of alive patients was 23.5 days (range: 9-81 days). **Conclusions** Pancreatic fistula after PD is frequent but only in a small percentage of cases requires re-intervention. The main indication to re-operation is bleeding (71.4%); it can occur late after PD. Breakdown of anastomosis is associated with a high mortality rate which can be controlled by an aggressive surgical and clinical management.

Reference

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Evaluation of CD1a Polymorphism Frequencies in Patients with Pancreatic Cancer

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Context CD1a is not a classic antigen presenting molecule showing a strong structural homology to classical MHC molecules. CD1a, mainly expressed on dendritic cells, actually is involved in gamma/delta T cell activation, stimulating the immune response against lipidic or glycolipoid antigens. Current reports show that CD1a molecules are expressed in the inflammation by infiltrating surrounding tumor cells and in some circumstances by transformed cells. It has been suggested that CD1a molecules induce tumor-specific immune responses by presentation of tumor cell glycolipoids to specific T cells and NKT cells. Modulation of the CD1a expression as a mechanism of tumor escape from immune system has been reported. CD1a gene shows in the exon 2, nt 622, a C->T substitution inducing an amino acid substitution with a modification of CD1a binding affinity. Substitution of threonine with isoleucine in the antigen binding groove of the CD1a protein, actually might affect antigen presentation potential of the molecule.

Objective This study was conducted to compare the genotypic frequencies of CD1a gene in pancreatic cancer patients compared to healthy controls in order to evaluate the role of this polymorphism in the pancreatic cancer susceptibility. **Methods** Polymorphism in exon 2 of CD1a (C622T) gene, was studied in 35 Sicilian pancreatic cancer patients compared to 75 healthy blood donors by a polymerase chain reaction sequence specific primer method. **Results** The frequencies of CC, CT and TT genotypes of CD1A gene among patients were not significantly different compared to the control group. The analysis of genotype distribution according to tumor grading do not show any significant association. **Conclusions** These preliminary results suggest that there are not correlation between CD1a genotypes and pancreatic cancer. To definitively exclude the role of CD1a polymorphisms in the susceptibility of pancreatic cancer the extension of the analysis to the polymorphism at codon 51 of the gene and recruitment of larger cohorts of patients and controls seems to be mandatory.

Pancreatic Cancer Pulls Down Lymphocyte Migration

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Context Tumor cells may neutralize the immune system by evading detection and/or by inhibiting immune cells function. **Objective** We verified *in vitro* whether pancreatic cancer (PC) cells conditioned media modify CD4⁺ T cell proliferation,

migration and activation. **Methods** CD4⁺ T lymphocytes were purified by negative selection using a RosetteSep[®] kit (StemCell Technologies). CD4⁺ cells were cultured for 4 days in control or Capan1 (a PC cell line) fresh conditioned media. To assess migration

a transwell system with or without hSDF-alpha was used; migrating cells were FACS counted. Proliferation was FACS analyzed using carboxyfluorescein succinimidyl ester as tracer, after 72 h of co-culture with allogenic PBMC. Control and conditioned CD4⁺ cells were co-cultured for 24 h with unpulsed or staphylococcal enterotoxins pulsed EBV-B cells. In the supernatants interferon-gamma (IFN- gamma) and IL4 were assayed. **Results** The number of control and conditioned migrating CD4⁺ T cells did not differ in the absence of hSDF-alpha (t=1.0, P NS). In the presence of hSDF-alpha, migrating Capan1 conditioned lymphocytes were less (3,337±390, mean±SEM) than control lymphocytes (6,413±660) (t=7.55, P<0.001). Capan1 conditioned medium stimulated CD4⁺ T cell proliferation both in the presence (t=2.27, P<0.05) or absence

(t=3.87, P<0.001) of allogenic PBMC. IL4 concentration did not significantly vary between conditioned or non conditioned EBV-B stimulated CD4⁺ cells. Stimulation of CD4⁺ T cells by pulsed or unpulsed EBV-B induced higher IFN-gamma concentrations in conditioned than in control cells (t=3.30, P<0.05, and t=2.56, P<0.05, respectively). Control and conditioned media were ultrafiltered (mw cut-offs = 30,000 and 10,000 Da). The effects of Capan1 conditioned medium on CD4⁺ T cell migration and IFN-gamma production were recovered in the mw fraction of more than 30,000 Da. **Conclusions** We demonstrated that PC cells release soluble mediator/s of more than 30,000 Da which inhibit CD4⁺ T cell migration, activate proliferation and Th1 differentiation, supporting the hypothesis that tumor cells alter immune cells function.

Association between Intraductal Papillary Mucinous Neoplasm (IPMN) of the Pancreas and Gastrointestinal Stromal Tumors (GIST): A New Extrapancreatic Malignancy to Search for in IPMN?

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Context Several reports have described an increased frequency of synchronous and metachronous extrapancreatic cancers in patients with IPMN, suggesting the possibility of a genetically inherited predisposition of these patients to develop tumors in other organs. Up to now, a single case of gastrointestinal stromal tumors (GIST) concurrent to IPMN has been reported in the literature. We report three additional patients in whom a GIST was found before, at the time and after the diagnosis of IPMN. **Case reports** First Case A 63-year-old female who presented with hemolytic anemia of unknown etiology. As part of the work up she underwent a CT scan that showed the presence of a 3 cm abdominal mass just above the gastric fundus. An endoscopic ultrasound with fine needle tissue acquisition (EUS-

FNTA) was performed. Histological examination with immunohistochemical staining positive for CD117 was diagnostic for GIST. At EUS a 17x5 mm cystic lesion in the pancreatic body was incidentally detected which was found to communicate with the main pancreatic duct (MPD) at secretin-MRCP consistent with the diagnosis of branch type IPMN. She underwent laparoscopic removal of the GIST which revealed a low malignant potential. Second case A 81-year-old female who was discovered to have a 6 cm lesion in the gastric wall at a CT performed to evaluate recurrent episodes of acute pancreatitis. Because of this finding she underwent partial gastrectomy with the diagnosis of a GIST after histological examination with immunohistochemical staining of the resected specimen. Recurrent

acute pancreatitis continued to occur during the following 3 years with an unknown etiology. At referral to our center, an EUS was performed which showed a dilated MPD with a 3cm cyst in the head of the pancreas both with mural nodules (mixed type IPMN). An FNA was diagnosed for carcinoma. She refused surgery and she is being treated with intraluminal brachytherapy. **Third Case** A 73-year-old female who was found to have diffuse pancreatic cystic lesion at S-MRCP performed after an episode of acute pancreatitis consistent with multifocal branch type IPMN. Because of a MPD dilation due to cystic compression at the level of the

pancreatic body, she underwent successful distal pancreatectomy which revealed IPMN adenoma. During surgery, two 5 mm and 8 mm subserosal nodules at the gastric body were incidentally found and removed. Both were GISTs with low malignant potential. **Conclusion** Our report of three cases of concomitant IPMN and GIST may indicate that this association could be more frequent than previously reported. Further studies to evaluate the prevalence of IPMN in patients with GIST and viceversa are needed to clarify if this association is significant and of clinical relevance.

Searching the Arianna Thread between TGF-beta and Pancreatic Cancer Down to the Smad Labyrinth: Only a Trivial Pursuit?

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Context Smad proteins are a group of intracellular signaling mediators of TGF-beta family members. Which play a complex bidirectional role in tumorigenesis. Nuclear translocation of Smad 2-Smad 4 and Smad3-Smad 4 complexes from the cytoplasm act as TGF-beta signaling pathways. On the other hand, Smad 6 and Smad 7 act as inhibitory proteins which downregulated TGF-beta pathway. It has been reported that Smad 7 deficiency and Smad 3 upregulation may be responsible of TGF-beta hyper-responsiveness. **Objective** The aim of this study was to get further insights into the role of Smad protein network in TGF-beta signaling in several pancreatic cancer cell lines, 2 highly metastatic (BxPC-3, SW 1990) and 2 non-metastatic (PaCa-2, Caspan-2). **Methods** We examined four cell lines (i.e., PaCa-2, BxPC3, Capan-2 and SW 1990) which were derived from human pancreatic carcinoma and all maintained in proper media. Cells were incubated for 3 days and then treated with 10 ng/mL of TGF-beta for 30 or 60 minutes. MTT assay (3-(4,5-

dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) was used to assess the proliferation activity. Quantitative real-time reverse transcription-polymerase reaction (RT-PCR) was applied by using different sense/antisense primers for Smad 2, Smad 3, Smad 4, Smad 6 and Smad 7. **Results** By MTT assay it appeared that, following TGF-beta incubation 3 out of 4 pancreatic cells lines (PaCa-2, Capan-2 and SW 1990) showed a significant proliferative activity (P<0.05). Expression of Smad 2 and Smad 3 mRNA significantly decreased in the PaCa-2, BxPC3, Capan-2 cell lines treated with TGF-beta-treated (P<0.05). SW 1990 cell lines showed a drop of Smad 2 (P<0.05) while there was no change in Smad 3 expression. Smad 4 had a dual behavior by increasing in PaCa-2 and decreasing in SW 1990 cell lines (P<0.01). Smad 6 were found significantly decreased in BxPC-3 and in PaCa-2 (P<0.05). Smad 7 expression was markedly inhibited in BxPC-3, Caspan-2 and in PaCa-2 cell lines. **Conclusion** Whatever the order of the variables considered, Smad modifications

were all conjuring up for a pro-oncogenetic role of TGF-beta. Such behavior was similar and comparable whether considering the highly metastatic and non-metastatic cell lines. Taken overall, these data support the

hypothesis that the proliferation of pancreatic cancer cells is strictly related to the decrease of Smad 7 gene expression. Tumor spread and metastatic seeding may follow the pleiotropic effect of TGF-beta.

Reconstruction after Pancreaticoduodenectomy. Results of Two Different Techniques

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Context Although an improved perioperative management reduced the mortality after pancreaticoduodenectomy (PD), the incidence of postoperative complications is still very high. Several techniques have been described to reduce morbidity. **Objective** We evaluated two different type of reconstruction after PD to analyze morbidity and mortality. **Methods** A retrospective review of 159 patients who underwent PD with pancreaticojejunostomy end-to-side between 1994 and 2006 was carried out. In the first 84 cases we performed a conventional Whipple procedure and all anastomoses are placed along a single jejunal loop with pancreaticojejunal anastomosis proximal followed at least 40 cm by biliary anastomosis and the gastrojejunostomy (1A group). This surgical procedure was carried out until to 2000. In the next 75 cases we used an isolated jejunal loop for pancreaticojejunal anastomosis and a second Roux loop for the biliary and gastric anastomosis (2A group). This type of reconstruction was made to avoid the risk of mixed pancreatic and biliary fistula. Both the groups were similar for gender, age, underlying pathologies, ASA score. We have considered the major

complications which pancreatic fistulas, biliary fistulas, hemoperitoneum and re-operations. Pancreatic fistula (PF) was defined in according with the International Study Group (ISGPF, 2005) and we used also the classification of clinical grading system (grades A, B, C). The outcomes for each group were compared. **Results** PF was the most important complication. The rate of PF has been lower in 1A group than in 2A group (25% vs. 34%). The rate of reintervention has been lower for 1A group than in 2A group (12% vs. 22%). The others complications were similar in two group. Mortality rate was higher in 1A group than 2A group (9% vs. 6%) and all cases were related to PF. The mean hospital stay was 22 days for both. All results have not been statistically significant. **Conclusion** No significant difference occurred between 1A group vs. 2A group about morbidity and mortality. Whipple procedure remains a good choice. A biliary anastomosis in 1A group performed to great distance from pancreaticojejunal anastomosis allowed to obtain the same results of a reconstruction with double loop.

Non-Functioning Pancreatic Endocrine Tumors: Clinical Features, Surgical Treatment and Outcome

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Context Non-functioning pancreatic endocrine tumors (NF-PETs) are heterogeneous, rare neoplasms histologically undistinguishing from functioning forms and

difficult to diagnose preoperatively. They account for 15-53% of pancreatic endocrine tumors (PETs) and show typical histological and immunohistochemical features of PETs without hormone-related symptoms. The interest about them has been increasing recently due to the progress of their knowledge and improvement in imaging technique. **Objective** We reviewed our series of NF-PETs in order to analyze clinical aspects, surgical approach and outcome. **Methods** All the patients were submitted to CA 19-9, NSE, Chromogranin A analysis, abdominal CT scan, surgical treatment and follow-up. All cases were fit for surgery because resectable or eligible to palliative procedure for symptoms. The resection were considered R0 or R1 according to microscopic residual disease and the specimens were collected according to WHO 2000 classification. The criteria of malignancy were local invasion, vascular and/or perineural microscopic infiltration, lymph nodal involvement and presence of metastases. **Results** Between January 1994

and March 2006 we observed 30 PETs; of these, 15 (50%) were NF-PETs. Twelve patients (80%) presented symptoms mimicking pancreatic ductal carcinoma. CT scan diagnosed NF-PET in 9 cases (60%). Thirteen patients underwent pancreatic resections (86.6%) and two were treated with palliative procedures. No postoperative mortality were registered. R0 resection was achieved in 8 cases and R1 in 5 cases. Histology showed 9 well-differentiated endocrine tumors with uncertain behavior, 3 well-differentiated endocrine carcinomas and in one patient two distinct types of pancreatic carcinoma (ductal carcinoma and poorly differentiated endocrine carcinoma). Twelve patients are alive (mean follow-up 69.5 months, range 11-159 months) and three died. Survival was 15 months for the patient with double carcinoma, 14 months for a case with hepatic metastases and 22 months for a case that developed liver metastases. **Conclusion** NF-PETs have similar clinical presentation to pancreatic ductal carcinoma but show high resectability and good prognosis.

Multidetector CT in the Assessment of Neuroendocrine Pancreatic Neoplasms Nature: Comparison between CT and Histological Findings

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Context Neuroendocrine pancreatic neoplasms are rare tumors which approach mainly depends on their clinical and morphological presentation. CT study of neuroendocrine of these neoplasms can evaluate the lesion nature and thus the eventual surgical treatment. **Objective** To evaluate the role of multidetector CT in differentiating malignant from benign lesions among neuroendocrine pancreatic neoplasms. **Methods** We evaluated 43 lesions in 25 patients (2 patients had MEN 1 syndrome). CT scans were performed before and after 120 mL iodine contrast medium administration (5 mL/min) in early arterial

(15''), pancreatic (30''), venous (70'') and delayed (180'') phases. Two different post-contrastographic patterns were considered: pattern A-nodules with early arterial enhancement and rapid wash-out; pattern B: lesions with low wash-in in arterial phases and increasing progressive enhancement or lesions with rapid wash-in and persistence of the hypervascularization. CT findings were compared with pathological results after surgical resections. **Results** At histopathology, 23 lesions resulted to be benign, 15 malignant, 5 borderline. At CT, 25/43 lesions showed pattern A (diameter ranging between 5 and 20 mm; average: 8.7

mm); at histopathology, 22/25 resulted to be benign (all less than 2 cm), 2/25 borderline (both greater than 2 cm) and 1 malignant (12 mm). Pattern B included 18/43 lesions (diameter ranging between 11 and 75 mm; average 38.7 mm); at histopathology 14/18 were malignant (all greater than 2 cm; average: 44 mm), 3 borderline (diameter range: 11-28 mm; average 16.3 mm) and 1 benign (15 mm). Pattern A showed a positive

predicting value (PPV) of 88% in predicting neuroendocrine pancreatic lesions benignity, while pattern B showed a PPV of 78% in predicting malignancy. **Conclusion** Multidetector CT study may suggest the nature of neuroendocrine pancreatic neoplasms on the basis of their post contrastographic enhancement pattern. Anyway, lesions dimensions must be always considered.

Enteral Nutrition in Severe Acute Pancreatitis: Nasogastric (NG) vs. Nasojejunal (NJ) Tube

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Context Severe acute pancreatitis (SAP) is an hyper-catabolic condition, requiring a non-oral appropriate nutritional support. Enteral feeding with a NJ tube has been proved to be safer and cheaper than total parenteral nutrition. Although NJ route should ensure pancreatic rest, it has recently been suggested that nutrition through a NG tube equally safe, being potentially easier to be administered.

Objective To compare safety of enteral nutrition with an elemental formula provided through NJ or NG tube in our Unit in patients with SAP. **Methods** From May 2006 to April 2007, we employed a NG tube in 6 consecutive patients with confirmed SAP. Their clinical outcome was compared to that of the previous 6 consecutive patients with confirmed SAP seen in our Unit who had had nutrition with a NJ tube. Inclusion criteria were diagnosis of SAP (abdominal pain + serum amylase greater than 3 times the reference upper value and Ranson score equal to, or greater than, 3 or Balthazar score equal to, or greater than, 4). Self-migrating tubes were placed in the stomach in all cases, and their position checked by plain X-ray. In the NJ group migration was helped by radiologic or endoscopic assistance if needed. All subjects received an elemental formula (Survimed[®]), starting at a rate of 20 mL/h

increasing to a caloric target of 2,000 kcal per day. All patients were treated with i.v. antibiotics (imipenem/metronidazole) and proton pump inhibitors. The end points were the occurrence of death, pancreatic or extrapancreatic complications, modification of pain and severity scores or presence of side effects after 7 days of nutrition and total hospital stay. **Results** The 2 groups were similar for sex (NG 3 females, NJ 2 females), and age distribution (means: NG 48 years, NJ 56 years). Mean Ranson score was 3.5 in NG and 1.6 in NJ; mean TC score was 6.6 in NG and 5.1 in NJ; mean CRP was 82.7 mg/L in NG and 103.5 mg/L in NJ. Etiology was: alcohol (n=5) and biliary (n=1) in NG; and alcohol (n=2), biliary (n=3), and idiopathic (n=1) in NJ. Outcomes are shown in the Table. **Conclusions** In this preliminary retrospective comparison we found no significant differences for major outcomes due to the small number of observed patients. However, differently from previous reports, more patients with a NG tube had infected necrosis, and needed a switch to parenteral nutrition. Hospital stay also seemed longer in the NG tube. More multicenter randomized trials comparing the two nutrition routes are needed to assess if NG tube is equally safe and effective.

	NG (n=6)	NJ (n=6)	P
Mortality	0	0	-
Infected necrosis	2	1	1.00
Need of surgery	0	0	-
Pseudocyst	4	4	1.00
Renal or respiratory failure	0	0	-
Pleuric effusions	1	1	1.00
Pain worsening after nutrition	1	0	-
Need to switch to parenteral nutrition	2	0	0.45
Diarrhea	4	2	0.56
Hospital stay (days: mean; 95% CI)	33.3 (3.7-62.8)	20.6 (16.9-24.4)	0.29

The Risk of Unnecessary Pancreatic Resection in Case of Misdiagnosed Intrapancreatic Accessory Spleen

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Context Intrapancreatic accessory spleens (IPAS) in 1-2% of cases are located in the pancreatic tail, so that they can be confused with primary pancreatic endocrine tumors.

Objective To assess the incidence of unnecessary pancreatic resections for a misdiagnosed IPAS. **Methods** We retrospectively analyzed clinical records of 45 consecutive patients who underwent a distal pancreatectomy for a preoperative diagnosis of an endocrine pancreatic tumor, in 9 cases (20%) with a laparoscopic approach, from 2000 and 2006. **Results** Overall mortality was 0%; morbidity was 40%; pancreatic fistula rate was 29%. In 3 cases (incidence: 6.7%) final histological diagnosis was an intrapancreatic accessory spleen. In one case it was a 1 cm diameter accessory spleen of the pancreatic tail in a 51-year-old woman; in the second case (a 51-year-old man) it was of 1.5 cm diameter; the third patient was a 50-year-

old woman with a 1.9 cm diameter IPAS. All the three cases presented common features: the preoperative imaging showed a asymptomatic, hypervascular, small (less than 2 cm of diameter) lesion, very distally in the tail of the pancreas at CT scan in one case and at MRI in the other two cases; OctreoScan in the first case and endoscopic ultrasound in the second case confirmed diagnosis of a nonfunctioning endocrine tumor. None of the three patients underwent ^{99m}technetium heat damaged red blood cells scintigraphy (HDRBC). **Conclusions** When at preoperative imaging it is suspected an endocrine tumor, not associated to a syndrome and the diameter of the lesion is less than 2 cm, located very close to splenic hilum, it is strongly recommended a ^{99m}Tc HDRBC scintigraphy. Surgery is indicated when there is no radiotracer uptake in the pancreatic tail near the hilum of the normal pancreas.

The Pancreatic Cancer Derived N-Terminal Peptide of S100A8 Stimulates Insulin Exocytosis and HepG2 Cell Growth

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Context We have previously isolated from pancreatic cancer tissues of diabetic patients

the 14 aminoacid N-terminal peptide of S100A8 (NT-S100A8). **Objective** To

ascertain whether NT-S100A8 interferes with insulin secretion and/or signaling and whether it affects cancer cell growth. **Methods** Beta-TC6 (rat insulinoma), HepG2 (insulin responsive human hepatocellular carcinoma) and four pancreatic cancer cell lines (BxPC3, Capan1, MiaPaCa 2, Panc1) were used. Control or 50, 200 and 500 nM NT-S100A8 added beta-TC6 cells were glucose-stimulated (20 mM) to release insulin, which was measured (RIA) in the supernatants after 2, 3, 5, 10, 15, 30 and 60 minutes and after 24 hours from stimulus. HepG2, stimulated or not stimulated with 50 mU/mL insulin, and pancreatic cancer cells were treated with 50, 200 and 500 nM NT-S100A8. The cells were counted after 24, 48 and 72 hours. **Results** Hyperglycemia induced a significant early (2-10 minutes) and late (24 h) insulin release from beta-TC6 cells. NT-S100A8 at any concentration induced insulin exocytosis from

secretory vesicles (2-5 minutes), being the difference significant for the 500 nM concentration (repeated measures analysis of variance: $F=3.53$, $P<0.05$). NT-S100A8 did not affect pancreatic cancer cell growth. HepG2 cell growth was insulin stimulated. NT-S100A8 at 500 nM significantly enhanced HepG2 cell growth ($F=3.73$, $P<0.05$), this stimulatory effect being more pronounced in insulin treated cells ($F=5.85$, $P<0.01$). **Conclusions** The pancreatic tumor derived peptide NT-S100A8 magnifies glucose stimulated insulin exocytosis (early response) and stimulates HepG2, not pancreatic cancer, cell growth. These actions might depend on interactions between NT-S100A8 and the insulin receptor: in beta cells it enhances glucose stimulated insulin secretion while in HepG2 cells it evokes the mitogenic signaling through MAPK phosphorylation and activation.

Antineoplastic Treatments in Advanced Pancreatic Cancer in Italy: A Survey from a Referral High Volume Center

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Context In the last 20 years pancreatic cancer incidence has progressively increased. Gemcitabine (GEM) has shown clinical benefit in patients with advanced pancreatic cancer with good tolerability, but with marginal effect on survival. Many clinical trials have recently tested the efficacy of a spectrum of antineoplastic agents in combination with GEM (fluorouracil (5-FU), cisplatin (CDDP), oxaliplatin (OX), erlotinib) but no survival advantage has been yet demonstrated. Moreover, the effectiveness of chemoradiation (CRT) is still unclear. **Objective** To assess the contemporary management of patients with advanced pancreatic cancer in Italy. **Methods** All consecutive patients with stage IVA or IVB pancreatic cancer observed at our Institution

between October 2006 and April 2007 have been enrolled. They have been interviewed and followed up by phone one month after diagnosis and later on every three months. **Results** Seventy-seven patients were enrolled: 39 (51%) men and 38 women with a median age of 64 years (range 41-83 years). Forty-six (60%) had stage IVA and 31(40%) stage IVB pancreatic cancer. Tumor site was the pancreatic head in 56 (73%) cases and the body-tail in 21 (27%). The referral oncological centers were nationwide distributed: 30 (39%) patients were treated in the Northern Italy, 23 (30%) in the Centre, and 24 (31%) in the Southern or Islands. Eleven patients (14%) received only supportive care. Sixty-five (84%) patients underwent first-line chemotherapy (CHT)

(GEM alone 35 (53%) patients, GEMOX 16 (24%) patients, GEM+CDDP 3 (4%) patients, GEM+erlotinib 2 (3%) patients, 5-FU alone 5 (7%) patients). Four (6%) patients underwent CR in association with GEM in 1 (1%) patients, GEM followed by 5-FU in 2 (3%) and 5-FU in another patient, respectively. At the moment 11 (14%) patients died of disease. **Conclusions** In Italy CHT seems to be the

preferred treatment for patients with advanced pancreatic cancer, even though a standard regimen is not nationwide accepted and applied. The type of treatment is still strictly related to both doctors' attitude and hospital facilities. Efficacy and cost effectiveness evaluation should be estimated in order to improve the health resources and their management.

Cystic Lesions of the Pancreas:

Evaluation with MR Imaging and MR Pancreatography

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Context MR pancreatography (MRP) is evolving as an effective non invasive imaging technique for examining patients suspected of having pancreatic disease. **Objective** To determine the usefulness of MR imaging and MRP in the evaluation of cystic pancreatic lesions and their relationship with the pancreatic ductal system. **Methods** Ninety-six patients with radiological diagnosis of cystic pancreatic lesions underwent MRI at 1.5T. After acquisition of axial T1/T2w sequences, MRP was obtained using coronal SS-FSE T2w sequences and in 42/96 patients also using secretin-stimulation. MR examinations were evaluated in conference by two observers to identify pancreatic abnormalities and their relationship with ductal system. Imaging results were correlated with ERCP, surgery, and/or imaging follow-up. **Results**

The cystic lesions were classified into two types: a) lesions related with pancreatic ductal system (50 patients): intraductal papillary mucinous tumor (n=48) and post-traumatic pseudocyst (n=2); b) lesions not related with pancreatic ductal system (13 patients): serous cystadenoma (n=7), mucinous cystadenoma (n=3), mucinous cystadenocarcinoma (n=1), cystic neuroendocrine tumor (n=2), all confirmed at surgery. The remaining indeterminate (less than 2 cm) cystic lesions (n=30) and pancreatic pseudocysts (n=3) underwent imaging follow-up. **Conclusion** Our study highlights the usefulness of MR imaging and MRP, particularly after secretin-stimulation, to detect cystic pancreatic lesions and establish their relationship with the ductal system.

Malignant Insulinoma: Report of Unusual Site of Recurrence

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Context Malignant insulinoma (MI) is a rare neuroendocrine neoplasia. It accounts for 5-

10% of all pancreatic insulinomas. There are no specific morphological, biochemical or

genetic features that clearly identify MI. Malignancy can be defined only by histological and immunohistochemical examination. **Case report** In 2002 a 28-year-old woman underwent a laparoscopic enucleation for a preoperative documented insulinoma. The histopathological examination revealed a neuroendocrine tumor with angioinvasive features and high mitotic index with clear resection margins. During follow up, levels of glucose, insulin and C-peptide were in range of normality; no hypoglycemic episodes occurred. In November 2006 the patient had a hypoglycemic episode. TC scan revealed an hypodense sub glissonian and hypervascularized lesion in VI hepatic segment and another focal lesion in the pancreatic body; a contrast-enhanced EUS confirmed the TC evidence of fibro-necrotic nature of the pancreatic lesion. At laparotomy, it was found an unknown nodular subgerotian mass, which was resected. No hepatic lesions were found. The histological examination revealed the presence of MI with

the same features of the previous one, examined in 2002. No complications were observed in postoperative period. **Conclusion** Laparoscopic approach is a feasible and safe procedure in neuroendocrine pancreatic tumor; in young patients and in case of single nodular lesion, laparoscopy could be the best choice. Recurrence of MI, mainly for hepatic localization, are well known even some years after the diagnosis of the primary tumor. However, a sub gerotian secundarism has never been described in the literature. This finding opens up this question: a real recurrence of the primary tumor or a new independent MI, deriving from aberrant pancreatic tissue? In this case the histological examination did not reveal pancreatic tissue, suggesting a recurrence of the primary MI in a unusual site. Patients who underwent a conservative local excision may need a surgical revision after the histological finding of malignancy in order to enlarge the resection margins. A more aggressive follow up for MI should be recommended.

Non Pylorus-Preserving *versus* Pylorus-Preserving Pancreaticoduodenectomy: Our Experience.

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Context Pancreaticoduodenectomy is considered the surgical procedure of choice for the resection of pancreatic head and periampullary region cancer and, sometimes, in case of chronic pancreatitis. In the late 70s, Traverso and Longmire reported their experience about a pylorus-preserving pancreaticoduodenectomy. These changes, according to the Authors, allow to preserve gastric function and to avoid some of the most important side effects of gastric resection. In 1985 Lygidakis and Brummelkamp postulated that the use of separate Roux-en-Y limbs for biliary and pancreatic anastomosis may allow the early oral feeding in case of a pancreatic leak, and that its incidence is lower when this

procedure is used. **Methods** Here, we reported our experience with pylorus-preserving pancreaticoduodenectomy *versus* pancreaticoduodenectomy with Roux-en-Y loop reconstruction as described by Lygidakis in the treatment of the peri-ampullary region diseases. **Results** From December 2000 to June 2002, 10 patients (four women and six men) underwent pancreaticoduodenectomy for peri-ampullary region cancer. In particular, 3 patients underwent pancreaticoduodenectomy according to Lygidakis (I group); they had their gastric resection done with linear stapler in order to decrease the risk of fistula. Seven patients underwent pylorus-preserving pancreaticoduodenectomy (II

group) with intra-operative distraction of pylorus in order to prevent the delayed gastric emptying. The average post-operative stay was 20.3 days in the I group and 14.4 days in the II group. Two patients in the I group and two in the II group required intra-operative blood transfusion; all the patient underwent Rx evaluation with radiopaque dye in VII DAS, and no dye leak was evidenced, so since VIII DAS all the patients have started a liquid diet *per os*. No patient died in this series during hospitalization or within 30 days after surgery. Five patients (one in the I group and four in the second group) are alive and disease-free after five years of follow-up. **Conclusions** Pylorus-preserving pancreaticoduodenectomy has gained wide acceptance

for both benign and malignant conditions. However, many authors are concerned about its high morbidity rates, mostly related to delayed gastric emptying (DGE) in the early post-operative course. Furthermore, some Authors sustain that, compared to the other procedures, it is associated with shorter operation times, less intra-operative blood loss and less overall morbidity rate, and that DGE, if present, should be related to other important co-morbidity factors. In conclusion, in our experience, pylorus preserving pancreaticoduodenectomy compared to Lygidakis procedure, does not show an increase risk of pancreatic leak and, besides, it offers better short and long-term outcomes.

Intraductal Papillary Mucinous Neoplasms and Pancreatic Cancer

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Context IPMN represent about 20% of the pancreatic cystic neoplasm (PCN). It is presumed to develop from adenoma to invasive carcinoma with a biological-morphological sequence similar to that one of colon-rectal cancer. Radical surgery with negative margins could allow a good prognosis. **Objective** To evaluate the incidence of association between IPMN and pancreatic cancer and to verify survival rates in patients with both lesions. **Methods** We retrospectively reviewed the demographic, clinical, laboratory, radiological, surgical and pathological characteristics of patients with a diagnosis of IPMN observed from 1990 to 2006 in our Institute. In all patients a transabdominal US and CT scan were performed. MRCP was carried out in all patients observed since 2000 (9 patients). We also analyzed the survival data of these patients. **Results** We operated 15 patients with IPMN: mean age was 64 years (range 49-75 years), 11 were male (73%). The most frequent presenting symptom was abdominal pain (60%), followed by weight loss (27%) and jaundice (14%). Tumor was located in the

head of the pancreas in 6 patients (40%), in the body-tail in 6 patients (40%) and the tumor was diffuse to the whole pancreas in 3 cases (20%). Main duct type IPMN was shown in 6 patients (40%), branch duct type in 3 patients (20%) and the remaining 6 patients (40%) were affected by a mixed type IPMN. Pathological examination in the 15 resected specimens revealed: 2 benign-IPMNs (13%), 8 borderline-IPMNs (53%), 2 in situ carcinoma (13%) and 3 invasive cancer (20%). Among these 3/15 (20%) were associated with ductal adenocarcinoma of the pancreas: one benign-IPMN, one borderline-IPMN and one invasive IPMN. Postoperative mortality was zero. Three patients died (mean follow-up: 42.3 months), 12 patients are alive at a mean follow-up of 51.4 months. **Conclusion** IPMN could be related with ductal adenocarcinoma in 20-25% of cases. This association changes its prognosis. Because of the high incidence of this association, several authors are considering IPMN like a risk factor or even a precursor for ductal adenocarcinoma.

Solid Serous Cystic Tumor of the Pancreas. A Case Report

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Context Pancreatic serous cystic tumors are uncommon pancreatic tumors. Their gross appearance is frequently microcystic or oligocystic. The solid form is rarely described in literature. **Case report** A 59-year-old female was admitted at our Institute for abdominal pain in the upper right quadrant. Her past medical history was not significant. Laboratory tests were within normal range. Transabdominal US showed a well circumscribed hypoechoic mass, 3 cm in diameter, in the pancreatic tail. CT confirmed the presence of the pancreatic solid mass. The mass showed marked contrast-enhancement in the early phase, it was dyshomogeneous and a hyperdense capsule was visible. The preoperative diagnosis was of a solid mass of the pancreatic tail. A distal pancreatectomy with splenectomy was performed. Post-operative course was uneventful. Grossly, the resected specimen demonstrated a solid well circumscribed, encapsulated mass of 3 cm in diameter of the pancreatic tail. The cut surface of the tumor contained a thick fibrous

band without necrosis nor hemorrhage. The surrounding pancreatic parenchyma was normal and surgical margins were negative. Histologically, on hematoxylin-eosin stain, the architecture of the mass was solid with cell arranged in nests, acini and trabeculae, separated by thick, hypocellular fibrous bands. Small cystic areas were seen microscopically. The cells contained abundant clear cytoplasm which was PAS-positive and diastase-sensitive suggesting the presence of glycogen. Diagnosis of solid serous microcystic adenoma of the pancreas was made. **Conclusion** Solid serous microcystic adenoma of the pancreas is a very rare entity. In fact, to our knowledge, only four cases are reported in the literature. Solid tumors of the pancreas are usually associated with a malignant behavior and they could be more frequently ductal adenocarcinoma or neuroendocrine tumors. Surgery should be mandatory in every patient with a solid pancreatic tumor even if the solid mass could be a benign tumor as in this case.