Pancreas Cancer 2004
April 24–26, Pisa, Italy

Abstracts

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Franco Mosca, Pisa
L. William Traverso, Seattle, Wash.
Ugo Boggi, Pisa

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Oral Presentations

01 Report of the National Cooperative Pancreatic Cyst Trial
W. Brugge, A. Warshaw, C. Fernandez
Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

Background: Cysts of the pancreas display a wide spectrum of histology, including inflammatory (pseudocysts), benign (serous), premalignant (mucinous), and malignant (mucinous) lesions. Endoscopic ultrasound (EUS) may offer a diagnostic tool through the combination of imaging and guided fine needle aspiration (FNA). The purpose of this investigation was to determine the most accurate test for differentiating mucinous from non-mucinous cystic lesions.

Methods: The results of EUS imaging, cyst fluid cytology, and tumor markers (CEA, CA 72-4, CA 125, CA 19-9, and CA 15-3) were prospectively collected and compared in a multi-center study using histology as the final diagnostic standard.

Results: Three hundred forty one (341) patients underwent EUS and FNA of a pancreatic cystic lesion; 112 of these patients underwent surgical resection, providing a histologic diagnosis of the cystic lesion (68 mucinous, 7 serous, 27 inflammatory, 5 endocrine, and 5 other). Receiver operator curve analysis of the tumor markers demonstrated that cyst fluid CEA (optimal cut-off of 192ng/ml) demonstrated the greatest area under the curve (0.79) for differentiating mucinous versus non-mucinous cystic lesions.

Conclusion: Of tested markers, cyst fluid CEA is the most accurate test available for the diagnosis of mucinous cystic lesions of the pancreas.

02 Inflammatory Cells Contribute to the Angiogenic Phenotype of Pancreatic Cancer
M. Menicagli, D. Campani, I. Esposito, L.E. Pollina, N. Funel, N. Decarli, U. Boggi, M. Del Chiaro, C. Croce, F. Mosca, G. Bevilacqua
Department of Oncology, of Transplantations and of Advanced Technology in Medicine, University and Hospital of Pisa, Italy

Introduction: Stromal alterations involving angiogenesis, extracellular matrix, inflammatory cells and proteasic activity, represent important factors in regulating the growth and invasion of the tumor.

Aim: Evaluation of vascular endothelial growth-factors (VEGF-A, -C), vascular endothelial growth factor receptors (VEGFR-2,-3) and basic fibroblast growth-factor (bFGF), in neoplastic and inflammatory cells of pancreatic cancer.

Methods: 145 paraffin-embedded tissue samples were immunostained for VEGF-A, VEGF-C, VEGFR-2, VEGFR-3 and bFGF. The intratumoral microvessel density (IMD) was evaluated by counting the number of vessels immunostained with CD34. Positive VEGF-A, VEGF-C and bFGF inflammatory cells, were characterized by a double immunostaining with antibodies against CD68 (macrophages) and tryptase (mast cells). In addition, intratumoral density of macrophages and mast cells has been evaluated and expressed by n/mm². The findings were compared to the clinico-pathological data of the patients.

Results: VEGF-A was expressed in tumor (134 cases, 92.4%) and in inflammatory cells (range 6.3–295.2/mm²). The over-expression of VEGF-A in tumor cells was correlated to the expression of VEGFR-2 (p = 0.01) and high IMD (p = 0.04). bFGF was expressed in tumor (112 cases, 77.2%) and inflammatory cells (range 4.2–137/mm²). bFGF in tumor cells was directly correlated to macrophage density (p = 0.03) and tumor size (p = 0.03). VEGF-C was expressed in tumor (74 cases, 51%) and inflammatory cells (range 4.2–162.3/mm²). The over-expression of VEGF-C in tumor cells was directly correlated to VEGFR-3 expression in tumor (p = 0.002) and endothelial cells (p = 0.0001). VEGFR-3 expression in tumor cells was correlated to N+ status (p = 0.02). A high number of VEGF-C+ inflammatory cells were present in N+ cases (p = 0.03). No correlation was found between tumor grade, stage, survival and all angiogenetic factors (IMD, macrophage or mast cells density, expression of VEGF-A, VEGF-C, bFGF) in tumor or in inflammatory cells.

Conclusions: Inflammatory cells produce pro-angiogenetic factors supporting the invasive capacity of the tumor and particularly, VEGF-C contributes to nodal metastases.
**03**

**ADAM9 Expression in Pancreatic Cancer is Associated With Tumour Type and is a Prognostic Factor in Ductal Adenocarcinoma**

C. Pilarsky, R. Grützmach, J. Lüttges, O. Ammerpohl, S. Kersting, R. Koch, H. Kalthoff, H.K. Schackert, G. Klöppel, H.D. Saeger

Department of Surgery, University Hospital, Dresden, Germany

Gene expression profiling revealed ADAM9 to be distinctly over-expressed in pancreatic ductal adenocarcinoma (PDAC). We examined the relevance of ADAM9 expression in PDAC diagnosis and prognosis. 59 infiltrating primary PDACs, 32 specimens of patients with chronic pancreatitis, 11 endocrine tumors and 24 acinar cell carcinomas were immunohistochemically analyzed for ADAM9 expression. Staining for ADAM9 was detected in 58/59 (98.3%) PDACs and in 2/24 (8.3%) acinar cell carcinomas, but not in endocrine tumors. In the nonneoplastic pancreas, whether normal or chronically inflamed, ADAM9 was expressed in centroacinar and intralobular duct cells, but not in interlobular duct cells and their hyperplastic lesions. Cytoplasmic expression of ADAM9 correlated with poor tumor differentiation and also with shorter overall survival than in cases showing only an apical membranous staining pattern (p = 0.001). Multivariate analysis identified cytoplasmic ADAM9 expression as an independent marker of shortened survival in a set of 42 curatively (R0) resected PDAC (P < 0.05, hazard ratio 2.85, 95% confidence interval: 1.21–6.71).

The results show that ADAM9 expression distinguishes PDAC from other solid pancreatic tumors. In addition, cytoplasmic ADAM9 overexpression is associated with poor differentiation and shortened survival. Therefore, ADAM9 overexpression might contribute to the aggressiveness of PDAC.

**04**

**NFκB Mediated Pancreatic Cancer Migration and Invasion**

H. Ito, M. Duxbury, M.J. Zinner, S.W. Ashley, E.E. Whang

Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

**Background:** Constitutive activation of the DNA binding protein nuclear factor kappa B (NFκB) has been reported to occur in most pancreatic cancers; yet, the significance of this finding is unclear. In this study, we tested that NFκB mediates pancreatic cancer migration and invasion.

**Methods:** A super-invasive subclone (PANC-1INV) was derived from the PANC-1 human pancreatic cancer cell line by serial passages through transwell filters. Cellular migration and invasion was determined using Boyden chamber without or with matrigel. NFκB binding activity was assayed using EMSA and luciferase reporter assay. MMP-2 expression and activity was determined using western blotting and zymography. MMP-2 promoter activity was using luciferase reporter assay.

**Results:** PANC-1INV cells had 2.9-fold higher migratory potential and 2.1-fold (p < 0.05) more invasive. It demonstrated 2.3-fold (p < 0.05) greater MMP-2 expression than native PANC-1 cells. Luciferase assay revealed 3.4-fold greater NFκB binding activity in PANC-1INV cells than native PANC-1 cells. PDTC (a NFκB inhibitor, administered at concentrations ranging from 10–1000 nM) induced dose-dependent reductions in NFκB activation, cellular migration/invasiveness, MMP-2 expression and MMP-2 promoter activities for both PANC-1 and PANC-1INV cells. In contrast, PDTC treatment did not show any significant effect on the cell migration and invasion of CAPAN-2 cells, which lacked constitutive NFκB activation.

**Conclusions:** NFκB mediates not only pancreatic cancer cellular migration but also cellular invasiveness by augmenting MMP-2 expression. Blockade of NFκB signaling may be a promising strategy for inhibiting pancreatic cancer invasiveness.

**05**

**DX-8951f in Advanced Pancreatic Cancer (APC)**

G. Abov-Alfa, E.M. O'Reilly, P. Hoff, R. Donehower, L. Hammond, D. Neville, A. Levin, D.P. Kelsen, K. Feit, A. Duggal, R. De Jager

Memorial Sloan-Kettering Cancer Center, New York, NY, USA

DX-8951f is a novel water soluble, hexa cyclic topoisomerase-I inhibitor with broad pre-clinical and clinical activity in a range of solid and liquid malignancies. A multi-center trial of DX-8951f administered at 0.5 mg/m² on a day 1-5 q 3 week schedule, was conducted in 39 patients with APC, (D’Adamo, et al., Proc. ASCO, 2001). A subset of 23 patients, who had no prior chemotherapy have been further analyzed. Three patients (13%) had confirmed PR’s lasting 2.8, 4.3 and 10.1 months. The median survival time (MST) for the 23 patients without prior therapy was 9.3 months. The 6-, 12- and 24-month survivals were 70%, 39% and 5%, respectively. Toxicity was primarily myelosuppression and fatigue. A phase I study of DX-8951f and gemcitabine in advanced solid tumor malignancies, yielded phase II-III doses of DX-8951f 2.0 mg/m² and gemcitabine 1,000 mg/m² with both drugs given on day 1 and 8 of a 3 week schedule, (O’Reilly, et al., Proc. ASCO, 2002). The toxicities were similar to single-agent DX-8951f with the exception of more thrombocytopenia. Activity was seen at multiple dose levels. Thirty-one patients in this trial with APC had no prior therapy. 1 CR, 6 PR’s (23%) were noted with a median duration of response of 9.3 months. The 6-, 12- and 24-month survivals were 70%, 39% and 5%, respectively. The combined results of these two trials demonstrate:

1. activity for single-agent DX-8951f in APC; 2. activity for the combination of DX-8951f and gemcitabine in APC; 3. a favorable historical comparison for both single-agent DX-8951f and a DX-8951f + gemcitabine combination compared to gemcitabine alone.

Two large-scale randomized trials in the U.S. (DX-8951f and gemcitabine compared to gemcitabine) and Europe (DX-8951f compared to gemcitabine) have completed their accrual and will answer the definitive contribution of DX-8951f to the treatment of APC.
06
LY293111: A Novel Approach to Pancreatic Cancer
K.L. Blanchard, A. Weitzman, C. Slapak, P. Paoloetti
Eli Lilly and Company, Indianapolis, IN, USA

Single agent Gemcitabine (GEM) is the only regimen with proven survival benefit in locally advanced or metastatic adenocarcinoma of the pancreas.

Since the introduction of GEM multiple anticancer agents have been evaluated either alone or in combination with GEM in randomized clinical trials of patients with pancreatic cancer. None of the agents has shown superior activity to that of GEM alone. LY293111 (LY) is a novel oral anticancer agent discovered at Lilly Research Laboratories that showed promising results both alone and in combination with GEM in pancreatic cancer xenograft models. In a phase I trial conducted in cancer patients the combination of GEM and LY was safe and well tolerated. LY is a known leukotriene B4 receptor antagonist and has peroxisome proliferators activated receptor [PPAR] gamma agonist properties.

The anticancer activity of LY is being evaluated in a randomized, double blinded, placebo-controlled phase 2 trial. Chemotherapy-naïve patients with locally advanced or metastatic adenocarcinoma of the pancreas were randomized to receive either GEM 1,000 mg/m² on days 1, 8 and 15 of a 28-day cycle and continuously-administered oral LY at a dose of 600 mg BID or GEM 1,000 mg/m² on days 1, 8 and 15 of a 28-day schedule plus placebo.

Randomization was performed using a minimization algorithm to balance the arms with respect to ECOG PS and disease stage. Six-month survival rates will be compared using the Pearson’s chi-squared test, and balance the arms with respect to ECOG PS and disease stage. Six-month survival benefit in locally advanced or metastatic adenocarcinoma of the pancreas were randomized to receive either GEM 1,000 mg/m² on days 1, 8 and 15 of a 28-day schedule plus placebo.

07
Determinants of Gemcitabine-Pemetrexed Synergism in Pancreatic Cancer Cell Lines
E. Giovannetti, V. Mey, R. Danesi, I. Mosca, M. Del Tacca
Division of Pharmacology and Chemotherapy, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa, Italy

The fluorinated deoxycytidine analog gemcitabine is now an established effective agent in the treatment of pancreatic cancer. The present study investigates whether pemetrexed, a new multitargeted antifolate that blocks folate metabolism and DNA synthesis, would be synergistic with gemcitabine against the MIA PaCa-2, PANC-1 and Capan-1 pancreatic cancer cell lines.

Cells were treated with gemcitabine (1 h), and pemetrexed (24 h), alone or in sequence, and the analysis by the combination index demonstrated synergism mainly with the sequence pemetrexed-gemcitabine. To assess the role of drug metabolism on gemcitabine cytotoxicity, further studies were performed with inhibitors of the activating enzyme deoxycytidine kinase (dCK), and the inactivating enzymes 5’-nucleotidase (5’-NT), and cytidine deaminase (CDA). The crucial role of dCK in gemcitabine citotoxicity was confirmed by a ten-fold increase in IC50 by adding the dCK inhibitor 2’-deoxy-cytidine in all cell lines, while there was a modest increase in cytotoxicity by inhibition of 5’-NT and CDA, with dihydro- pyrrocarbonate and tetrahydrouridine, respectively. Cell cycle analysis by flow cytometry demonstrated that pemetrexed increased cells in the S phase (from 15.3 to 46.6% in MIA PaCa-2, from 10.6 to 80.1% in PANC-1 and from 46.4 to 63.2% in Capan-1 cells), which is the most sensitive phase of cell cycle to gemcitabine. Furthermore, all the pemetrexed-gemcitabine combinations significantly enhanced the occurrence of apoptosis, as detected by fluorescence microscopy. Finally, quantitative RT-PCR analysis demonstrated that pemetrexed, at the IC50 level, significantly enhanced the expression of dCK (+227.9%, +86.0% and +135.5% in MIA PaCa-2, PANC-1 and Capan-1 cells, respectively), potentially facilitating gemcitabine activation. These data provide evidence that the combination of gemcitabine and pemetrexed displays schedule-dependent synergistic cytotoxic activity in vitro against pancreatic cancer cells, associated with favorable modulation of cell cycle, induction of apoptosis and enhanced expression of dCK.

08
c-Src-Mediated Cross-Talk Between Carcinoembryonic Antigen-Related Cell Adhesion Molecule 6 (CEACAM6) and αvβ3 Integrin Enhances Pancreatic Adenocarcinoma Cellular Adhesion to Extracellular Matrix Components
M. Duxbury, H. Ito, S.W. Ashley, E.E. Whang
Department of Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Introduction: CEACAM6 is an important determinant of tumorigenicity and cellular metastasis. Previously, we reported that inhibition of CEACAM6 expression suppresses pancreatic adenocarcinoma aneuploidy-resistance in vitro and prevents metastasis in vivo. The purpose of this study was to characterize the role of CEACAM6 in modulating interactions between cancer cells and extracellular matrix (ECM) components, a critical component of the metastatic process.

Methods: The pancreatic ductal adenocarcinoma cell lines BxPC3 (overexpresses CEACAM6 and c-Src) and Capan2 (low CEACAM6 and c-Src expression) were studied. CEACAM6 crosslinking was performed using CEACAM6-specific monoclonal antibodies. Cellular adhesion to the ECM components fibronectin and vitronectin was quantified by colorimetric assay. PP2 and RNA interference (RNAi) were used to inhibit c-Src kinase activity and expression. The effects of transfection of c-Src and CEACAM6 were determined in Capan2. The roles of the archetypal fibronectin (α5β1-integrin) and vitronectin (αvβ3-integrin) receptors were characterized using integrin subtype-specific blocking monoclonal antibodies.

Results: CEACAM6 crosslinking increased BxPC3 cellular adhesion to fibronectin and vitronectin. Enhanced adhesion was
suppressed by blocking αvβ3, but not αvβ1-integrin. CEACAM6 crosslinking increased c-Src kinase activity and c-Src inhibition attenuated the increase in fibronectin and vitronectin adhesion induced by CEACAM6 crosslinking. PP2 suppressed adhesion to fibronectin by 86% (P < 0.05) and vitronectin by 96% (P < 0.05), versus DMSO control. Src siRNA suppressed adhesion to fibronectin by 80% (P < 0.05) and vitronectin by 84% (P < 0.05), versus mismatch control siRNA. In Capan2 cells, transfection of CEACAM6 or c-Src alone did not increase αvβ3-integrin-mediated ECM component adhesion following CEACAM6 crosslinking. In contrast, co-transfection of CEACAM6 and c-Src conferred this property on Capan2 cells (mean fibronectin adhesion 4.25-fold greater than control, P < 0.05; mean vitronectin adhesion 5.85-fold greater than control, P < 0.05).

**Conclusion:** CEACAM6 crosslinking induces a c-Src-dependent increase in αvβ3-integrin-mediated adhesion to fibronectin and vitronectin. This characteristic of CEACAM6 may contribute to its pro-metastatic effects.

**09**

**PEFG (Cisplatin, Epirubicin, 5-Fluorouracil, Gemcitabine) Regimen Followed by Radiotherapy after Curative Surgery for Pancreatic Adenocarcinoma**

M. Reni, A. Zerbi, G. Balzano, M.G. Panucci, P. Passoni, M. Ronzoni, E. Villa, V. Di Carlo

Department of Radiochemotherapy, ‘S. Raffaele’ Hospital Scientific Institute, Milan, Italy

**Background:** Postoperative management of patients with pancreatic adenocarcinoma (PA) is controversial.

**Methods:** Patients aged 18–70 years with histologic diagnosis of stage II-IVA ductal PA, and Karnofsky performance status >70 were eligible for this study. Treatment consisted of cisplatin and epirubicin 40mg/m2 on day 1, gemcitabine 600mg/m2 over 1 hour on day 1 and 8, and 5-FU 200mg/m2/day as protracted infusion for the duration of chemotherapy (PEFG regimen). Cycles were repeated every 28 days for a maximum of 4. Thereafter, radiotherapy associated or not to concomitant chemotherapy, was administered. The primary endpoint of the study was 1-yr failure-free survival (FFS). The target enrollment was 51 patients and the strategy would be considered to deserve further analysis if at least 30 patients were FF at 1-yr from surgery (minimum rate of interest 65%; maximum rate of low interest 45%; α = 0.05; β = 0.10).

**Results:** Between September 1997 and June 2002, 51 patients were enrolled. Altogether, 179 cycles of PEFG were delivered. Main grade 3/4 toxicity consisted of neutropenia in 51%, thrombocytopenia in 18%, anemia in 4%, grade 3 cardiovascular, vomiting, mucositis, diarrhea, hand-foot syndrome, non-neutropenic fever, fatigue, deep venous thrombosis, and liver toxicity in 1% of cycles. External beam RT was delivered to 40 patients (median dose 54.9 Gy). One-yr FFS was 67 + 7%. Two-yr overall survival was 53 + 7%. Sixteen patients were alive at a median follow-up of 34 months (range 20–76).

**Conclusions:** Postoperative management of PA with PEFG regimen followed by RT was well tolerated and yielded a promising outcome. These findings warrant further study of this strategy in the adjuvant setting.

**10**

**Genistein Reduces Neoangiogenesis and VEGF Production in Pancreatic Cancer in vivo and in vitro by Inhibition of Hypoxia Inducible Factor-1**

M.W. Müller, P. Büchler, O.J. Hines, M.W. Büchler, H.A. Reber, H. Friess

Department of General Surgery, University of Heidelberg, Germany

**Background:** Pancreatic cancer is one of the deadliest diseases which shows a very aggressive and resistant tumor growth. For local and metastatic tumor growth neoangiogenesis is a basic requirement. Low oxygen levels can activate Hypoxia inducible factor-1 (HIF-1), which upregulates vascular endothelial growth factor (VEGF), in vitro. Genistein, a naturally occurring isoflavonoid, exhibits strong antiangiogenic activity.

**Aim:** To analyze the effects on pancreatic tumor neoangiogenesis in vitro and in vivo by inhibition of the HIF-1 activation by genistein.

**Methods:** The human pancreatic cancer cell lines Capan-1 (C1) and Mia PaCa-2 (MP2) were grown either under normoxic or hypoxic conditions. VEGF protein secretion was measured using ELISA, DNA binding of HIF-1 was studied with electrophoretic mobility shift assay, and mRNA quantification was performed using Northern blot analysis. Tumor growth in vivo was studied using an orthotopic murine model. Microvessel density was analyzed by anti-Factor-VIII immunohistochemistry.

**Results:** Hypoxia significantly (p < 0.01) upregulates VEGF production in C1 and in MP2. DNA binding activity of HIF-1 to the promotor region of the VEGF gene was activated within 60 min after onset of hypoxia. This effect was dose dependently suppressed by genistein. Protein levels of VEGF significantly (p < 0.05) dropped in both cell lines [C1 (4.2 fold), MP2 (2.4 fold)] upon genistein treatment. In vivo genistein suppressed VEGF mRNA expression significantly (p < 0.05) in all animals treated. Reduced VEGF expression was also accompanied by a significant lower microvessel density (37.2 vs. 21.2) in immunohistochemistry.

**Conclusion:** This study indicates one likely mechanism on a molecular basis by which the previously reported antiangiogenic activity of genistein is mediated. Inhibition of HIF-1 downregulates VEGF production and leads to a decreased microvessel density in tumor xenografts. The regulatory unit of the transcription factor HIF-1 and its target gene VEGF may be a possible therapeutic target in future.

**11**

**Relevance and Classification of Pancreatic Leakage after Pancreatic Resection**

F. Makowiec, U. Adam, H. Riediger, U.T. Hopt

Department of Surgery, University of Freiburg, Germany

**Background:** In most centers leakage of the pancreatic anastomosis (PaLeak) represents a leading cause of morbidity after pancreatic resection. PaLeak is usually defined as a leak or dysfunction of the pancreatic anastomosis with or without transudation of pancreatic enzymes into the peripancreatic fluid collection. The incidence varies from 3% to 10% and outcomes range from minor to major complications including life-threatening mediastinal, retroperitoneal, or pericolic collection. A comprehensive review of the literature and our clinical experience guided us to accept a very strict definition of PaLeak: a leak is a surgical complication that requires specific and vigorous medical and interventional therapy. At our institution, PaLeak is defined as an active extravasation of pancreatic enzymes into the peripancreatic fluid collection with or without a collection requiring drainage and/or intervention. PaLeak requires immediate medical and technical attention from the interventional radiology team, the medical team, and the surgical team in order to prevent complications such as infection, pseudoaneurysm formation, and life-threatening hemorrhage. This strict definition of PaLeak leads to a reduction in false-positive rate. The overall complication rate from PaLeak decreases significantly from 10% to 3% per patient year.
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Methods: 452 pancreatic resections (54% PPPD, 19% DPHR, 14% Whipple, 11% distal resections and 2% other) were performed for chronic pancreatitis (51%), malignancy (38%) and others (11%). The pancreatic anastomosis was drained for at least five days. All patients received octreotide postoperatively. Reconstruction consisted of pancreato-jejunostomy. PaLeak was defined as (a) anastomotic insufficiency found during relaparotomy, (b) need of a CT-guided drainage for symptomatic fluid collections with high amylase concentration or (c) secretion of amylase-rich fluid from the drainage beyond day six. The perioperative course was documented prospectively.

Results: Mortality was 2.4%. Any complication occurred in 41%, surgery-related complications in 29% and PaLeak in 11.7% (n = 41). PaLeak was more frequent in patients with tumors compared to chronic pancreatitis (15% vs. 8.6%; p < 0.04). Of the 53 cases with postoperative PaLeak, 26 (49%) required no further therapy other than prolonged drainage. Fourteen patients (26%) required a CT-guided drainage and 13 patients (25%) were re-operated. Mortality was zero and PaLeak healed in all 40 patients not re-operated. Of the 13 patients requiring re-operation seven underwent salvage pancreactectomy (three of those died). Two further patients died after re-operation due to cardiac complications. All patients who died with PaLeak had malignant disease. Overall mortality of patients with pancreatic fistula was 5/53 (9%). Mortality of PaLeak was 5/28 (18%) in malignant disease but zero in patients with chronic pancreatitis.

Conclusions: Because of their clinical presentation and prognostic consequences, leakages of pancreatic anastomosis may be classified as 'biochemical' with no need for intervention and good outcome or 'clinical' requiring further therapy.

12 Five Year Actual Survival Following Extended or Standard Lymphatic Clearance in Cancer of the Head of the Pancreas

U. Boggi, M. Del Chiario, M. Massa, C. Croce, F. Gremmo, G. Marangoni, A. Sgambelluri, F. Vistoli, S. Signori, A. Campatelli, G. Di Candio, D. Campani, G. Bevilacqua, F. Mosca

Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa, Italy

Background: Despite pancreatic cancer (PC) spreads early and frequently to regional lymphatic nodes, there is no general consensus on whether an extended (ELC) or a standard (SLC) lymphatic clearance should be added to 'curative' pancreaticoduodenectomy (PD).

Aim: To analyze the 5-year actual outcome of two cohorts of patients undergoing ELC or SLC following PD for PC.

Methods: Between November 1987 and December 1998, 87 consecutive patients undergoing PD for locally non-advanced PC (T1-3 according to the last revision of UICC staging) received either an ELC (n = 44) or a SLC (n = 43). ELC and SLC were defined as proposed by Ishikawa. No patients received either neo-adjuvant or adjuvant treatments. Minimum follow-up period was 5 years. The two groups were comparable regarding all baseline characteristics.

Results: No significant difference was recorded regarding the mean duration of surgery and the number of transfusions. Postoperative hospital stay averaged 20.9 ± 8.9 days for ELC as compared to 19.6 ± 6.2 days for SLC (p = NS). ELC morbidity and mortality rates were 47.6% and 2.3% as compared to 33.3% and 4.5% for SLC (p = NS). Severe diarrhea, requiring medical treatment, was recorded more frequently following ELC (33%) than after SLC (2%) (p = 0.001). Actual survival rates at 1, 3 and 5 years following ELC were 70.7%, 25.2% and 14%, respectively. Equivalent figures for SLC were 56.8%, 14.6% and 7.8%, respectively (p = NS). In patients diagnosed with lymph nodes metastases survival was 60.9%, 23.6% and 14% following ELC as compared to 52.2%, 10.4% and 0% after SLC. Incidence and pattern of cancer recurrence were similar after ELC and SLC.

Conclusions: Five-year actual follow-up of patients undergoing PD for locally non-advanced PC confirms that survival is not enhanced significantly by ELC as compared to SLC. Severe diarrhea limits the quality of life of patients undergoing ELC.

13 Prognostic Implications of Vascular Infiltration in Pancreas Cancer

U. Boggi, M. Del Chiario, C. Croce, F. Gremmo, G. Marangoni, A. Sgambelluri, F. Vistoli, S. Signori, A. Campatelli, G. Di Candio, S. Mazzeo, C. Cappelli, D. Campani, G. Bevilacqua, F. Mosca

Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa, Italy

Background: Traditionally, pancreatic resections are contraindicated for pancreas cancers infiltrating the main vascular trunks.

Aim: To evaluate the prognostic implications of vascular infiltration in pancreas cancer.

Methods: Between November 1987 and January 2004, 123 pancreatic resections associated to vascular resection were performed, including 90 venous resections (73.2%), 15 arterial resections (12.2%), and 18 venous/arterial resections (14.6%).

Results: Overall, morbidity was 37.3% and mortality 3.2%. Morbidity of patients who underwent venous resection alone, arterial resection alone, and combined venous/arterial resection were 31.1%, 50%, and 33.3%, respectively. Equivalent figures for mortality were 2.2%, 0%, and 11.1% (p = NS), respectively.

Pathology confirmed the diagnosis of ductal adenocarcinoma (DA) in 98 specimens (79.7%) while the remaining cases were diagnosed with other tumor types (23; 18.7%) or with chronic pancreatitis (2; 1.6%). Actual vascular infiltration was diagnosed in 52.8% of cancerous specimens. Infiltration reached the tunica adventitia, media, and intima in 25%, 33.1% and 41.9% of specimens, respectively. Survival at 1, 3 and 5 years for DA was 49.9%, 21.6%, and 11.1%, respectively. Equivalent figures for other tumor types were 80%, 50%, and 33.3%, respectively. At the same time points, survival for DA undergoing venous resection was 52.4%, 18.5%, and 12.7%, respectively, as compared to 55.5%, 55.5%, and 13.8% for arterial
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resection and to 32.4%, 0%, and 0% for venous/arterial resection, respectively. Finally, actual vascular infiltration was associated to decreased survival rates at 1, 3 and 5 years (41.4%, 4.7% and 0%) as compared to nonconfirmed vascular involvement (56.4%, 26.3%, and 26.3%).

Conclusions: Not all vascular segments deemed involved at pre- and intra-operative evaluation have actual pathological infiltration, and not all patients thought to bear a pancreas cancer are eventually diagnosed with DA. Resection of multiple vascular segments and/or documentation of actual vascular infiltration are associated to poor outcome.

14
Is there any Benefit of Venous Resection for Ductal Adenocarcinoma of the Pancreatic Head?
M. Niedergethmann, M. Farag-Soliman, S. Post
Department of Surgery, University-Hospital Mannheim, University of Heidelberg, Germany

Objectives: To evaluate, who benefits from venous resection during pancreaticoduodenectomy for ductal pancreatic adenocarcinoma we analyzed 271 consecutive patients. The outcome of patients with (n = 68) and without (n = 203) concomitant resection of major veins (portal vein and/or superior mesenteric vein) were compared.

Material and Methods: Data examined comprised 1) demographics, 2) pathology report, 3) TNM-stage, 4) UICC classification, 5) details of the surgical therapy, and 6) hospital course and follow-up until December 2003.

Results: Both groups differed significantly regarding T-, UICC-, R1-stage, perineural infiltration, lymphangiosis carcinomatosa, operation time, blood loss, and blood transfusion. However, there was no difference in perioperative morbidity (27% vs. 22%), mortality (4% vs. 3%), and long-term survival (at 5 years postoperative 23% vs. 24%). Subgroup analysis of patients with free margins (R0-resections) revealed that those patients with venous resections and no tumorous infiltration (histopathologically) had the most favorable outcome.

Conclusions: Pancreaticoduodenectomy with portal or mesenteric superior vein resection can be performed with low perioperative mortality and morbidity rates. Therefore, extended venous resection is not an additional risk for the patients, but keeps the chance for cure, likewise in patients with less advanced disease.

15
Expression Profiling of Microdissected Pancreatic Ductal Carcinomas Using High-Density DNA Microarrays
R. Gruitzmann, C. Pilarsky, O. Ammerpohl, J. Lüttges, H. Kalthoff, B. Kremer, H.K. Schackert, G. Klöppel, H.D. Saeger
Department of Surgery, University Hospital, Dresden, Germany

Introduction: The aim of the study was to search for new molecular markers of pancreatic ductal adenocarcinoma (PDAC) leading to novel diagnostic as well as therapeutic targets for this dismal disease. Despite recent progress in our understanding of the molecular basis of PDAC further studies are needed to find new molecular markers for diagnostic and therapeutic purposes.

Methods and Materials: We investigated the mRNA-expression profile of microdissected cells from 11 normal pancreatic ducts, from 14 samples of PDAC and of 4 established pancreatic cancer cell lines. We applied DNA microarray technology with the Affymetrix U133 GeneChip set representing roughly 33,000 genes. The RNA was extracted from microdissected samples and cell lines, amplified and labelled using a repetitive in vitro transcription protocol. Hybridisation and detection were performed according to Affymetrix recommendations. Differentially expressed genes were identified using the SAM (significance analysis of microarrays) program.

Results: We found 616 differentially expressed genes. Within these, approximately 30% were also identified in other gene expression profiling experiments and 10% have been associated with pancreatic cancer by other analysis techniques, like the Galectins 1 and 3 and the MT-SP2. We have validated the differential expression of several genes in PDAC by immunohistochemistry and RT-PCR.

Summary: We present the first whole genome expression study of microdissected tissue from PDAC, from microdissected normal ductal pancreatic cells and pancreatic cancer cell lines using high-density microarrays. Within the panel of genes we identified novel differentially expressed genes, which have not been associated with the pathogenesis of PDAC before.

Posters

P01
Impact of Centralization on Results of Resection for Exocrine Pancreatic Cancer
Å. Andrén-Sandberg
Department of Surgery, Central Hospital of Rogaland, Stavanger, Norway

Complications of pancreatic resections are dangerous and costly. A literature review was therefore done to investigate the evidence for improving the results by regionalizing this demanding surgery.
Studies from four countries (USA, UK, the Netherlands and Finland) with advanced health care systems have universally shown a significant inverse correlation between case volume for pancreatic cancer resection and post-operative mortality. Further analysis reveals lower complications, reduced hospital stay, reduced hospital costs and improved survival of patients treated in high-volume hospitals. The relationship between volume and outcome is with institutional volume rather than single surgeon caseload. The evidence therefore strongly supports the regionalization of pancreatic cancer surgery into large specialized multi-disciplinary units. In the UK, the national health service executive has instructed regional health authorities to concentrate pancreatic cancer surgery into designated regional centers ideally with catchment populations of 2–4 million. There is now considerable pressure to adopt a similar policy in all countries with advanced health care systems.

There is today enough evidence in the literature to advocate a regionalization of pancreatic cancer resections.

P02
Importance of Age at Pancreatoduodenectomy for Exocrine Pancreatic Cancer
Ä. Andrén-Sandberg
Department of Surgery, Central Hospital of Rogaland, Stavanger, Norway

Compared to other gastrointestinal malignancies, exocrine pancreatic cancer is a fairly common malignancy, and account for well over 185,000 new cancers per year world-wide. However, only approximately 20 percent of these cancers are seen before age 60 and pancreatic cancer must be understood as a disease of the elderly.

Pancreatoduodenectomy must be looked upon as a major surgical procedure and was once associated with mortality rates of 33–41 percent in patients over 70 years of age. More recently studies have demonstrated lower morbidity and mortality rates of 14–45 percent and 5–9 percent, respectively. Today studies have now shown that an age of 70 years or more does not preclude pancreatoduodenectomy.

Most of the studies do not show increased operative morbidity or mortality. The cumulative survival rate is not different from that obtained in younger patients. However, it must be remembered that the older patients always are well selected, probably better selected than the younger.

Available data strongly indicate that with appropriate selection older patients today have an acceptable mortality and morbidity also after pancreatoduodenectomy. Age and well-controlled comorbid conditions are no longer contraindications to surgical resection. These patients recover to a state of health that is equal to their age-matched counterparts without cancer.

P03
Quality of Life after Pancreatoduodenectomy for Cancer
Ä. Andrén-Sandberg
Department of Surgery, Central Hospital of Rogaland, Stavanger, Norway

Pancreatoduodenectomy must be looked upon as a major surgical procedure and when today the mortality and morbidity related to the surgical procedure are more limited than before, attention has turned to postoperative quality of life. Outcomes such as pain, stool habits, diabetes, working capacity, leisure activity levels, or with evaluation of physiology such as gastric emptying and gastrointestinal function, and other measurable variables will then be of interest not only in a discussion on which priority pancreatic resection have in an economically limited health care section, but also if palliative resections are indicated, which type of operation technique that shall be favored etc.

There are today no randomized studies measuring quality of life in patients operated on with pancreatoduodenectomy, but when non-randomized comparisons are made (and there are several of good quality) it is obvious that the resected patients – if they are free from cancer – achieve a normal, or almost normal, quality of life according to measurements with evaluated scales or by noting their postoperative symptoms.

Publications using quality of life in the palliative setting of unresectable pancreatic cancer usually show that the proposed treatment maintain the quality of life at a higher level for a longer time even though the total survival time is little increased. If this is the effect of higher grade of hope for the treated patients, a real effect of the treatment given, or a selection bias for positive results to be published is not known.

In conclusion, it can today be stated that after rehabilitation after pancreatoduodenectomy for malignancy the quality of life is equal or almost equal to healthy persons of the same age as long as the patients are free from their disease.

P04
Preoperative Interleukin-2 Immunotherapy Improves Survival in Pancreatic Cancer
C. Angelini, C. Mussi, G. Bovo, S. Crippa, F. Romano, G. Piacentini, R. Caprotti, Fr. Uggeri
Department of General Surgery, ‘San Gerardo’ Hospital, University of Milan-Bicocca, Monza, MI, Italy

Background and Objectives: It is known that the outcome of cancer patients do not depend upon tumor characteristic alone, but also on the immune status of the patient. Besides blood lymphocyte counts, infiltration and activation of lymphocytes and other inflammatory cells around the tumor have been recognized as a positive tumor-host reaction in several neoplasms, such as lung, breast, melanoma, colorectal and gastric cancer. Aim of this study is to evaluate the effectiveness of preoperative interleukin-2 treatment to improve local immune resistance and survival in pancreatic cancer patients.
Methods: 19 patients with pancreatic cancer who underwent radical surgery were randomized into two groups. Group 1: 9 patients treated with preoperative administration of human recombinant IL-2 subcutaneously at 9 million UI/day for 3 days starting 4 days before surgery; group 2: 10 patients underwent surgery alone. Semi-quantitative evaluation of neutrophils and lymphocytes infiltration on the resected specimens, presence of necrosis and of desmoplastic reaction were studied.

Results: There were no significant differences between two groups about age, sex, stage of disease, preoperative hematological assessment and postoperative complications. Histological parameters showed no significant differences between the two groups, whereas overall survival curves showed a 1 year survival of 40% in treated group compared with 10% in control one (p = 0.009). Median follow up was 18 months.

Conclusions: This preliminary results suggest that a short-term preoperative IL-2 immunotherapy may improve survival of pancreatic cancer patients. Although we didn’t found a significant difference in local inflammatory cells number between control and treated group, these preliminary data suggest that IL-2 administration could improve immune function, leading to a more effective response against tumor, since IL-2 is not only the main growth factor for lymphocyte cells, but is able to regulate lymphocyte activation and differentiation too.

P05
Prognostic Factors after Surgical Resection for Pancreatic Carcinoma
A. Antinori, L. Ciccocitti, P. Giustacchini, F. Castri, R. Coppola, P. Magistrelli, A. Picciocchi
Department of Surgery, Policlinico ‘A. Gemelli’, Catholic University, Rome, Italy

Introduction: Surgical resection has a primary role in the treatment of pancreatic carcinoma. Several recent studies have emphasized the importance of patient selection based on different prognostic factors.

Methods: Eighty-seven patients with pancreatic carcinoma treated at the Department of Surgery of the Catholic University of Rome during 1988–2001 were analyzed. Immediate results and survival data were reviewed. Clinico-pathological predictive factors, and molecular markers (p53, Bcl-2, Bax, apoptotic index) in a subgroup of cases, were compared statistically by univariate and multivariate analysis.

Results: Operative mortality rate was 2.7% while surgical related morbidity was 28%. Intraoperative blood loss (BL) was associated with higher surgical morbidity. Analysis of disease-specific survival (DSS) showed that grading (p = 0.02) and nodal status (p = 0.03) significantly affected DSS at the univariate analysis. The median survival time was higher in patients with overexpression of p53 and low apoptotic index, even if the difference was not significant. Multivariate analysis with Cox model confirmed the role of grading and nodal status as independent prognostic factors.

Conclusion: Grading and nodal status were the strongest independent predictors of survival. As concern others molecular factors a trend of positive influence on survival suggest further investigations.

P06
Immediate Outcome and Survival after Pancreaticoduodenectomy for Periampullary Cancer
A. Antinori, P. Giustacchini, L. Ciccocitti, R. Coppola, P. Magistrelli, A. Picciocchi
Department of Surgery, Policlinico ‘A. Gemelli’, Catholic University, Rome, Italy

Introduction: Surgical resection remains the foundation of treatment for patients with potentially curable periampullary carcinoma. Recently an encouraging operative mortality and survival after pancreaticoduodenectomy have been reported. The purpose of the study is to investigate the real impact on immediate and long-term results of different prognostic factors.

Methods: From 1988 through 2001, 145 patients with peri-ampullary carcinoma underwent pancreaticoduodenectomy at the Department of Surgery of the Catholic University of Rome. Perioperative morbidity, mortality and survival data were reviewed and potential prognostic factors were compared statistically by univariate and multivariate analysis.

Results: Of the 145 with resected periampullary cancer, 62 were pancreatic carcinoma (PC), 60 were ampullary carcinoma (AC), 15 were distal bile duct carcinoma (BDC), and 8 were duodenal carcinoma (DC). Operative mortality rate was 6.9% while surgical morbidity was 39.3%. Patients with pancreatic cancer had a significantly lower mortality (3.2% vs. 8.4%) and surgical morbidity (25.8% vs. 48.3%) in AC. 66.7% in BDC – p = 0.007). Patients that underwent a preoperative biliary drainage had a higher surgical morbidity.

Univariate analysis on disease-specific survival (DSS) showed that intraoperative blood loss (p = 0.003), type of tumor (p = 0.0001), nodal status (p = 0.0007), surgical margins (p = 0.0001), and grading (p = 0.009) significantly affected survival at the univariate analysis. Multivariate analysis confirmed blood loss, pancreatic origin, nodal status and surgical margins as independent prognostic factors.

Conclusions: In patient with periampullary carcinoma the origin of the tumor influences immediate and long-term results. Indications for biliary drainage should be adequately selected. Intraoperative blood loss, type of tumor, nodal status and surgical margins are significant prognostic factors.

P07
Pancreatic Cancer Resection in Elderly Patients
G. Balzano, A. Zerbi, P. Veronesi, F. Scaltrini, A. Beneduce, M. Reni, V. Di Carlo
Department of Surgery, ‘San Raffaele’ Hospital, Milan, Italy

Background: Pancreatic cancer resection is considered a high-risk procedure in patients aged 70 years or older.

Methods: 319 patients with pancreatic adenocarcinoma, who underwent resection between 1990 and 2002, were reviewed. Data were prospectively collected in our pancreatic surgery data-base.
Operative outcome and survival of 95 patients aged 70 years or more were compared with findings in 224 younger patients.

**Results:** Mortality rate was 2.1% in patients aged 70 years or more and 2.2% in younger patients; morbidity was 44.3% and 49.2%, respectively (NS). Postoperative pancreatic fistula was less frequent and 2.2% in younger patients; morbility was 44.3% and 49.2%, respectively.

Pathologic prognostic factors were similar between the two groups (UICC classification, nodal involvement, grading, radicality, tumor diameter). However, patients aged 70 years or more underwent less frequently postoperative chemo- and radiotherapy (p < 0.01) with respect to younger patients. Median postoperative survival was 15 months in elderly patients and 18 months in the younger group (log-rank test p = 0.26). Multivariate analysis considering age, pathologic factors and adjuvant therapies as covariates demonstrated that tumor diameter, grading and UICC stage were independent prognostic factors, whereas age was not (p = 0.2).

**Conclusion:** Patients aged 70 years or more can benefit from pancreatic cancer resection similarly to younger patients.

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**P08**

**Toxicity and Technique of Multimodality Treatment in Advanced Pancreatic Adenocarcinoma: A Retrospective Study**

S. Barra, T. Scolaro, A. Bacigalupo, F. Giannelli, S. Chiara, V. Vitale

IST, Genova, Italy

We reviewed advanced pancreatic carcinoma from 2000 through 2003 to verify acute toxicity in 28 pts, m/f: 15/13, treated by chemoradiotherapy (CT/RT). 11 pts had unresectable tumors (A) and 17 pts had resectable disease (B). CT was: 5-FU c.i. (200–500 mg/m²) twice a week during RT (15 pts). Radiotherapy was delivered previous simulation with oral contrast agent and CT scan with 5 mm slice. Three or four fields were used with 3D conformal technique, 1.8–2.0 Gy/fraction per day, 5 times a week; each pt dose-volume histogram was calculated to verify and optimize the radiation plan. In group A clinical tumor volume (CTV) was performed by a margin of 2–3 cm on gross tumor volume and local regional lymphnodes were included. In group B CTV was the tumor bed plus 2–3 cm margin. Doses to the critical organs should not exceed for liver 30 Gy to more than 50% of its volume and equivalent to whole kidney has been excluded from all irradiation fields if possible, or at least limited to 18 Gy. 26 pts received a total dose more than 45 Gy (range 45–60 Gy), 1 pt stopped RT at 7.2 Gy and 1 pt at 32 Gy. Grade III hematological toxicity was observed in 3 pts. No gastrointestinal toxicity grade III-IV were registered; one pt stopped RT at 7.2 Gy because of brain stroke and another at 32 Gy for myocardial ischemia. In our experience chemotheraphy associated with radiotherapy is feasibility and well tolerated when a careful radiation treatment planning is warranted.

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**P09**

**Unusual and Rare Tumors of the Pancreas: Spindle Cell Hemangioendothelioma: A Case Report**

M. Benedetti, E. Devecchi, E. Ticozzelli, G. Rossi, R. Vailati, P. Forti, F.P. Tinozzi, M. Abelli, C. Bianchi, P.L. Colombo, S. Tinozzi

Chirurgia Generale Gastroenterologica e Mammaria e dei Trapianti d’organo, IRCCS Policlinico ‘S. Matteo’, Pavia, Italy

Hemangioendotheliomas of the pancreatic gland are rare non-functioning tumors usually discovered incidentally at autopsy or during US – CT examinations. The rarity of the disease is underlined by Chiari and Gruber who reviewing the cumulative necropsy experience of over 30,000 patients didn’t find any connectival tumor of the pancreas and by Laverdiere who found evidence for about 25 spindle cell tumors of the pancreas in reviewing the literature.

**Case Report:** A 66-year old female presented with intermittent epi-mesogastric pain with irradiation to the back. A CT scan of the abdomen showed a prevalent exophitic solid mass of the body of the pancreas 5.4 cm in diameter. After contrast injection, evident enhancement appeared hypervascularized. At surgery conferme round mass of the body of the pancreas. Subtotal distal pancreatectomy with splenectomy and loco-regional lymphadenectomy was performed. The patient was discharged on the tenth postoperative day. After 18 months follow-up the patient was alive and well. Microscopically the tumor contains strikingly elongated and spindle-shape cells in a dense and fibrous stroma, with multiple little and medium size cavernous vessels. The tumor presents expansive multimodular growth, and focally shows compression of adjacent parenchyma. No metastatic involvement was present.

**Discussion:** Hemangioendotheliomas of the pancreas present like other tumors of the gland. They occur approximately one-half of patients are <25 years of age. Although these tumors may be quite large on presentation, the biology of some is favorable; thus metastatic disease may not be present at exploration. Surgical resection allows for accurate histologic evaluation of the entire specimen and may be curative in those tumors with low to moderate malignant potential. This would support aggressive surgical resection for cure (pancreatoduodenectomy or subtotal distal pancreatectomy). In this view, recently, interferon-alpha-2a was effective in inducing early regression of spindle cell hemangioendothelioma of the pancreas in infants.
P10
Phase I Study of Gemcitabine (GEM) as Prolonged Fixed Dose Rate i.v. Infusion with Peripheral Blood Progenitor Cell (PBPC) Support in Advanced Pancreatic Carcinoma (APC)

C. Bengala, E. Fontana, E. Giovannetti, R. Danesi, M. Lencioni, S. Fogli, A. Fontana, U. Boggi, M. Del Chiaro, S. Ricci, F. Mosca, M. Del Tacca, P.F. Conte
Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa, Italy

GEM has shown clinical antitumor activity in APC; this activity appears to be due to intracellular formation of triphosphate metabolites. The formation of triphosphate metabolites and intracellular accumulation are dose rate dependent with a saturation at 10 mg/m²/min. Data from randomized phase II study showed that GEM given as prolonged fixed dose rate i.v. infusion may improve response rate and survival in patients with APC in comparison of standard infusion. Moreover prolonged infusion of GEM can significantly increase mielotoxicity. We designed a phase I dose finding study of increasing doses of GEM given at i.v. fixed infusion dose rate of 10 mg/m²/min with support of PBPC + G-CSF 5 mg/kg/day for 5 days. Starting dose of GEM was 3,000 mg/m² with a dose escalation of 500 mg/m² every 21 days. Nineteen of 23 patients were evaluable for response: 3 pts achieved CR lasting 21 months. Our data show that the treatment is feasible and well tolerated. The recommended dose for further phase II study is 6,500 mg/m².

P11
Antiangiogenic versus Cytotoxic Therapeutic Approaches to Human Pancreas Cancer: An Experimental Study with a VEGFR-2 Tyrosine Kinase Inhibitor and Gemcitabine

G. Bocci, R. Danesi, G. Marangoni, A. Fioravanti, U. Boggi, I. Esposito, A. Fasciani, E. Boschi, D. Campani, M. Del Chiaro, G. Bevilacqua, F. Mosca, M. Del Tacca
Division of Pharmacology and Chemotherapy, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa, Italy

Pancreatic adenocarcinoma is a leading cause of cancer death in the United States and represents a challenging chemotherapeutic problem. The pharmacological control of angiogenesis might represent a novel approach to the management of pancreas cancer, since the pathological development of vascular supply is a critical step for tumor growth and may affect its prognosis. In order to test this hypothesis, SU5416 [3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one] – selective inhibitor of the vascular endothelial growth factor receptor-2 tyrosine kinase – and gemcitabine (2', 2'-difluorodeoxycytidine) were tested on endothelial (HUVEC) and pancreatic tumour cells (MIA PaCa-2) in vitro and in vivo alone and in simultaneous association. SU5416 inhibited HUVEC cells stimulated to proliferate by VEGF but not MIA PaCa-2 cells; the drug concentration that decreased cell growth by 50% (IC50) was 0.14 µM. Furthermore, SU5416 reduced the development of microvessels from placental explants (IC50, 0.23 µM). Gemcitabine inhibited the growth of both HUVEC and MIA PaCa-2 cells with an IC50 of 0.08 and 0.1 µM, respectively. A synergistic effect (combination index <1 and dose reduction index >1) on anti-proliferative and pro-apoptotic activity was calculated with the simultaneous combination of the two drugs on endothelial cells. A marked in vivo antitumour effect on MIA PaCa-2 xenografts was observed with SU5416 at a protracted schedules, as well as with gemcitabine; furthermore, the combination between the two drugs resulted in an almost complete suppression of tumour growth and relapse. In conclusion, the present results provide the evidence of an effective anti-endothelial/antitumour activity of protracted administration of SU5416 on human pancreas cancer xenografts, which is comparable with the one obtained by gemcitabine; moreover, the synergistic combination between these drugs on endothelial cells and the promising association in pancreatic cancer xenografts could be used in future studies and translated into the clinical setting.

P12
The Impact of Age on the Outcome of Pancreatectomies

U. Boggi, M. Del Chiaro, F. Gremmo, C. Croce, A. Sgambelluri, L. Morelli, F. Vistoli, S. Signori, G. Di Candio, A. Campatelli, F. Mosca
Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa, Italy

Background: Despite improvements in intra- and post-operative care, pancreatectomies (PC) continue to be associated with significant morbidity and, occasionally, with mortality. Despite advanced age is no longer deemed an absolute contraindication to PC, controversy continues regarding the upper age limit above which a PC should not be performed.

Aim: To analyze the outcome of PC according to four age groups starting with individuals younger that 60 years and ending up with those older than 80 years, with increments of 10 years between each study group.

Materials and Methods: Between November 1987 and October 2003 646 PCRs were performed for either pancreatic or periampullary neoplasms. Patients were classified into four groups based on their age at surgery. Group A comprised 215 patients aged less than 60 years, group B 231 patients aged between 60 and 69 years,
group C: 168 patients aged between 70 and 79 years, and group D: 32 patients aged over 80.

**Results:** Hospital stay averaged 10.8, 13.1, 13.2, and 16.9 days in the four study groups (p = NS), respectively. Morbidity was 33.1% in group A, 35.5% in group B, 41.7% in group C, and 46.8% in group D. Equivalent figures for mortality were 2.2%, 2.3%, 3.5%, and 6.6%, respectively. Survival rates at 1-, 3-, and 5-years for patients with pathologically proven ductal adenocarcinoma were: 51.3%, 15.8% and 15.8% for group A; 59.4%, 23.7% and 4.3% for group B; 70.4%; 18.4% and 14.6% for group C; and 46.7%, 8% and 8% for group D.

**Conclusions:** Our experience confirms that age per se has a little impact on the outcome of PCR. Post-operative complications, however, may pursue a more aggressive course in elderly patients due to either decreased healing powers or associated disease. Exhaustive pre-operative work-up and careful patient selection are both fundamental.

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**P13**

**First Report of Xenograft from Intraductal Papillary Mucinous Neoplasm of the Pancreas (IPMN): Only an Experimental or maybe a Clinically Remarkable Model too?**

A. Bonora¹, C. Sorio², R. Salvia³, D. Lissandrini², G. Maraia², A. Mafficini², A. Cavallini², P. Capelli², A. Scarpa³, P. Pederzoli³

Departments of ¹Surgical Sciences, ²Pathology and ³Medical Research Laboratories, University of Verona, Italy

Even if considered a fairly recent and rare clinical entity, nowadays IPMNs appear to be a continuously increasing disease, thus amounting nearly to 10% of the overall patients observed for pancreatic tumors in a high volume centre.

This led us to get a deeper knowledge of the clinical features of IPMN, so largely improving our skill on diagnostic and surgical management of these patients. Nevertheless, little is still known about biology of IPMNs and their behavior in the progress to the malignancy. Up to now, surgery is the only curative treatment and therefore a proper assessment, a limited pancreatic resection could be performed.

Because of the surprising long-life survival of the patient (over 5 years), we decided to check the pathological samples and so diagnosis was turned to an invasive IPMN. Both primary and xenografted tumor showed no mutations in K-ras, p53 and p16 genes typical of ductal carcinoma, this furthermore proving that invasive component was not of ductal origin. The characterization of phenotypic profile is still in process.

In our opinion, the availability of an experimental model for IPMN could be an effective help in understanding the biology and the behavior in time to malignancy of this tumor, this leading us to better select the patients undergoing resective surgery, and finally in testing chemotherapeutic drugs and adjuvant treatments for unresectable patients.

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**P14**

**Total Pancreatectomy for Misdiagnosed Mucinous Papillary Tumor of the Pancreas**

D. Borzoni, S. Valeri, M. Cicala, C. Rabitti, F. Rea, A. Rosignoli, D. Caputo, R. Coppola

Area di Chirurgia Generale ‘Campus Bio-Medico’ di Roma, Rome, Italy

Papillary Mucinous Tumors (PMT) of the pancreas are increasing in frequency clinical entities. The key-points of their management are difficult differential diagnosis with benign (chronic pancreatitis) and malignant (cystoadenocarcinoma) diseases and prolonged long-term survival rates if compared with other pancreatic malignancies. In September 2002 we observed a 59-year-old man affected by obstructive jaundice, upper abdominal pain and weight-loss. Clinical notes revealed an intricate surgical history.

In 1984 the patient underwent BII sub-total gastrectomy for duodenal ulcer; in 1992 because of gallstone and concomitant bile duct stones cholecystectomy and trans-duodenal papillectomy were performed; in 1997, the patient underwent pancreatic biopsy that showed ductal hyperplasia; for the suspect of chronic pancreatitis a lateral pancreatocojenunostomy was performed at that time. He was also affected by mellitus diabetes since 1995. At admission, severe cholestasis and a ten-fold increase of CA 19-9 were detected. Abdominal CT-scan showed a cystic/solid lesion involving the whole gland in absence of distant metastases or locoregional lymph-nodes. According to patient's history and clinical evaluation PMT was suspected and surgical radical excision planned.

Intraoperative frozen section confirmed this diagnosis. Total pancreatectomy, standard lymphadenectomy and Roux-en-Y hepatico-jenunostomy were performed. Uneventful postoperative course and discharge in the 16th post-operative day were recorded. Histology showed a diffuse intraductal PMT without extra-capsular invasion. Seventeen months after surgery the patient is alive and free of disease. PMT have been recently defined ‘the new kid on the block’ among pancreatic neoplasms. It is often arduous to differentiate this tumor with chronic pancreatitis and benign cystic lesions, but correct diagnosis and early radical surgical excision warrants high survival rates.

In 1997 our patient underwent pancreatic biopsy that showed ductal ectasia that is an histological entity frequently associated to PMT. If properly assessed, a limited pancreatic resection could be performed at that time so avoiding risks of total pancreatectomy.

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Carcinoids are serotonin-secreting neuro-endocrine tumors. Less than 5% are located in the pancreas and, to our knowledge, less than 50 cases of pancreatic carcinoids have been described in literature.

We report the case of a 70 years-old man admitted for flushing, lacrimation and hypoacusia. During the diagnostic work-up a solid lesion in the right hepatic lobe and multiple small nodules in the left one were found. A 2 cm solid resectable nodule was also found in the right upper pulmonary field. No pancreatic lesions and no abnormalities of the duct of Wirsung could be detected.

At laparotomy, a multinodular metastatic liver was found, with a bigger lesion located in the right lobe and multiple sub-centimetric lesions in the left one. Per-operative histopathology documented a neuro-endocrine carcinoma. The intra-operative echography confirmed the biliar involvement of the liver and permitted to find out a 1 cm nodule in the body of the pancreas. A spleen-sparing distal pancreatectomy with synchronous right hemihepatectomy and six wedge resection on the left hemi-liver were performed. Histopathology confirmed a metastatic neuro-endocrine carcinoma. The post-operative course was uneventful, the clinical syndrome disappeared and the patient was discharged on the 11th day p.o. He is now scheduled for pulmonary wedge resection.

A case of aggressive surgical therapy for a rare carcinoid tumor of the pancreas is reported. The only possibility to cure such a disease is offered by surgery and patients with endocrine tumors metastatic to the liver may have an actuarial 5-years survival of 62–76% when curative surgery is performed compared to 29% if untreated. Aggressive surgery to remove locally advanced or metastatic neuro-endocrine tumors may then result in improved duration and quality of life but low morbidity and mortality rates are mandatory since the natural history of these tumors is long (mean 5–10 years).

Although the operative mortality of pancreaticoduodenal resection has decreased recently, operative morbidity from the leakage of the pancreaticoduodenal anastomosis remains high (10–20% Strasberg 1997). Optimizing anastomotic function, preservation of adequate blood supply of the cut surface of the pancreas, and of jejunal loop is necessary. Alternative modalities for management of pancreatic stump did not improve results.

We describe experience in 27 consecutive cases, treated from January 2000 with DCP (Wipple 14, Traverso Longmire 13), for non acute pancreatic disease (ADK 20, Non malignant 5, Neuroendocrine 1, Metastatic 1) located in the head (19), duodenum (2), ampulla (6), end distal common bile duct (1).

There were 13 female and 14 male, median age 66.5 years (30–90), 13 pts showed jaundice at the diagnosis and 3 were treated with stent before surgery. Median duration of operatory time was 420 min (285–540), median blood loss replacement 150cc (0–900), median hospital stay 14.5 days (10–24).

Three patients had extended surgery, (2 resection of mesenterico-portal axis, and 1 subtotal gastrectomy). Median number of resected lymphonode was 15 (10–46).

Telescopic pancreaticojejunostomy, end to side, with end to side Wirsung-jejunal anastomosis was performed in all patients. Only in one pancreatic stump was ligated.

In all patients pancreatic transection was performed over portal vein without coagulatory device, hemostasis with fine suture, and minimal mobilization of stump.

All patients were treated postoperatively with Octreotide Seven (26%) patients showed major surgical complications (3 pancreatic leakage, and 3 bleeding requiring reintervention) 1 pt (0.4%) died, from abdominal non pancreatic abscess.

P16
Obstructive Jaundice as Clinical Onset of Von-Hippel Lindau Disease
M. Caricato, D. Borzomati, S. Valeri, C. Rabitti, F. Ausania, G. Giarratano, S. Greco, R. Coppola
Area di Chirurgia Generale ‘Campus Bio-Medico’ di Roma, Rome, Italy

The Von-Hippel Lindau (VHL) disease is a rare genetically determined syndrome characterized by the occurrence of multiple tumors and cysts.

Central nervous system tumors, phaeochromocytoma and renal cell carcinoma are the most frequent malignancies diagnosed at the onset of the disease usually during the fourth decade of life; as the disease burdens several organs and systems can be involved. Pancreatic neuroendocrine tumors can typically affect VHL patients, but they are not usually diagnosed at the beginning of the disease. For this reason these tumors are usually diagnosed during the screening survey. In 2001 we observed a 16 year old man affected by obstructive jaundice with a familial history of VHL. No clinical signs of VHL had been previously observed. Abdominal CT-Scan showed a pancreatic solid lesion highly suspected for neuroendocrine tumor. This hypothesis was confirmed by the result of a biopsy performed during ERCP. In October 2001, the patient underwent pancreaticoduodenectomy. After a follow up of 26 months the patient is alive and free of disease. This is the second case in the literature reporting about a patient affected by a pancreatic neuroendocrine tumor as the first clinical sign of VHL disease. Patients affected by this syndrome have a poor prognosis and mean life does not exceed the sixth decade. It has been showed that only a strict follow-up can effectively improve survival. Based on the present case, the follow-up of subjects with familial history of VHL syndrome should routinely include functional tests and imaging exams of the pancreas.
Pancreas Cancer 2004

Very important leakage (>80 ml/day for 40 days) was observed only in patients with ligation of stump, other two leakage (50 ml/day) recovered in 15 days.

The relatively low rate of anastomotic leaking (8%) led us to adopt telescopic technique on routine basis.

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**P18**

**Palliative Therapy of Obstructive Jaundice in Cancer of the Pancreatic Head**

*M. Colombo-Benkmann, T. Mundel, A. Brinkmann, C. Schleicher, H. Wolters, D. Tübergen, N. Senninger*

Department of General Surgery, University of Munster, Germany

**Introduction:** Obstructive jaundice in pancreatic cancer can be treated by several procedures. The objective of this prospective study was to compare results of biliodigestive bypass (BDB) vs endoscopic transpapillary drainage (ETD).

**Patients and Methods:** BDB was performed in 19 patients (pts) (m:f 15:4; 58 yrs [40–73]) with obstructive jaundice due to unresectable cancer of the pancreatic head, 14 of whom had undergone preoperative ETD (1990–2000). In 26 pts (m:f 19:7; 63 yrs [39–73]) ETD was left in place (n 23) or performed postoperatively (n 3). Outcome parameters were therapeutic efficacy, re-interventions and complications. All pts experienced tumor related death with a median survival of 11.7 months [2–29] (BDA) vs 6.9 months [1–23] (p 0.001).

**Results:** Inoperability was due to retroperitoneal/vascular infiltration in 18 (95%) (BDB) vs 25 (96%) (ETD) pts, 7 (37%) vs 9 (35%) pts had preoperatively unapparent systemic spread.

Therapeutic complications occurred in 2 BDB pts, but not after ETD (p 0.05). Preoperative median bilirubin was 8.6 mg/dl [3.1–20.7] in BDB pts, despite preoperative ETD in 14 of them. Preinterventional bilirubin in ETD pts was 9.7 mg/dl [1.2–25.3] (p 0.05). Bilirubin dropped significantly after a median of 10 days [3–48] (BDB) vs 15 days [1–38] (ETD) (p < 0.0001) with a median lowest level of 2 mg/dl [0.4–5.0] vs 2.2 mg/dl [0.2–14.2] (p 0.05). Bilirubin normalized in 14 pts (74%) after BDA and in 12 pts (46%) after ETD (p = 0.077). Obstructive jaundice reoccurred in 2 (10.5%) BDB pts and 10 (38.5%) ETD pts (p = 0.046), cholangitis in 3 vs 5 pts (p 0.05).

Re-interventions were performed in one (5%) BDB patient, however in 15 (58%) ETD pts (p = 0.001).

**Conclusions:** BDB and ETD are equally effective in obstructive jaundice in cancer of the pancreatic head. However normal bilirubin levels are reached more often after BDB, which has a lower incidence of recurrent obstruction than ETD. BDB should be preferred in palliative therapy for obstructive jaundice, if operative exploration is performed.

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**P19**

**Relevance of Prognostic Factors in Ductal Adenocarcinoma of the Pancreas: A Matched Pair Analysis**

*M. Colombo-Benkmann, C. Hecker, C. Schleicher, H. Wolters, T. Mundel, N. Senninger*

Department of General Surgery, University of Munster, Germany

**Introduction:** Patients with ductal adenocarcinoma of the pancreas (PC) may differ significantly in survival despite identical tumor stages. The objective of this study was to evaluate factors with an influence on prognosis besides tumor stages.

**Patients and Methods:** Twenty-one pairs matched for gender, age (±4 years) and tumor stage (UICC 2002) were selected out of 200 patients who underwent curatively intended hemipancreatectoduodenectomy for PC (1985–2000). One partner of each pair was alive tumor free for >24 months (m) (median survival 52 m [40–193]) (group A), while the other had deceased within 24 m after surgery due to PC (median survival 10.8 m [2–23]) (p < 0.001) (group B). Statistical analysis for 38 factors was carried out by logistic regression corrected for tumor stage.

**Results:** In both groups gender distribution (male:female) was 13:8, median age 60.2 years [group A: 44–71; group B: 44–69]. Tumor stages were distributed equally (group A/B): Ia (pT1pN0) n 1/1, Ib (pT2pN0) n 3/3, IIA (pT3N0) n 7/7, IIB (pT1–T3pN1) n 10/10. Median tumor diameter in both groups was 3 cm [group A: 1–9 cm; group B: 2–6 cm]. R-category (p = 0.039), abdominal pain (p = 0.032) and preoperatively elevated transaminases (p = 0.014) were the only factors of prognostic significance in univariate analysis. Comorbidities, preoperative laboratory parameters, tumor specific characteristics and operative complications did not predict prognosis. Multivariate analysis identified abdominal pain (p = 0.03; odds ratio 0.153, 95% confidence interval 0.03–0.83) and pathological transaminases (p = 0.024; odds ratio 0.971, 95% confidence interval 0.947–0.996) as only parameters of independent significance for tumor free survival.

**Conclusions:** Classical prognostic factors in PC cannot differentiate patients with significantly different survival. In contrast parameters indicating extrapancreatic tumor extension (R-category, abdominal pain) and hepatic dysfunction are associated with prognostic differences. This indicates that other factors such as tumor biology not being investigated in the present study may be more relevant for predicting prognosis than classical parameters evaluated in survival analyses.

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**P20**

**Early Pancreatic Cancer Diagnosis with Guided FNAB-US**

*R. Costantini, A. Sardellone, G. Mancino, P. Innocenti, A.M. Napoletano*

Patologia Chirurgica, Policlinico ‘SS. Annunziata’, Chieti, Italy

Guided FNAB-US (Fine Needle Biopsy – Ultrasonically) still remains a very important test for early diagnosis of pancreatic cancer.
We prefer guided FNAB-US (and not guided CT) because of the possibility to control the progression of the tip of the needle for biopsy in real-time and in the absence of X-rays.

Forty patients (40) were evaluated. All underwent a US investigation of the upper abdomen and particularly of liver, bile ducts and pancreas. A real-time ultrasonograph with a linear 3 MHz probe was used.

In 24 patients cancer of the pancreatic head was present and in 16 a pancreatic neck-tail cancer was found.

These cancers appeared at US investigation with the following features:

Echo-poor, finely dishomogeneous, with definite borders; there was an alteration of the pancreatic structure in all the cases.

In the first cases we used a Surecut needle by which we obtained a fragment of tissue for histologic examination. By Surecut the biopsy is obtained in aspiration by a single puncture while keeping the pancreatic cancer mass under US control.

At present we use Chiba needles to obtain cells for cytology.

We prefer this kind of needle because:

1. it is possible to make five–six punctures in different directions in the tumoral mass to avoid false negative; 2. the cytologic evaluation is faster than the histologic one.

**P21**

**The Traverso-Longmire Procedure for Pancreatic Head Cancer and Periampullary Cancer**

*R. Costantini, A. Sardellone, P. Innocenti, A.M. Napoletano*

Patologia Chirurgica, Policlinico ‘SS. Annunziata’, Chieti, Italy

The pylorus-preserving pancreaticoduodenectomy preserves the distal stomach and proximal centimeters of the duodenum. Therefore, this procedure prevents the complications that can occur with the loss of gastric reservoir and improves the patients’ nutritional status. Initially, indication to pylorus preservation was restricted to benign conditions, but subsequently it was used also for periampullary tumors. Then this technique was applied also to radical surgery for limited pancreatic adenocarcinomas.

Since 1981 we have performed pylorus-preservation in all operable cancers of pancreatic head, and in periampullary tumors. In a series of 42 consecutive operable cases, pylorus-preservation was done in 31. 23 were carcinomas of the head of the pancreas, 6 of the papilla, 2 of the distal common duct. Postoperative delayed gastric emptying, for more than 8 days, was noted in 50% of the cases. It is believed that ligation of gastroduodenal, right gastroepiploic artery and sometimes right gastric arteries may cause circulation defects in cases without large anastomotic connections between such arteries and left gastric and left gastroepiploic arteries.

After a few days adequate bloodflow is re-established through the rich submucosal network. For this reason it is safer to leave a duodenal stump no longer than 2 cm.

We also experienced a postoperative blow-out of duodeno-jejunostomy made on a 4 cm long duodenal stump. Radiologic, endoscopic and cholescintigraphic studies have demonstrated a good pyloric function, which is not disturbed by the close duodeno-jejunostomy.

Patient diet has been comfortable and adequate. 70% of patients have reached the original body weight.

In our opinion the advantages of this procedure are:

1. shortened operating time, which permits application in elderly patients; 2. short jejunal loop for pancreatic and bile duct anastomosis that reduces bowel tract excluded from alimentation transit with better neutralization of acid chymus and lower incidence of peptic ulcerations.

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**P22**

**Successful Laparoscopic Intermediate Pancreatectomy**

*S. Crippa, E. Orsenigo, P. Baccari, S. Di Palo, M. Carlucci, A. Tamburini, R. Sampietro, C. Staudacher*

Dipartimento di Scienze Chirurgiche, Divisione di Chirurgia Gastroenterologica, Università Vita e Salute – IRCCS Ospedale San Raffaele, Milan, Italy

**Background:** Laparoscopic surgery is generally considered contraindicated in order to perform intermediate pancreatectomy.

**Case Report:** A 75 years old woman was deemed for laparoscopic intermediate pancreatectomy for a solitary neuroendocrine tumor of the pancreatic body.

**Methods:** Under general anesthesia, the patient was put in supine position with the legs abducted. Carbon dioxide pneumoperitoneum was established using Hasson's method through a 10 mm over the umbilicus vertical incision. A 30° telescope was inserted to examine the peritoneal cavity. No macroscopic peritoneal seeding was found. First the body and tail were exposed anteriorly through a window in the gastrocolic ligament. The inferior border of the pancreas was dissected from the retroperitoneal fat using the harmonic scalpel. The tumor was identified in the middle of the pancreatic body. Traction was applied anteriorly and the superior mesenteric vein was gently dissected from the pancreas. The pancreas was transected with harmonic scalpel. An appropriate 5F pediatric tube was inserted into the lumen as a temporary stent. A duct-to-mucosa anastomosis was laparoscopically performed to a jejunal limb. The distal stump was closed by interrupted suture. Histological findings showed a well differentiated neuroendocrine tumor and resection margin free from disease. Operating time was 330 minutes and blood loss 300 mL. Hospital stay was 17 days. In the postoperative period the patient developed a low-output pancreatic fistula.

**Conclusions:** With increasing experience with the laparoscopic technique, solitary lesions of the pancreatic body can be treated safely and successfully with laparoscopic intermediate pancreatectomy.
**P23**

Safety and Efficacy of Laparoscopic Pancreaticoduodenectomy

S. Crippa, E. Orsenigo, P. Baccari, S. Di Palo, M. Carlucci, A. Tamburini, R. Sampietro, C. Staudacher

Dipartimento di Scienze Chirurgiche, Divisione di Chirurgia Gastroenterologica, Università Vita e Salute – IRCCS Ospedale San Raffaele, Milan, Italy

**Background:** In the past few years, minimally invasive therapy for pancreatic diseases has made significant strides but the role of laparoscopic pancreaticoduodenectomy is still controversial.

**Methods:** 4 patients with a mean age of 44 ± 11 years were deemed for a laparoscopic pancreaticoduodenectomy. Pathological diagnosis were ductal adenocarcinoma in one, neuroendocrine tumor in two and metastatic malignant melanoma in one.

**Results:** The procedure was laparoscopically completed in all with a mean operating time, blood loss and hospital stay of 416 ± 77 minutes, 325 ± 50 mL, and 12 ± 2 days respectively. There were no complications attributable to this surgery and there were no deaths. The average number of dissected lymph nodes was 26 ± 17 (range 16–47). All the patients remain well at a median follow-up of 4.5 months (range 1–10).

**Conclusions:** It can be inferred from this small but successful experience that laparoscopic pancreaticoduodenectomy can be considered for the treatment of tumors of the pancreas or periampullary region.

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**P24**

Laparoscopic Surgical Treatment of Pancreatic Neuroendocrine Tumours

S. Crippa, E. Orsenigo, P. Baccari, S. Di Palo, M. Carlucci, A. Tamburini, R. Sampietro, C. Staudacher

Dipartimento di Scienze Chirurgiche, Divisione di Chirurgia Gastroenterologica, Università Vita e Salute – IRCCS Ospedale San Raffaele, Milan, Italy

**Background:** Laparoscopic resection is not an established treatment for tumours of the pancreas. Aim of this work is to evaluate the results of laparoscopic pancreatic resection for non-secreting pancreatic neuroendocrine tumors. Per-operative data, surgical outcomes and techniques are presented.

**Methods:** Four women and one man underwent laparoscopic pancreatectomy and were collected retrospectively from June 2002 to January 2004.

**Results:** Pancreaticoduodenectomy (n = 2), intermediate pancreatectomy (n = 1) and distal pancreatic resection with splenectomy (n = 2) were successfully performed. Operative mortality was nil. The postoperative morbidity included two low-output pancreatic leaks. The mean operating time, blood loss and hospital stay was 305 minutes, 284 mL and 15 days respectively. There were no cases that required conversion to conventional open procedure. Histological findings showed non-secreting well differentiated neuroendocrine tumor in all cases. All patients remain well at a median follow-up of 5 months (range 1–19).

**Conclusion:** Patients appear to benefit from laparoscopic pancreatectomy for neuroendocrine tumor. Minimally invasive approach ensures an adequate treatment despite it requires the expertise of highly skilled laparoscopic surgeons.

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**P25**

Low versus High Doses of Preoperative Interleukin-2 Immunotherapy in Pancreatic Cancer: Preliminary Results

L. Degrate, C. Nobili, E. Perego, C. Mussi, F. Romano, F. Uggeri, Fr. Uggeri

Department of General Surgery, ‘San Gerardo’ Hospital, University of Milan-Bicocca, Monza, Milan, Italy

**Background and Objectives:** A cell-mediated immunodeficiency status is demonstrated to occur in malignancies. Cancer-related immunodeficiency is clinically relevant, in fact, low count of total and T helper lymphocytes predicts a poor prognosis, like as disease extent and performance status. Moreover, the surgical trauma can worsen the impaired immune surveillance and favor the growth of the few residual cancer cells spread before or during surgery. This study investigates in pancreatic cancer patients the effectiveness of pre-operative interleukin-2 administration to improve lymphocyte counts postoperative recovery, comparing two different doses of the drug.

**Methods:** 28 patients with pancreatic cancer who underwent radical surgery were randomized in 3 groups. Group 1: 9 patients treated with preoperative human recombinant IL-2 subcutaneously at 9 millions UI/day for 3 days starting 4 days before surgery; group 2: 9 patients treated with preoperative human recombinant IL-2 subcutaneously at 12 millions UI/day for 3 days starting 4 days before surgery; group 3: 10 patients treated with surgery alone. Assessment of total and T helper lymphocyte counts were studied at hospital admission and in 7th, 14th and 50th postoperative day.

**Results:** Toxicity of IL-2 treatment was mild in both groups. There are no statistical differences in total and CD4+ lymphocyte counts between the group treated with IL-2 at 9 millions UI/day and the control group, whereas the group treated with IL-2 at 12 millions UI/day had higher lymphocyte levels than the other groups, with a mean lymphocyte level within the normal values in the postoperative period.

**Conclusions:** This preliminary results suggest that preoperative subcutaneously IL-2 immunotherapy at 12 millions UI for 3 consecutive days before surgery is able to recover a count of total and CD4+ lymphocytes within normal values after surgical stress in pancreatic cancer patients. Toxicity of the treatment is mild and well tolerated.
P26

An Italian Study on Genetic Susceptibility to Pancreatic Cancer

M. Del Chiaro¹, L. Bertacca², A. Zerbi², B. Longoni³, A. Giovannetti¹, G. Cipollini², M.A. Caligo², U. Boggi¹, G. Bevilacqua², G. Casari³, M. Polese³, V. Civellic, V. Di Carlo⁴, G. Cavallini⁵, S. Presciutti⁵, F. Mosca¹

¹Div. Chirurgia Generale e Traintanti, ²Div. Anatomia Patologica, ³Dip. to di Patologia Sperimentale Biotecnologie Mediche, Infettivologia ed Epidemiologia, Università di Pisa, ⁴IRCCS, Ospedale ‘S. Raffaele’, Milano and ⁵University of Verona, Italy

It is estimated that 3–5% of all pancreatic cancer cases are caused by germline mutations in known predisposing genes, and it is increasingly recognized that some families carry an inherited susceptibility for pancreatic cancer unrelated to any currently identified syndrome. The Associazione Italiana Studio Pancreas (AISP) has recently launched a study on the genetic susceptibility to pancreatic cancer to investigate these issues in the Italian populations. Family history of cancer and blood samples are collected from all incident cases with pancreatic ductal adenocarcinoma ascertained by the participating groups. Pedigrees are recorded in a centralized database (Progeny 5). This currently includes families of 183 probands (75 females and 108 males); 8 probands had previously been diagnosed with other cancers: 5 breast, 2 prostate, and 1 duodenum. Pancreatic cancer in first-degree relatives of the probands was present in 9.3% of the families (two including 2 affected relatives); one family included 3 affected relatives when considering second-degree relatives. A total 2,033 informative relatives were recorded in the database, for 262 of whom (13%) malignant cancer was reported. Pancreatic and prostate cancers were present in high excess among males (more than 4-fold the cumulative risks published by Italian Cancer Registries for the 0–64 years age group), followed by cancers of the lower gastrointestinal tract (LGI, 2-fold increase); among females, pancreatic cancer was also in large excess (5-fold), followed by LGI and uterine intestinal tract (LGI, 2-fold increase); among females, pancreatic cancer was also in large excess (5-fold), followed by LGI and uterine cancer (2-fold increase). To investigate the role of BRCA2 in susceptibility to pancreatic cancer, the probands with at least one first-degree relative with pancreatic cancer, or with breast cancer if <60 years (even of second-degree if in the paternal line), were selected. Among nine out of a total of 28 eligible cases analyzed with full sequencing, a missense mutation not previously described was detected.

P27

Pancreatic Stump Management after Pancreateoduodenectomy

M. Del Chiaro, U. Boggi, C. Croce, F. Gremmo, A. Sgambarli, E. Vasile, F. Vistoli, S. Signori, G. Di Candio, A. Campatelli, F. Mosca

Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa, Italy

Background: Management of pancreatic stump (PS) remains the ‘Achille’s heel’ of pancreateoduodenectomy (PD).

P28

Treatment of the Pancreatic Stump: An Alternative Choice

G.B. Doglietto, S. Alfieri, F. Prete, F. Rotondi, D. Di Miceli, F. Rosa

Div. di Chirurgia Digestiva, Dip. to Scienze Chirurgiche, Policlinico Gemelli Università ‘Cattolica Sacro’, Roma, Italy

Introduction: The present work describes our technique of pancreatic duct occlusion with synthetic glue after pancreateoduodenectomy.

Patients and Methods: Between 1998–2002, 35 consecutive non-selected patients underwent pancreateoduodenectomy, with occlusion of pancreatic duct regardless of pancreatic disease, Wirsung’s diameter or pancreatic remnant consistency. The limit of pancreatic resection was forwarded from the left of the portal vein (n. 22 patients) to the left margin of the aorta (n. 13 patients) in the most recent operations. A 14–16 gauge radiopaque catheter, 3 cm long, is then introduced in the Wirsung duct to inject the synthetic glue [N-Butyl(2)cianoacrilate-monomer + Metacrillossolfolan-monomer]. Solidification begins 1–2 seconds after the application and is complete about 60 seconds later. A 3/0 suture is then tied around the Wirsung duct. At the end, two abdominal drainages are routinely placed close to the pancreatic stump to permit an adequate surveillance and to provide efficient drainage of an eventual leak.

Results: The median recovery time from a pancreatic fistula was 33 days (range 18–63). Post-operative hemorrhage occurred in 3 cases (8.5%). No post-operative bleeding occurred in the 14 patients with pancreatic fistula. Neither hospital mortality, nor clinical or laboratory

Abstracts Pancreatology 2004;4:91–121
evidence of pancreatitis occurred. Five patients taking antidiabetic drugs before surgery continued with the same regimen postoperatively. Eight (23%) patients with laboratory signs of pancreatic endocrine insufficiency required post-operative insulin, while the remaining 22 showed a normal endocrine function one year after the operation. CT scan of the pancreas at 6 months and one year after surgery showed in 7 patients (5 with pancreatic fistula and 2 with uneventful recovery) a clinically asymptomatic pseudocyst of the pancreatic edge, without biochemical alterations.

Conclusion: The reported technique is in our experience a suitable alternative to anastomosis in the treatment of the pancreatic stump in patients with friable pancreas and with narrow Wirsung duct.

P29
Ductal Adenocarcinoma of the Pancreas in Young Patients
I. Esposito, R. Penzel, S. Aulmann, M. Wente, H. Friess, H.F. Otto, F. Bergmann
Institute of Pathology, University of Heidelberg, Germany

Pancreatic ductal adenocarcinoma (PDAC) rarely affects patients before the age of 40 years. The aim of the present study was to determine if the clinical, pathologic and genetic features of PDAC occurring in young patients (≤40 years) differ from those in elderly patients.

Six patients, all females, with a mean age of 38 years (range 35–40) were included in the study. No one had a family history of either pancreatic cancer or hereditary pancreatitis. Three patients were smokers. The pathologic features of the tumors did not differ from those occurring in elderly patients.

The molecular analysis revealed that PDAC of young patients share a similar, although not identical profile with PDAC of elderly patients. Interestingly, the rate of K-ras codon 12 mutations was lower (2 of 6 patients, 33%) compared to that commonly observed in elderly patients. Immunohistochemical analysis revealed p53 nuclear overexpression in 4/6 cases (66%) and transforming growth factor beta-1 (TGFbeta-1) overexpression in all cases. The loss of Smad 4 expression in 5/6 cases (83%) confirmed a dysregulation in the TGFbeta-1 signaling pathway. The epidermal growth factor receptor (EGFR) was expressed on the tumor cell membrane in 4/6 cases (66%). The membranous pattern of beta-catenin expression in all 6 cases, as well as the expression of mismatch repair gene products (MLH1, MSH2 and MSH6), the latter suggesting a microsatellite-stable phenotype, are also typical features of PDAC of elderly patients. None of the tumors was positive for the estrogen and progesterone receptors.

In conclusion, the results of this study show that the rare PDAC of young patients shares genetic similarities with that of elderly patients. The lower rate of K-ras mutations, when confirmed in larger series, would suggest the existence of another initiating event of pancreatic carcinogenesis in at least a subgroup of patients.

P30
No Evidence for Germline Mutation of the LKB1/STK11 Gene in Familial Pancreatic Carcinoma
R. Grützmann, D.K. Bartsch, M. Sina-Frey, R. Koch, H.D. Saeger, C. Pilarsky
Department of Surgery, University Hospital, Dresden, Germany

Introduction: As many as 10% of pancreatic cancer cases may have an inherited component. However, familial pancreatic cancer has not been linked to defects in any specific gene. Inactivating germline mutations of the tumor-suppressor gene LKB1/STK11 at 19p13.3 have been shown to cause Peutz-Jeghers syndrome (PJS), an autosomal dominantly inherited disease characterized by a predisposition to mucocutaneous pigmentations, as well as various benign and malignant neoplasms. It has been assumed, that LKB1/STK11 might play a role in familial pancreatic cancer, because PJS patients have a higher risk in developing pancreatic cancer. To elucidate the role of LKB1/STK11 in the familial pancreatic cancer, a total of 27 index patients were analyzed using genomic DNA sequencing of the complete coding region of LKB1/STK11.

Methods: We identified 27 German families in which at least two first-degree relatives had a histologically confirmed diagnosis of pancreatic ductal adenocarcinoma. None of the families in our study met the criteria for the Peutz-Jeghers Syndrome. We sequenced the complete coding region of LKB1/STK11 using the genomic DNA isolated from peripheral blood lymphocytes obtained from index patients to identify germline mutations in LKB1/STK11.

Results: No germline mutation was found within the complete coding region of LKB1/STK11. However our approach revealed four intronic polymorphisms, which are two-allelic 1-bp substitution/deletion polymorphisms (IVS2+24, IVS2–49, IVS3–51, IVS7+7).

Conclusions: Our data suggests that germline alterations of LKB1/STK11 seem to play no role in a subgroup of families with familial pancreatic cancer.

P31
Diabetes Reduces Pancreatic Tumour Detection by [18F]FDG-PET: Is it so?
P. Izzo, U. Boggi, T. Kalliokoski, M. Del Chiaro, A. Sambelluni, P. Erba, S. Pardini, E. Ferrannini, G. Sambuceti, C. Croce, F. Gremma, P. Salvadori, P. Nuutila, F. Mosca
Regional Referral Center for Pancreatic Diseases, Treatment, University of Pisa, Italy

The relevance of PET and [18F]-2-fluoro-2-deoxyglucose ([18F]FDG) in the diagnosis of pancreatic adenocarcinoma is widely recognized. However, diabetes, which is often associated with this malignancy, is viewed as potential confounder. Hyperglycaemia during PET scan sessions may lower [18F]FDG uptake, via substrate competition. If plasma glucose levels are acutely normalized, the toxic effect of prior hyperglycaemia may persist. Conversely, pancreatic inflammation,
accompanying some forms of diabetes, may enhance tracer uptake in a tumor-free organ. To establish the diagnostic impact of these factors, we performed [18F]FDG PET studies in 16 patients with histologically-confirmed adenocarcinoma, spanning over a wide glycaemic range, 7 healthy controls (C), and 9 patients with recently diagnosed (antibody positive) type 1 diabetes (Ty1D), who were in sub-optimal metabolic control, and were rendered nearly normoglycaemic by low-dose insulin infusion — for the duration of the PET session. Subjects were studied after an overnight fast, and underwent PET imaging of the pancreas ~1 h after [18F]FDG injection. Magnetic resonance imaging was used to locate the pancreas in C and Ty1D, in whom the organ is not PET-visible. Standardized tracer uptake values (SUV) were calculated in the areas of interest. In C, and in Ty1D, pancreatic SUV were 1.2 ± 0.32 and 1.3 ± 0.24, respectively (range 0.87–1.83, NS). Thus, tracer uptake in Ty1D was within the normal range, regardless pancreatic islet inflammatory infiltration, and mild hyperinsulinaemia. In adenocarcinoma, the SUV was 5.6 ± 1.7 (range 3.0–8.5, p < 0.01 vs other groups), and it was inversely correlated with systemic glycaemia (r = −0.55, p = 0.03). Still, the lowest SUV value in cancer was nearly two-fold higher as compared with the highest pancreatic value in the other groups.

In conclusion, though our data support the concept of substrate competition between endogenous glucose and [18F]FDG, pancreatic adenocarcinomas showed such remarkable [18F]FDG-avidity, that the counteracting effect of mild-to-moderate hyperglycaemia caused no diagnostic interference.

P32
Pancreatic Cancer: A Consequence of Undiagnosed and Untreated Celiac Disease?
R. Khurana, V. Khurana
Louisiana State University Health Science Center, Shreveport, LA, USA

Introduction: Celiac sprue is a malabsorption disease that carries an increased but underestimated risk of gastrointestinal malignancy. Diagnosis of celiac disease in the elderly is difficult as the manifestations are often subtle and nonspecific.

Case Presentation: A 77-year-old white man presented with a 2 year history of progressive intermittent abdominal pain, bloating, vomiting, severe reflux and 20 lb wt loss without diarrhea. He had a history of Non Hodgkin’s Lymphoma 10 years prior and constipation since childhood. His physical exam was significant for cachexia. An upper endoscopy revealed dilated stomach with retained food content and significant edema with narrowing of the duodenum, but no obstruction. Duodenal Biopsies revealed focal villous atrophy. Serum antiendomysial antibodies were strongly positive. CT of the abdomen revealed only a dilated stomach. After 3-week trial of gastric decompression, repeat endoscopies and barium studies revealed persistent narrowing of the duodenum. Surgery was consulted and at laparotomy a hard and indurated segment encasing second portion of duodenum was noted. Whipple’s resection was performed. Pathology revealed well-differentiated infiltrating adenocarcinoma of the pancreas.

Discussion: Ten to 15% of the patients with celiac sprue will develop a gastrointestinal malignancy. Immunologic perturbation, pre-malignant changes in the damaged epithelium, increased permeability to oncogenic substances and malabsorption of protective substances have been implicated in the pathophysiology.

Conclusion: Early treatment on strict gluten free diet decreases the risk of malignancies, hence it is necessary to diagnose and treat celiac disease at an early age. Pancreatic cancer as a consequence of celiac disease is under appreciated; the link should be further investigated, given the recent studies suggesting markedly increased prevalence of celiac disease.

P33
Diffuse Carcinoma with ‘Jump’ Lesion and Neuroendocrine Tumor of the Pancreas: Intraoperative Trap
G. La Greca, F. Barbagallo, A. Fasone, S. Latteri, T. Guastella, A. Galia, M. Scuderi, D. Russello
Cannizzaro Hospital, Università di Catania, Italy

We report a case of a diabetic patient submitted to surgery because of pancreatic cancer. A preoperative CT showed a 35 mm tumor limited to the head of the pancreas. A Whipple procedure was planned. During surgery a 4 mm suspect nodule of the liver was diagnosed by intraoperative ultrasonography. The intraoperative frozen sections excluded a metastasis. After duodeno-pancreatectomy the resected pancreas was controlled by the pathologist showing that free margins were only 3 mm but otherwise the pancreas remnant appeared macroscopically normal. Other 20 mm pancreas were anyway resected to increase the negative margin. The distal margin was controlled again by the pathologist but resulted surprisingly invaded by adenocarcinoma. A total pancreatectomy was then performed. The definitive pathology showed a micrcystic mucinous carcinoma involving the whole pancreas (pT3N1M0), characterized by some ‘jump’ lesions alternating normal pancreas and carcinoma, showing also diffuse neuroendocrine proliferation and a 4 mm neuroendocrine tumor. This rare association of neuroendocrine tumors with carcinoma of the pancreas is exclusively described for the serous type of adenoma/adenocarcinoma. To our knowledge this is the first report concerning the association of a neuroendocrine tumor with a micrcystic adenocarcinoma of the mucinous type. Retrospectively analyzing this case about the suspect liver nodule together with the rare association of two different cancers with different prognosis, but both possible cause of liver metastasis with different prognostic significance we would like to stress out the importance of intraoperative pathological examination specimens to avoid strategical mistakes. There is also the risk to leave cancer in the pancreatic remnant estimating R0 a resection that is unfortunately R1. The possibility of the ‘jump’ of the cancer, and of the association of different cancers underlines also the possible multifocal and multiclional origin and/or development of pancreatic cancer that we believe should be better investigated.
P34

Our Experience in the Treatment of Carcinoid Pancreatic Tumors

S. Lanzara, P. Carcovofo, M. Giaconelli, L. Feggi, K. Maravegias, G.C. Pansini, A. Liboni
Sez. Chirurgia Generale, Arcispedale ‘S. Anna’, Ferrara, Italy

The aim of this study is to review our experience with pancreatic carcinoid tumors. Between January 1990 and September 2003, 7 patients with pancreatic carcinoid tumor were operated on our institutions. Of these patients, we reviewed preoperative symptoms, diagnostic technique, treatment, postoperative complications and survival.

Nobody had a typical ‘carcinoid syndrome’; everybody had an aspecific symptomatology. Only 2 patients (29%) had a preoperative diagnosis of pancreatic carcinoid tumor, made with fine needle agglomeriposy in 1 case and radionuclide scintigraphy in 1 case. The other 5 patients (71%) had an aspecific diagnosis of pancreatic tumor, made with abdominal CT. Nobody had metastatic disease.

We performed a duodenoccephalopancreatectomy in 2 cases (29%); a distal pancreatectomy in 2 cases (29%); a distal pancreatectomy plus splenectomy in 1 case (14%); enucleation of the tumor in 1 case (14%); a total pancreatectomy in 1 case (14%).

The postoperative complications were: stenosys of the biliobiliary anastomosis in 1 case (14%); intraabdominal abscess in 2 cases (29%); biliary lake in 1 case (14%). One patient died 9 days after the operation for acute pancreatitis of the distal residual pancreas; 6 patients (86%) are still alive without recurrent disease, with a mean postoperative survival of 74 months (4–168 months). According with the international literature, these data show that the prognosis for patients with carcinoid pancreatic tumor fully resected is excellent.

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P35

Pancreatoduodenectomy with MesentericPortal Vein Resection: Postoperative Morbidity and Long-Term Survival

F. Makowiec, U. Adam, H. Riediger, U.T. Hopt
Department of Surgery, University of Freiburg, Germany

Background: The value of superior mesenteric-portal vein resection (SM-PVR) for vein invasion or tumor adherence during pancreatoduodenectomy (PD) is still under debate. We investigated morbidity, mortality and long-term survival in patients who underwent PD with or without SM-PVR.

Methods: Between 7/1994 and 8/2003 169 PD (77% pylorus preserving, 21% Whipple and 2% pancreatectomy) were performed for malignant disease. Thirty-nine patients (23%) had SM-PVR. Twenty-five of those 39 patients (64%) with SM-PVR had histologically proven malignant vein invasion. Long-term survival was available and compared in 126 patients with pancreatic or periampullary cancer using univariate (log-rank) and multivariate (Cox regression) methods.

Results: A margin-negative resection was obtained in 72% (63% in SM-PVR vs 75% without SM-PVR; p = 0.15). In patients with SM-PVR vs patients without SM-PVR median duration of surgery was 500 vs 455 mins (p < 0.01) and the units of blood transfused in median four vs three (p = 0.1). Postoperative complications/mortality were found in 36%/5.1% (SM-PVR) vs 44%/3.8% in patients without SM-PVR (p = 0.38/p = 0.6). Three-year survival was 20% (pancreatic cancer), 27% (ampullary cancer) and 15% (distal bile duct cancer).

In subgroup analysis undifferentiated tumors (p < 0.04 univ./ p < 0.02 multiv.) and positive resection margins (p < 0.04 univ./ p < 0.05 multiv.) were significantly associated with poorer survival. The lymph node status, portal vein resection and histologically proven vein invasion did not show any independent influence on survival rate.

Conclusion: After PD, morbidity and long-term survival in patients with concomitant resection of the portal vein were similar to those of patients not requiring vein resection. Combined resection of the pancreatic head with the portal vein, therefore, should always be considered in the absence of other contraindications for resection.

P36

Pancreatic Resection after Primary Chemo-Radiotherapy for Locally Advanced Adenocarcinoma: Preliminary Results

P. Massucco, A. Melliano, L. Viganò, D. Ribero, L. Capussotti
Surgical Oncology, IRCC, Torino, Italy

Background: Primary chemo-radiotherapy for locally advanced pancreatic cancer (LAPC) may occasionally be associated with tumor downsizing enough to permit a surgical exploration but the experience with pancreatic resections after combined treatment is still limited.

We analyzed pancreatic resections performed in the setting of a phase II study evaluating combined treatment in LAPC (vessel infiltration).

Patients and Methods: From 8/1998 to 7/2003, 23 LAPC patients received GEM 100 mg/m² twice-weekly in the first 15 cases and 50 mg/m² in the remaining, concurrently with RT (45 Gy; 1.8 Gy/d). All patients had biopsy proven disease, measurable by CT-scan and were restaged by CT-scan 45 days after the end of the treatment. Patients showing PR or SD with normalization of CA19.9 were surgically explored.

Results: Six patients (26%; 4 PR and 2 SD with normalization of CA19.9) were explored. A pancreatoduodenectomy was performed in 3 cases, a total pancreatectomy in the other 3. A vein resection was necessary in 2 cases. Mean operative time was 1 hour longer than
Abstracts

Pancreatic resections consecutively performed in the same period for 40 resectable ductal carcinomas (6.6 h ± 0.5 vs 5.6 h ± 0.9; p < 0.02). One patient died 2 months after surgery for the consequences of a biliary leak. Morbidity: 1 pancreatic fistula and 1 delayed gastric emptying. Pathologic findings: microscopic cancer foci in 1 case; pT3/N0 in 4; pT4/N1 in 1. Median and 24-months survival were 23 and 32.6% for resected cases vs 13 and 9.3% for non-resected. In the group of 40 patients with localized cancer these figures were 18 and 35.1%.

Conclusions: Pancreatic resection after combined treatment is feasible but more technically demanding. Both CT scan and serum CA19-9 were useful in the selection of patients to be surgically explored. Patient undergone a pancreatic resection experienced a survival longer than non-resected and comparable to patients resected for localized cancer.

P37
Extended Lymphadenectomy and Vein Resection for Pancreatic Head Cancer: Operative Outcome and Survival
P. Massucco, A. Mellano, L. Viganò, D. Ribero, L. Capussotti
Surgical Oncology, IRCC, Torino, Italy

Methods: Since 1988 we prospectively collected clinical and pathologic data of all the patients consecutively submitted to macroscopic radical resection for periampullary adenocarcinoma. Since 1994, we performed an extended lymphadenectomy in patients with intraoperative diagnosis of ductal adenocarcinoma. Data about postoperative outcome, final pathology and survival were analyzed comparing patients with or without an extended lymphadenectomy or a vein resection.

Results: From January 1988 to December 2000, 162 patients were resected for periampullary adenocarcinoma. An extended lymphadenectomy was performed in 45 cases and a venous resection in 24 (15%). In-hospital and 60-days operative mortality was 5.6%. Morbidity was 38.3%. Mortality, morbidity and postoperative stay were not significantly modified by extended lymphadenectomy or venous resection. Vein resections were associated to significantly longer operative time and higher blood transfusion rate. In 110 patients with ductal adenocarcinoma, the extended lymphadenectomy yielded a mean of 32 nodes compared to 11 for the standard resection (p < 0.001). Nodal metastases were identified in 67 patients. Extended resection identified a significantly higher percentage of regional nodal metastases and clinically unapparent metastases to distant nodes in 9 cases (20%). Patients requiring a vein resection had a significantly higher rate of retroperitoneal margin involvement. Median survival was 15 months. Five-year actual survival was 6.4%. A trend toward a better survival after the extended resection was observed in the first 2 years from surgery compared with the standard resection both in node positive and in node negative patients. Perineural invasion and nodal status were the most powerful predictors of overall survival.

Conclusions: Extended resection was associated to an early advantage in survival that was no longer evident after about 2 years from surgery. Patients requiring a vein resection were less likely to receive a curative operation. Long-term survival was related to cancer biology rather than to the extension of resection.

P38
Vascular Involvement in Pancreatic Neoplasms: Multidetector CT Evaluation
S. Mazzeo1, C. Cappelli1, A. Belcari1, P. Torri1, A. Giannini1, M. Del Chiaro1, F. Gremmo1, D. Campani1, U. Boggi1, F. Mosca2, C. Bartolozzi1
1Diagnostic and Interventional Radiology, 2Division of General and Transplantation Surgery, 3Pathology, University of Pisa, Italy

Purpose: To evaluate the role of multidetector CT in the detection of vascular involvement of pancreatic cancer.

Methods and Materials: CT studies were performed in 78 patients (January ’02-August ’03) with suspect pancreatic lesion. The multidetector CT scanner was used before and after and injection of 120 ml non ionic contrast medium. The CT acquisition was done in pancreatic (35) and venous phases and all acquired images were post-processed with MPR and MIP software tools.

In the neoplastic vascular involvement the following critical vessels were considered: portal vein, superior mesenteric vein, celiac trunk, and superior mesenteric artery.

The relation between neoplastic lesion and vessels were classified using the following grading: grade 0: none contact between lesion and vessel; grade I: focal contiguity between vessel and cancer, without modification of the vessel caliber; grade II: lesion surrounding the vessel, without reduction of the caliber of the vessel; grade III: cancer surrounding the vascular structure with reduction or obstruction of the lumen of the vessel.

Results: Surgery was performed in 69/78 patients and final histologic diagnoses was: 52 ductal adenocarcinoma, 3 neuroendocrine carcinoma, 6 mucinous carcinoma, 2 others neoplastic lesions, 6 benign lesions.

The vascular resection was performed in 16 patients, and a total of 25 vessels were resected. In these cases CT grading showed: grade 0 in 4 cases; grade I in 3 cases; grade II in 8 cases; grade III in 10 cases. Histo-pathologic results were: none vascular infiltration in 4/4 cases with grade 0, vascular involvement in 0/3 cases with grade I, in 5/8 cases with grade II and 9/10 cases with grade III.

Conclusion: In the patients affected by pancreatic cancer the multidetector CT represents an accurate technique. When the neoplastic lesion surrounds the vascular structure, a vascular infiltration must be suspected.
Multidetector CT in the Assessment of Pancreatic Solid Masses

S. Mazzeo, C. Cappelli, A. Giannini, A. Belcaro, P. Torri, R. Bertini, M. Del Chiara, D. Campani, C. Croce, U. Boggi, F. Mosca, C. Bartolozzi
1Diagnostic and Interventional Radiology, 2Division of General and Transplantation Surgery, 3Pathology, University of Pisa, Italy

Purpose: To evaluate the role of multidetector CT in the assessment of pancreatic solid masses.

Methods and Materials: The study includes 76 patients submitted to surgical resection or biopsy for pancreatic solid mass. In these patients we retrospectively analyzed the multidetector CT images to evaluate the enhancement pattern of the pancreatic masses and to correlate the result with the histopathological finding. CT studies were done before and after 120 ml of highly concentrated non ionic contrast medium in pancreatic (35%) and venous phases (70%), using in all cases the same technical CT parameters. All acquired images were post-processed with MPR e MIP software tools. Four CT patterns of post-contrast enhancement were considered: hypodense, hyperdense, isodense, and mixed aspect.

Results: The histopathological results demonstrated: 52 ductal adenocarcinoma, 5 neuroendocrine lesion, 6 mucinous carcinoma, 2 pseudopapillary neoplasm, 4 metastasis (1 breast, 3 kidney), 4 undifferentiated carcinoma, 3 cholelcoad cancer.

The evaluation of CT enhancement pattern showed hypodense aspect in 57/76 cases (75%), hyperdense in 9/76 (12%), isodense 2/76 (3%), mixed 8/76 (10%). Ductal adenocarcinomas and undifferentiated carcinomas were hyperdense in 90% and 100% of cases respectively; mucinous cancers resulted hypodense in 67% and mixed in 33%; hyperdense aspect was observed in 60% of neuroendocrine neoplasms and 71% of tranpancreatic lesions (metastases and cholelcoad cancers).

Conclusion: In our experience CT multidetector study represents an accurate technique to characterize the pancreatic masses, and the CT enhancement pattern can be related to the histopathological type. When an hyperdense aspect is observed, a neuroendocrine or tranpancreatic origin of the lesion must be considered.

Rare but Significant Mutations of Tumor Suppressor Genes (TP53, p16INK4 and DPC4) in a Minority of Chronic Pancreatitis Cases

W. Meike, A. Bockholt, M. Ziemer, O. Stoss, K. Homayounfar, A. Müller, B.M. Ghdim, J. Faß, J. Rüschhoff, E. Heinmöller
1Institut für Pathologie, Klinikum Kassel, 2Klinik für Allgemeinchirurgie Universität Göttingen, 3Klinik für Allgemeinchirurgie, Klinikum Kassel, Kassel, Germany

Aims: Patients suffering from chronic pancreatitis (CP) are at increased risk for developing pancreatic cancer (PC). The molecular mechanisms underlying this process are poorly understood.

Methods: Formalin-fixed paraffin-embedded tissue from patients suffering from CP (n = 24) were used for laser microdissection of pancreatic intraductal lesions (PanIN). Whole genome amplification (I-PEP-PCR) of microdissected PanIN-lesions (50–500 cells) was performed prior to specific microsatellite PCR for loss of heterozygosity (LOH) analysis. Selected PanIN’s were screened for mutations in TP53 and p16INK4 by ABI-sequencing. In addition, protein expression of p53, p16INK4 and DPC4 was examined by immunohistochemistry (IHC).

Results: Of informative PanIN-lesions, LOH of TP53 was found in 0.91% (4/438), DPC4-LOH was seen in 3.61% (14/388) respectively. LOH of p16INK4 was detected in 3.68% (19/516). One of 24 cases exhibiting PanIN-3-lesion, protein overexpression of p53 and loss of p16 and DPC4-protein was found. Sequence analysis showed a C > T nucleotide exchange in exon 8 (bp-14501) of the TP53 gene with an amino acid change from Prolin to Leucin. Furthermore a supposed splice site mutation at bp-12 (G > A) in intron 1 of the p16INK4 gene was detected.

Conclusion: In CP, mutations of TP53, p16INK4 and DPC4 seem to be a rare but significant event in the progression to PC and thus may represent a favorable marker for risk assessment of patients suffering from longstanding CP. To our knowledge, this is the first report where the proposed molecular genetic progression model for PC was demonstrated in a case of CP without evidence of infiltrating cancer.

Peritoneal Cytology in Patients with Potentially Resectable Adenocarcinoma of the Pancreas

I. Meszoely, J.S. Lee, J.C. Watson, M. Meyers, H. Wang, J.P. Hoffman
Fox Chase Cancer Center, Philadelphia, PA, USA

The prognostic significance of malignant cells in the peritoneal washings of patients with pancreatic adenocarcinoma remains poorly defined. Prior reports suggest that positive peritoneal cytology (PPC) is associated with advanced disease and reduced survival.

To determine the prognostic value of PPC in patients with pancreatic cancer, we retrospectively reviewed our data base between July 1987 and September 2002 and identified 168 patients who had undergone exploration for potentially resectable pancreatic cancer with peritoneal washings performed at the time of exploration. 135 patients underwent resection, 33 were considered unresectable. PPC was reported for 27 patients (16.1%), 13 (9.6%) in the resected and 14 (42.4%) in the unresected group. Median time to macroscopically detected recurrence in the resected group was not significantly different in the PPC vs NPC patients (10 vs 12 months, p = 0.46). Median overall survival of patients with PPC vs negative peritoneal cytology (NPC) approached, but did not reach significance (15 vs 19 months, p = 0.055). Peritoneal cytology status was not associated with administration of chemotherapy, margin status, antecedent FNA, stage, or site of recurrence.

These data suggest that malignant cells in peritoneal washings of patients with potentially resectable pancreatic adenocarcinoma should not preclude resection. Long term survival may be achieved, therefore aggressive treatment should be strongly considered.
P42 Detection of Alternative Splicings of dCK Gene in Microdissected Ductal Pancreatic Carcinoma Samples

M. Morelli, G. Bertacca, A. Cavazzana, D. Campani, G. Bevilacqua, C. Di Cristofano, N. Funel, M. Menicagli, L. Pollina, U. Boggi, F.A. Sgambelluri, F. Gremmo, C. Croce, M. Del Chiaro, C. Bengala, E. Fontana, F. Mosca

Department of Oncology, of Transplantations and of Advanced Technology in Medicine, University and Hospital of Pisa, Italy

Gemcitabine is the most common chemotherapeutic treatment for ductal pancreatic carcinoma (DPC). Gemcitabine (2',2'-difluorodeoxycytidine; dFdC) is a deoxycytidine analog with two fluorine substitutes for the two hydrogen atoms in the 2' position of the deoxyribose sugar. Gemcitabine activity is dependent upon the formation of a triphosphorylated metabolite that is subsequently incorporated into DNA. The first step of activation of this compound is the phosphorylation into dF-dCMP by an enzyme called deoxy-cytidine kinase (dCK). The triphosphate metabolite (dF-dCTP) is incorporated into DNA preventing replication.

This study was performed to develop an efficient method for RNA extraction from microdissected tissues in order to identify the presence of alternative splicing of dCK gene.

The advantage of using laser capture microdissection (LCM) is evident by comparing the results obtained by microdissected and non microdissected tissue.

So far the expression of dCK was studied in 12 tumor samples. RNA was extracted from microdissected and non microdissected samples and then RT-PCR was performed. In all the non microdissected samples the PCR fragment of 857 pb corresponding to the normal transcript was present. After LCM we were able to detect alternative splicing in 3/12 (25%) cases: the sequencing of abnormal transcripts confirmed the absence of exons 3, 4, 5, 6 in two cases and the absence of exons 4, 5, 6 in one case. We can conclude that the normal contaminant RNA, that masked the results, was removed by using LCM.

This data are satisfying regarding the setting up of the method, but more cases have to be analyzed to determine the clinical impact of the dCK alternative splicings.

P43 Molecular Characterization of Ductal Pancreatic Carcinoma

M. Morelli, G. Bertacca, A. Cavazzana, D. Campani, G. Bevilacqua, C. Di Cristofano, N. Funel, M. Menicagli, P. Aretini, L. Pollina, U. Boggi, F.A. Sgambelluri, F. Gremmo, C. Croce, M. Del Chiaro, C. Bengala, E. Fontana, F. Mosca

Department of Oncology, of Transplantations and of Advanced Technology in Medicine, University and Hospital of Pisa, Italy

Pancreatic carcinoma (PC) represents a challenge in surgical and medical oncology. Prognosis of the patients has not change in the last years despite the important accomplishments in the surgical approach to disease. The majority of patients has tumors at not operable stage. The 5 years survival of affected patients that undergo surgery or chemotherapy is approximately 1–2%. One of the reasons of this low rate of survival is the lack of responsiveness to most common oncologic therapies such as chemotherapy, radiotherapy and immunotherapy.

Molecular analysis of pancreatic tumors has always been difficult because of the low cellularity due to the host characteristic desmoplastic reaction. This problem has been in part solved by the use of several techniques of cell enrichment such as laser capture microdissection (LCM) of primary lesions.

Since December 2001 by the U.O. of Molecular and Ultrastructural Diagnostic and Pathology 40 cases of ductal pancreatic carcinoma were collected and subjected to LCM; nucleic acids were extracted from enriched samples.

Sequencing analysis was performed for detection of p53, k-ras and bax alteration. Mutations of p53 gene were found in 55% (22) of the cases. Alteration at codon 12 and codon 13 of k-ras gene were found in 83% (33) of patients. Among the 7 non mutated cases for k-ras, 6 cases were p53 mutated (86%).

Microsatellite instability was also investigated according to the NCI consensus criteria in 28 cases: 21% (6/28) showed high instability; 32% (9/28) show only one altered locus and 45% (13/28) were MSS cases. Nevertheless Bax gene was never altered.

PC therefore appears to be characterized by a high frequency of k-ras mutation, although k-ras wild type tumors may occur. p53 is significantly associated with k-ras wild type tumors suggesting an alternative pathway of ductal cell tumorigenesis.

P44 Whipple Pancreatoduodenectomy for Malignant Disease of the Pancreas: Our Experience

L. Mori, E. Rescigno, F. Razzetta, A. Vercesi, G. D'Ambrosio

Div. Chirurgia Generale, Ospedale di Lavagna (GE), Italy

According to recent surveys pancreatic carcinoma is the 4th leading cause of death for malignant tumors. Resection is the only chance of cure for pancreatic cancer but 5 years survival rate after surgery remains poor. Pancreatoduodenectomy appears to be safer in the last decade and postoperative mortality in HPB specialized units is about 6%. The aim of this study is the analysis of postoperative morbidity and survival results in pancreatic neoplasm resective surgery in our experience. From May 1997 to January 2004, 97 patients with ductal adenocarcinoma of the pancreatic head were admitted to our surgical department and 38 underwent to Whipple pancreatoduodenectomy (resectability rate 39.1%). Standard D1 resection was performed in whole cases. One patient underwent to portal complete resection and vascular graft substitution. Main complications were two cases of pancreatic fistula (1 patient surgically treated), 1 case of postoperative occlusion from stenosis of gastrojejunal anastomosis, 2 cases of delayed gastric emptying, 1 case of ischemic colonic perforation in XX p.o. after patient dismission, and 1 case of acute pancreatitis. Postoperative mortality rate was 7.9% and occurred in three patients.
Median hospital stay was 19 days (range 11–32). Patients with stage I tumors survived curative pancreatic resection for about 15.2 months, compared with those with stage II and III tumors who survived for about 9 and 6 months respectively. There were no 5 years survivors. Thanks to acceptable morbidity and mortality postoperative rates, Whipple pancreatoduodenectomy, offers improvement of survival in I–II stage and, in the presence of lymphonode metastases represents a good palliative option.

### P45
**A Twenty-Two Year Experience with Pylorus Preserving Pancreatoduodenectomy in the Treatment of Pancreatic and Periampullary Tumors**

F. Mosca, U. Boggi, M. Del Chiaro, F. Gremmo, C. Croce, A. Sgambelluri, F. Vistoli, S. Signori, A. Campatelli, G. Di Candio
Regional Referral Center for Pancreatic Diseases, Treatment, University of Pisa, Italy

**Introduction:** In 1978 Traverso and Longmire revived Watson’s original idea of preserving the pylorus during pancreatoduodenectomy. This procedure, originally described for the treatment of chronic pancreatitis, was soon employed also for pancreatic and periampullary tumors.

**Aim of the Study:** To describe our 22-year experience with pylorus preserving pancreatoduodenectomy (PPPD) in the treatment of pancreatic and periampullary tumors.

**Materials and Methods:** Between January 1982 and January 2004 we performed 493 pancreatoduodenectomies for the treatment of pancreatic and periampullary tumors, including 139 (28.2%), Whipple procedures (PD) and 354 (71.8%) PPPD. The two groups were comparable regarding all baseline characteristics. The technique of PPPD was slightly modified, as compared to the one originally described in 1978, to meet with oncological criteria: the right gastric vessels were divided to allow adequate exposure for soft tissue clearance, and the duodenal stump was trimmed as short as possible.

**Results:** Mean postoperative hospital stay was 13.4 days for PD and 14.6 for PPPD (p = ns). Morbidity and mortality rates were 41.5% and 5.8% for PD as compared to 35.9% and 3.8% for PPPD. Delayed gastric emptying occurred in 3.8% and in 4.4% of patients following PD and PPPD, respectively. Equivalent figures for marginal ulcers were 10.8% and 10.1% respectively. After a mean follow-up period of 10.2 years (range 22–0.1 years), 1-, 5-, and 10- year survival of patients diagnosed with ductal adenocarcinoma was not improved with PD (57%, 14.2% and 0) as compared to PPPD (58.2%, 15.5% and 0). Equivalent figures for periampullary tumors were 78%, 38.6%, and 8% for PD as compared to 77.8%, 36.2%, and 7.4% for PPPD.

**Conclusions:** PD and PPPD achieve equivalent early and long-term results. More specifically, resection of gastric antrum does not improve survival of cancer patients. Both techniques should be retained in the repertoire of pancreas surgeon.

### P46
**Pancreatic Cancer Cell Growth is Inhibited by the Selective Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor ZD1839 (IRESSA)**

M.W. Müller, J. Kleeff, J. Li, M. Korc, M.W. Büchler, H. Friess
Department of General Surgery, University of Heidelberg, Germany

**Background:** Pancreatic cancer is steadily increasing in incidence and has the worst prognosis of all GI-tract cancers. It is characterized by low responsiveness to conventional chemotherapy and radiotherapy. This resistance is partly due to the overexpression of several tyrosine kinase receptors and their ligands, like epidermal growth factor receptor (EGFR). ZD1839, a new tyrosine kinase inhibitor of EGFR, has shown clinical activity against EGFR-expressing tumors.

**Aim:** Our aim was to investigate the potential role of ZD1839 in pancreatic cancer.

**Methods:** Using the MTT assay we analyzed the effects of ZD1839 on growth factor actions in different human pancreatic cancer cell lines and the GI50 of ZD1839 as well. FACs analysis using Annexin and PI staining was performed to study cell cycle, apoptosis, and cell death. EGFR expression levels, MAP kinase and EGFR phosphorylation was investigated by Western blot analysis. Colony formation and invasion was analyzed in soft agar assays and Matrigel coated filters.

**Results:** ZD1839 inhibited cell proliferation of pancreatic cancer cell lines with GI50 concentrations ranging from 2.5 to over 10 μM. The EGF induced cell proliferation was completely inhibited by ZD1839 but not IGF induced mitogenesis. ZD1839 completely abolished EGF induced phosphorylation of EGFR and MAP kinase and inhibited basal and EGF induced anchorage-independent cell growth and invasion.

**Conclusion:** ZD1839 inhibits pancreatic cancer cell growth through EGFR dependent pathways. ZD1839 also inhibits anchorage-independent growth and invasiveness. ZD1839 may offer a new approach for the treatment of pancreatic cancer.

### P47
**Carcinoid Tumors of the Pancreas**

C. Mussi, C. Angelini, S. Crippa, F. Romano, A. Fontana, P. Sartori, A. Sormani, L. Degrate, Fr. Uggeri
Department of General Surgery, ‘San Gerardo’ Hospital, University of Milan-Bicocca, Monza, Milan, Italy

Carcinoid tumor of the pancreas is a very rare disease with less than 50 cases reported in the world literature. The high incidence of distant metastasis (69%) at the time of the diagnosis prevents long-term survival in the majority of patients. Nevertheless patients with distant disease can also undergo resection for potential cure or
symptomatic palliation because of the slow growth rate of many carcinoid tumors. We report here new four cases of pancreatic carcinoid tumors. Abdominal pain was the most common symptom complained (75%). Two patients presented carcinoïd syndrome and had raised levels of urinary serotonin degradation product 5-hydroxyindoleacetic acid (5-HIAA). Only one patient had liver metastasis at the time of surgery. Tumor diameters did not correspond with the presence or absence of metastases. Partial pancreatectomy was performed in three cases, while in one case only a palliative by pass procedure was possible. Two patients were treated with postoperative Octreotide. One patient had a chemo-embolisation of the hepatic metastasis and was treated also with high dose radiolabeled somatostatin analogues. Patient with non resectable disease died after four months. One patient died after two years, one is alive and disease free after seven years and the patient with liver metastasis at diagnosis is alive after 40 months.

The analysis of our experience and literature review underline the importance of an aggressive and multimodal therapy of this rare tumor. In fact, combination of a surgical debulking, chemo-embolisation, Octreotide and high dose radiolabeled somatostatin analogues administration improve survival and is effective in the palliation of symptoms and liver metastasis.

P48

The Transjejunal Drainage of Wirsung Duct after Child Pancreatic Resection for Cancer could Reduce the Risk of Pancreatic Fistula

S. Neagu, R. Costea, V. Dinca, S. Gradinaru, M. Neagu, M. Vlase, G. Iana, M. Pelmus
IAP, University Hospital, Bucharest, Romania

Background: The pancreatic fistula is one of the major and frequent complications after pancreatic resection for cancer. Multiple protective methods of the pancreaticojeyunal anastomosis were developed.

Patients and Methods: We present the case of a 43 years-old male patient operated for carcinoïd of the head of the pancreas, without jaundice, in which we performed, in order to protect the pancreaticojeyunal anastomosis after Child radical pancreaticoduodenectomy, an enteral drainage of the Wirsung duct with a polyten transjejunal tube according to Witzel’s method. Another particularity of this case is the biliary-intestinal anastomosis: because the bile duct was normal and not suitable for anastomosis, we performed a choledochojejunostomy.

Results: The postoperative evolution was excellent. We suppressed the external drainage of the Wirsung duct after 10 days and the patient was discharged after 14 days. The histopathologic analysis established the diagnostic of ductal adenocarcinoma.

Conclusion: The external drainage of the Wirsung duct after pancreatic resection could protect the pancreatic anastomosis from fistula.

P49

Microarrays-Based Study in Pancreatic Carcinoma

D. Pantalone1, I. Giotti1, E. Pelo1, B. Minuti1, E. Mazza2,3, M. Falchini2, B. Neri2, G. Nesi4, L.R. Girardi5, F. Torricelli1

1Laboratory of Genetic and Cytogenetic Medicine, Careggi Hospital (AOC), Florence; 2Department of Physiopathology – Section of Radiology; 3Centre of Experimental and Clinical Oncology, Oncologic Day Hospital, Department of Internal Medicine; 4Department of Human Pathology and Oncology, University of Florence, Italy

Pancreatic cancer is still predominantly diagnosed in advanced stages, and most patients are not eligible for surgery at diagnosis. This is mainly due to the great difficulty in detecting the tumor at an early stage and presently no satisfactory results have been obtained to overcome this problem.

Studies on molecular genetic of pancreatic cancer represent an important approach. In a previous study we focused on the mutations of p53 and DPC4 detectable in the bile of patients with histopathologically proven pancreatic cancers [1]. p53 and DPC4 mutations are present in a late stage of pancreatic cancer progression. We analyzed specimens of bile collected through percutaneus transhepatic biliary catheters, placed to treat malignant biliary obstruction in 25 patients. Rates of mutation was: 43% for the microsatellite D17S945 (p53), 54% and 50% for D18S46 and D18S474 (DPC4) respectively. Amplification rates were 67%, 93.6% and 80%. These results are encouraging and we decided to enlarge the number in order to evaluate a possible clinical application of the technique. Moreover we have a second group of study, microarrays based. We enrolled 15 patient. A blood sample for each patients was also collected. We examined RNA expression levels of frozen and paraffin-embedded specimens of the tumor and frozen and paraffin-embedded specimen of normal pancreatic tissue (surgical specimens). Total RNA was extracted and studied according to the procedure protocols at website: www.microarray.org/protocols.html and cmgm.stanford.edu/pbrown.

The experiments were conducted twice or more time and validated by Real Time PCR.

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P50
Use of an Omental Flap to Reinforce Pancreaticojejunal Anastomosis after ‘P’ Loop Pancreatectoduodenectomy: Surgical Technique and Preliminary Data
G. Pescio, M. Abete, M. Dogliotti, V. Ronchetti, A. Casano, S. Cesaro
Dipartimento Chirurgico, ASL 1 Liguria, Struttura Complessa di Chirurgia Generale, Imperia, Italy

Background: Operative mortality following Pancreatectoduodenectomy (PD) has been dramatically reduced over the last three decades. However, pancreatic fistula remains the first factor of morbidity (6–16%). In General Surgery, omentoplasty has been used for a long time to protect anastomoses and sutures. The aim of this study is to evaluate our case series retrospectively and to assess the usefulness of an omental flap in protecting the pancreaticojejunal anastomosis following a ‘P’ loop PD.

Methods: At the Hospitals of Genoa, Bordighera and Imperia, between 1991 and 2003, 31 pancreaticoduodenectomies were performed. Twenty-one males and 10 females (mean age: 63.2 years) underwent surgery for periampullary adenocarcinoma (93.5%) and chronic pancreatitis (6.5%). The personal reconstructive method consisted in a double ‘Roux-en-Y’ on the jejunal loop without mesenteric interruption and in a third anatomic ‘Roux-en-Y’ to reconstruct the alimentary tract. The gastric stump was anastomosed with the jejunum with a reconstruction of Billroth II-type in older patients. In 9 patients (29%) the pancreaticojejunal anastomosis was protected by means of a 360° omentoplasty with ‘slipknot-shaped’ flap when possible (6 cases) or ‘fork-shaped’ flap (3 cases).

Results: Perioperative mortality was 0; leakage of the pancreaticojejunal anastomosis occurred in 3 patients (9.7%), one of them died because of bleeding 48 days after surgery. In two of the patients with complications a protection omentoplasty was performed. In all the cases the treatment of fistula was conservative.

Conclusions: The severity of pancreatic fibrosis and the size of the main duct represent the most important risk factors for complications following PD. Pancreatectoduodenectomy is currently the standard technique; anastomosis protection by means of an omental flap is quick and easy to perform. Further prospective and randomised studies will be necessary to confirm its usefulness in reducing complications as well as their severity.

P51
Pancreatic Neuroendocrine Tumors (NET): The Effect of Surgical and Medical Therapy on Survival
R. Pizzilli, R. Tomassetti, L. Piscitelli, D. Campana, R. Ceciliato, R. Corinaldesi
Department of Internal Medicine, ‘Sant’Orsola-Malpighi’ Hospital, Bologna, Italy

Aim: To evaluate the efficacy of the various treatment modalities in a consecutive series of patients with pancreatic NET.

Patients: Seventy-nine (43 M, 36 F, mean age 59.1 years, range 28–82) patients with pancreatic NET. A clinical check-up and abdominal ultrasound were made every 3 months during the first year after the diagnosis and every 6 months thereafter; surgical and medical procedures and survival rates were recorded. Kaplan-Meier curves were used to estimate the survival.

Results: Two patients were lost at follow-up; the mean follow-up of the 77 patients was 55.7 months (range 2–252). Fifty patients (64.9%) had non-functioning NET, 15 (19.5%) had functioning NET, 12 (15.6%) had MEN 1 disease with pancreatic involvement. The tumor was localized in the pancreatic head in 27.3% of the cases, in the head and body in 10.4%, in the body in 10.4%, in the body and tail in 26%, diffuse throughout the gland in 5.2%. The size of the tumor was <30 mm in 31.1% of the cases and >30 mm in 54.4%; the tumor size was not available in 14.5% of the cases. Forty-five percent of the patients had distant metastases at the time of diagnosis and 10% developed metastases during the follow-up period. Twenty-three patients had radical surgery, 42% had debulking surgery and 35% were treated medically (11 chemotherapy, 13 chemoembolization, 51 somatostatin-anzalogues). The size of the tumor was not significantly related to the survival (P = 0.110), whereas there was a statistically significantly longer survival in patients without metastases at diagnosis (P < 0.01) and in those who did not develop metastases at follow-up (P < 0.01). Patients who underwent surgery had a longer survival than patients who had no surgery (P < 0.05). Medical treatment did not affect survival.

Conclusions: Surgery continues to have a central role in the therapeutic approach to NET of the pancreas.

P52
The Prognostic Impact of Clinical Staging in Pancreatic Adenocarcinoma
V. Picardi, G. Gallusso, G. Costamagna, G. Brizi, G. Mattiucci, F. Deodato, G. Macchia, V. Perri, V. Valentini, N. Cellini, A.G. Morganti
Radiation Therapy Department, Università Cattolica, Campobasso, Italy

Introduction: The importance of pancreatic cancer’ staging remain uncertain since state-of-the-art treatments have demonstrated little impact on survival. The aim of this report was to evaluate the accuracy of combined standard imaging techniques in predicting the pathologic stage, and to evaluate the prognostic impact of clinical staging in order to identify patients groups where laparoscopy and laparotomy could be beneficial.

Materials and Methods: In the 54 patients included in this analysis, the techniques employed for clinical staging were ERCP, abdominal CT scan and US. All patients underwent both clinical (presurgical staging) and surgical-pathological staging, based on the AJCC staging system. A comparison was performed between presurgical stage and surgical-pathologic stage. The prognostic impact of different factors on survival was evaluated with both univariate (logrank) and multivariate (Cox) analysis.

Results: Sensitivity and specificity for vascular involvement were 73.9% and 91.3%, respectively. Sensitivity and specificity for nodal involvement were 63.6% and 95.4%, respectively. 33.3% of the
patients showed higher than expected pathological stage, and 3.7% showed lower than expected pathological stage, by comparing clinical and pathologic evaluation. A highly significant correlation was observed between clinical T staging (p = 0.0067) and tumor diameter (p = 0.0037) and patients survival. Maximal prognostic differentiation was observed by dividing patients into two groups based on imaging results: group A (favorable prognosis: cT1-3 and tumor diameter <30mm) and group B (unfavorable prognosis: cT4 and/or tumor diameter >30 mm). Median survival was 25.1 and 8.0 months, respectively. Five-year survival was 20.1% and 0%, respectively (multivariate analysis: p = 0.0007).

**Conclusions:** In category A-patients, laparotomy seemed justified and novel adjuvant treatments should be tried. In category B-patients, innovative treatment strategies should be tested, and particularly combined neoadjuvant chemoradiation, thus avoiding laparotomy as first therapy.

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**P53**

**5-FU-Based Chemoradiation in Unresectable Pancreatic Carcinoma: A Phase I-II Dose-Escalation Study**

V. Picardi, G. Costamagna, G. Mattiucci, F. Deodato, G. Macchia, M. Mutignani, C. Digesù, M.G. Mangiacotti, V. Valentini, N. Cellini, A.G. Morganti

**Purpose:** To evaluate the possible impact of the dose on response, toxicity, pain relief and outcome in patients with unresectable pancreatic carcinoma by a phase I-II dose escalation study.

**Methods and Materials:** 50 patients entered the study. External beam dose was 39.6 Gy in the first 15 patients, 50.4 Gy in the successive 15 patients, and 59.4 Gy in the remaining 20 patients, five 1.8-Gy fractions weekly. Patients received concurrently continuous infusion of fluorouracil (1,000 mg/m²/day). After 4 weeks, patients were evaluated for surgical resection. In resected patients, electron-beam intraoperative radiation therapy (10 Gy) was given before reconstruction. Therewith, in resected patients, adjuvant chemotherapy was prescribed (6 courses: 5-FU, mitomycin C, Adriamycin).

**Results:** During chemoradiation, 1 patient (3.6%) developed grade 3 acute gastrointestinal toxicity and 2 patients (7.1%) developed grade 3 hematologic toxicity. Three out of 19 patients with unresectable tumors had tumor downstaging. Two patients (7.1%) showed partial response and 4 patients (14.3%) had minimal tumor response. Four patients (14.3%) showed disease progression after chemoradiation (liver or peritoneal metastases). Nine patients underwent surgical resection and IORT, with 1 postoperative death. The median survival time for the 28 patients was 11.3 months (21.5 and 9.0 months in resected and unresected patients, respectively).

**Conclusion:** Our preliminary results suggest that preoperative 5-FU chemoradiation was well tolerated and may result in tumor downstaging but the response-rate is still low. Based on the impact of surgical resection on survival, an improvement in local response rate is necessary.

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**P54**

**Preoperative 5-FU Based Chemoradiation + IORT in Pancreatic Carcinoma: A Phase II Study**

V. Picardi, G. Macchia, S. Alfieri, F. Deodato, G. D’agostino, C. Digesù, V. Valentini, N. Cellini, G.B. Doglietto, A.G. Morganti

Radiation Therapy Department, Università Cattolica, Campobasso, Italy

**Purpose:** The prognosis of pancreatic cancer remains poor. Surgery, when feasible, is rarely curative. Radiation therapy (RT) and concomitant 5-fluorouracil (5-FU) have been shown to improve survival in locally advanced pancreatic cancer. In an attempt to improve resectability and disease control, we used preoperative chemoradiation in a combined modality therapy protocol. The purpose of this study was to evaluate our definitive results in terms of acute toxicity and response.

**Materials and Methods:** 28 patients (12 males, 16 females; mean age: 62 years) with unresectable (cT4: 19 patients) or resectable (cT3: 9 patients) non-metastatic pancreatic tumors, received external beam radiation (39.6 Gy) plus 5-FU (96 hours continuous infusion, days 1–4 at 1,000 mg/m²/day). After 4 weeks, patients were evaluated for surgical resection. In resected patients, electron-beam intraoperative radiation therapy (10 Gy) was given before reconstruction. Therewith, in resected patients, adjuvant chemotherapy was prescribed (6 courses: 5-FU, mitomycin C, Adriamycin).

**Results:** During chemoradiation, 1 patient (3.6%) developed grade 3 acute gastrointestinal toxicity and 2 patients (7.1%) developed grade 3 hematologic toxicity. Three out of 19 patients with unresectable tumors had tumor downstaging. Two patients (7.1%) showed partial response and 4 patients (14.3%) had minimal tumor response. Four patients (14.3%) showed disease progression after chemoradiation (liver or peritoneal metastases). Nine patients underwent surgical resection and IORT, with 1 postoperative death. The median survival time for the 28 patients was 11.3 months (21.5 and 9.0 months in resected and unresected patients, respectively).

**Conclusion:** In a phase I-II study the association of high radiotherapy doses with the incidence of severe toxicity in the treatment of unresectable pancreatic carcinoma, was confirmed.

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**P55**

**Pancreatic Metastasis of Renal Cell Carcinoma**

G. Pozzo, B.M. Marino, U. Parisi, E. Castagna, C. Moro

Department of Surgery, Asti Hospital, Asti, Italy

The pancreas is an uncommon site of metastasis from renal cell carcinoma.
We describe herein the case of a 60 year old woman in whom metastases arising from renal cell carcinoma developed in the pancreatic tail. The patient had a nephrectomy twenty-two years ago for a renal cell carcinoma, and in the 2003 have developed a metastasis in the pancreatic tail. We made a total pancreatectomy and we found two metastasis in the pancreas, one in the neck and one in the tail.

We advocate aggressive surgical resection when possible, because as showed in the literature the metastasis could be multi-focal.

**P56**

**Cell-Mediated Immunodeficiency in Pancreatic Cancer Patients**

F. Romano, F. Uggeri, S. Crippa, M. Conti, A. Scaini, C. Angelini, C. Mussi, R. Caprotti, Fr. Uggeri

Department of General Surgery, ‘San Gerardo’ Hospital, University of Milan-Bicocca, Monza, Milan, Italy

It is known that lymphocytes play a fundamental role in mediating tumor cell destruction. Cancer patients show often a cell-mediated immunological impairment that predicts a poor prognosis and poor survival rates. Furthermore major surgery induces a transient immunodeficiency too that may favor metastatic spread. Aim of this study is to evaluate the cell-mediated IL-2 dependent immune status in operable pancreatic cancer patients and to compare it with other gastrointestinal tumors. One hundred and twenty-one cancer patients (22 pancreatic, 48 gastric and 51 colorectal), with median age of 66 years (range 42–83), 55 males and 66 females, were enrolled. Total and CD4+ lymphocyte counts were assessed preoperatively and at 14th and 50th postoperative days. Results obtained were compared between the groups and related to nodal involvement (N0 versus N+). Colorectal and gastric cancer patients showed quantitative lymphocyte deficiency at baseline in 29% and 41% of cases respectively. Fourteen days after surgery values below normal range were found in 44% and 54% (Total) and 53% and 67% (T helper) Recovery of post-operative lymphocytopenia occurred late only in patients with normal count at baseline. According to regional nodal involvement (pN0/N+) T helper deficiency was significantly more frequent in patients with nodal involvement than in patients without.

In pancreas cancer percentage of immunodepressed patients at baseline was higher compared to the other two groups (71%). Lymphocyte count was significantly different between pancreatic and gastric/colorectal cancer, reaching a statistical significance at baseline and on 14th and 50th postoperative day. No differences of T helper deficiency were noted according to nodal involvement (N0 versus N+) neither at baseline nor in the postoperative period. Immunodepression was significantly greater in pancreatic cancer in which is always a systemic disease even in early stages and independently from the nodal involvement and from the tumor load.

**P57**

**Eight-Years Experience with Surgical Treatment for Pancreatic Cancer at the National Cancer Institute of Milan**

D. Sarli, M. Schiavo, A. Russo, T. Camerini, H. Giordano, C. Badalotti, J.C. Coppa, C. Battiston, V. Mazzaferro

GI Surgery and Liver Transplantation Unit, Istituto Nazionale Tumori, Milan, Italy

**Background:** Pancreatic cancer is still a challenging disease to deal with in surgical oncology. Early diagnosis, surgical skill and multimodal treatments may affect outcome and morbidity. We analyzed prognostic factors and survival of a consecutive series of potentially curative pancreatic resections.

**Patients and Methods:** From 1994 to 2002 at INT-Milan 116 consecutive patients underwent potentially curative pancreatic resection for cancer. M/F ratio was 1/1. There were 102 (89%) adenocarcinoma (adk) and 13 (11%) neuroendocrine tumors. Ampullary tumors represented 32% of the series (29 pts). Pancreatocoduodenectomy (PD) and distal pancreatectosplenectomy (DPS) were performed in 85 cases (73%) and in 30 (27%), respectively. Pylorus-preserving procedures were carried out in 32 pts (38%).

Following DP, pancreatico-jejunal/gastric reconstruction was applied in 84% of pts, while chemical treatment of pancreatic stump (neoprene® injection) was decided in 14 pts.

Forty patients (34%) received post-operative CT/RT. Twenty-five different (pre- and post-operative, surgically and histologically-related) prognostic factors were correlated to both patients and recurrence-free survival.

**Results:** After a median follow up time of 37 months, 3- and 5-year overall (OS) and recurrence-free (DFS) survival for adenocarcinoma were 45%, 36% and 37%, 29%, respectively. Poor outcome was significantly associated with high tumor markers level (p = 0.001), presence of symptoms (p = 0.003), pre-operative biliary drainage (p = 0.0003), tumor size (T1 vs others, p = 0.02) and stage (stage I–II vs II–IV, p = 0.008), hospital stay longer than 30 days (p = 0.001). Adjuvant CT/RT had a significant effect on OS (p = 0.03), although such a strategy was not applied in a randomized fashion. Post-operative complications occurred in 44 pts (38%); among those, 19 (16%) were pancreatic fistulas.

**Conclusions:** Careful patient selection and multidisciplinary approach may improve general results of surgery for pancreatic cancer.

**P58**

**The Role of Endoscopy in the Vater Ampulla Neoplasm**

C. Savlovschii, D. Turbatu, D. Serban1, M. Comandasu, C. Branescu, L. Musat1, G. Smarandache, S. Mircea Oprescu1

1University Emergency Hospital, Bucharest, Romania

The digestive fibroendoscopy brought the most important contribution to the pathology of the Vater papilla, by directly observing it,
because it could describe not only the color modifications, but also the ones belonging to the dinamica of the papilla, alterations that appear in inflammations and other cases. We diagnosed 12 cases of neoplasm of the Vater papilla, while performing 4,800 duodenoscopies. The clinical symptoms of the patients were loss of weight, jaundice and loss of appetite. We used paraclinical investigations like ultrasound, CT, ERCP and PTC and in some cases hypotonic duodenography (which was normal). ERCP and PTC were useful in the diagnosis, while the confirmation of the disease was histopathological. The treatment of all cases was surgical or endoscopic: 4 cases with ampulectomy, 3 cases with anastomosis between the coledocum and the duodenum, while 5 cases were solved in an endoscopic manner with papilosphincterotomy and pigtail protesis. The role of endoscopy in the Vater ampulla neoplasm is very important because it can not only perform biopsy but also decide for an endoscopical or surgical manner of solving this case.

P59
Endoscopic Management of Neoplastic Bilio-Duodenal Stricture with Self-Expanding Metal Stents (SEMS)
A. Tringali, M. Mutignani, C. Spada, P. Familiari, G. Spera, M. Marchese, V. Perri, G. Costamagna
Digestive Endoscopy Unit, Catholic University, Rome, Italy

Background and Aim: Since recently endoscopic palliation of neoplastic biliary strictures was not possible in the presence of a concomitant duodenal stricture. With the advent of duodenal SEMS it is now possible to palliate bilio-duodenal strictures endoscopically.

Materials and Methods: From October 1998 to September 2003 endoscopic duodeno-biliary drainage was attempted in 37 patients (20 M; mean age 69 years) with pancreatic cancer (n = 25), metastatic cancer (n = 4), gastric cancer (n = 3), gallbladder, bile duct cancer (n = 2 cases each) and ampullary cancer (n = 1). Thirty-two (86.5%) patients had already a biliary stent in place and developed the duodenal stricture on average 117 days (range 15–412) after stenting. In 10 cases biliary drainage was attempted at the same time of duodenal stenting. When the papilla was covered from the duodenal stent, access to the papilla was obtained through the meshes of the duodenal stent by balloon dilation or by removal of some meshes of the duodenal stent with a rat tooth forceps. Enteral Wallstent (Boston Scientific) were used.

Results: Thirty-two (86.5%) patients had a stricture of the middle/distal common bile duct, whilst 5 patients (13.5%) had a hilar stricture. Duodenal stenting with SEMS was technically successful in all cases. Morbidity related to the procedure was 8% (1 cholangitis, 1 acute pancreatitis due to biliary SEMS, 1 bleeding from the tumor after duodenal stenting).

Follow-up:

| n% mean days | Death without symptoms 2773123 |
|-------------|-------------------------------|
| 30-day mortality 7 19 13 |
| Death with symptoms 6 16 217 |
| 30-day mortality 4 11 15 |
| Alive without symptoms 2 5 120 |
| Surgical bypass 1 3 |
| Lost to follow-up 1 3 |

Conclusions: Endoscopic palliation of duodenal-biliary strictures is feasible and may be effective in obtaining relief of jaundice and gastric-outlet obstruction. Selection of patients according to their life expectancy is necessary to reach cost-effectiveness.
