

consisted of 1) gliadin-sensitized & -challenged mice and 2) gliadin-sensitized & -challenged mice with supplementary intraperitoneal cerulein.

Results: Gliadin-sensitized & -challenged mice showed features of chronic pancreatitis including mixed inflammatory infiltrates, proliferation of fibroblasts, and acinar atrophy. In gliadin-sensitized & -challenged mice with cerulein injection, more severe inflammatory infiltrates, fibrosis and acinar atrophy were documented than those found in gliadin-sensitized & -challenged mice. By immunohistochemical analysis using mice IgG1, having homology with human IgG4, gliadin-sensitized & -challenged mice showed IgG1-stained plasma cells in the inflammatory infiltrates. In those with supplementary cerulein injection, strong IgG1 staining was observed not only in the plasma cells but also in the stromal, acinar and ductal cells. Serum IgG1 showed a significant elevation in gliadin-sensitized & -challenged mice. Mice with severe pancreatitis showed IgG1-stained inflammatory cell infiltrates in the extrapancreatic organs including bile duct, salivary gland, kidney and lung.

Conclusion: Gluten-sensitive HLA-DQ8 transgenic mice showed histological and serological features of autoimmune pancreatitis similar to those of human AIP.

Proteomic Biomarkers for the Early Detection of Pancreatic Cancer – An Analysis of Pancreatic Duct Fluid

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Objectives: We previously identified a panel of proteins in pancreatic cyst fluid that appeared to have the potential to assist in the classification of the lesions. However, many pancreatic cancers do not arise from cysts. Hence proteomic analyses were performed to look for proteins in pancreatic duct fluid that may segregate different pancreatic lesions.

Methods: Pancreatic duct fluid was aspirated at the time of pancreatic resection for 28 patients for varying pathologies. Mass spectrometry (GeLC-MS/MS) was used for protein identification. Only about 20 microliter samples were required. Clinical information, outcomes, pathology results and biomarkers were compared.

Results: 34 potential biomarker proteins were found at varying levels. They were variably observed in pancreatic cyst fluids obtained by EUS-FNA, from cysts that contained mucinous cystic neoplasm or adenocarcinoma but not from control cysts.

The proteins are: Mucin-1, Mucin-2, Mucin-5AC, Mucin-5B, Mucin-6, Mucin-13, CEACAM 1, CEACAM 5, CEACAM 6, CEACAM 7, CEACAM 8, S100-A6, S100-A8, S100-A9, and S100-A11, Anterior gradient protein 2 homolog, Galectin-3-binding protein, Gelsolin, Neutrophil gelatinase-associated lipocalin, Leukocyte elastase inhibitor, Deleted in malignant brain tumors 1 protein, Polymeric-immunoglobulin receptor, Histone H4, Tetraspanin-1, Tetraspanin-8, Ezrin, Annexin A2, Annexin A4, Annexin A1, Annexin A3, Annexin A5, Galectin-3, Galectin-4, and Alpha-enolase.

Conclusions: Variably combinations of these 34 potential pancreatic biomarkers correlate with the presence of premalignant lesions or cancers whether cysts are involved or not. The tiny samples required may facilitate analysis of small lesions for pancreatic cancer diagnosis and cancer risk-stratification. S100A8 and A9 in duct fluid correlated with poor post-surgery DFS and OS. Further research is required to understand the presence of these proteins.

Effect of Adjuvant Treatment on Recurrence of Intraductal Papillary Mucinous Neoplasm With an Associated Invasive Carcinoma After Operation

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Introduction: The role of adjuvant treatment for invasive intraductal papillary mucinous neoplasm (IPMN) is unclear. The aim of this study was to evaluate the role of adjuvant treatment in invasive IPMN and to find the risk factors that are associated with postoperative recurrence.

Methods: From January 2004 through April 2011, medical records of 62 patients who had pathologically confirmed invasive IPMN were reviewed retrospectively. Median age was 67 (45-85) years and 30 patients (57%) were male. Potential prognostic factors that can affect the tumor recurrence such as stage, vessel or nerve invasion, and adjuvant treatment were analyzed.

Results: Curative resection was done in 53 patients (85%). 45 patients underwent R0 resection and 8 patients underwent R1 resection. Pathologic stages were as follows: IA (8), IB (11), 2A (19), 2B (14) and 3 (1). Twenty-seven patients (51%) underwent adjuvant chemotherapy (6) or radiation therapy (11) or both (10). During median follow-up of 23 months (4-105), IPMN recurred in 16 patients (30%) and 5 patients (9%) died due to cancer recurrence. Lymph node positive, angiolymphatic invasion, perineural invasion, preoperative CA 19-9 and postoperative CA 19-9 were significant risk factors associated with recurrence-free time in univariate analysis. There was no significant difference in tumor recurrence or survival rate between adjuvant-treatment group and surgery-only group. In multivariate analysis, postoperative CA 19-9 was the significant risk factor associated with recurrence-free time (hazard ratio 17.9, $p=0.001$).

Conclusion: The role of adjuvant treatment after operation of invasive IPMN is inconclusive in this study. Serum CA 19-9 should be checked after operation in invasive IPMN to predict recurrence.

Clinical and Morphological Aspects of Parenchyma-Preserving Operations in Chronic Pancreatitis Surgery

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Introduction: Resection operations in patients with chronic pancreatitis (CP) compound or facilitate the development of exocrine and endocrine pancreatic insufficiency.

Aims: To present the morpho-functional advantages of parenchyma-preserving operations in relation to the resection interventions.

Patients and Methods: We operated 101 patients with CP. In 48 (48/101, 47.5%) patients (study group) a parenchyma-preserving operation (total longitudinal pancreaticoduodenopapillotomy with longitudinal Roux-en-Y pancreaticojejunoduodenostomy) performed. In 53 (53/101, 52.5%) patients (control group) resection types of surgery (Frey operation - 35, Beger - 18) performed. The material for the morphological study was taken at once from the head, body and tail of the pancreas. It used US, CT, ERCP, C-peptid, endogenic insulin, CA 19-9, IgG, pancreatic fecal elastase-1.

Results: Morphological changes in the head, body and tail of the pancreas were the same in all patients: periductal fibrosis with multiple focuses of immunocells infiltration with formation of a thick sheath of connective tissue along of the main pancreatic duct. The activated α -SMA-positive stellate cells were observed in large numbers in all areas of fibrosis of the pancreas. In all patients after parenchyma-preserving surgery (5 years) exocrine insufficiency had no progressed, and in the absence of exocrine insufficiency before the operation - its development was not observed after surgery. In all patients of control group exocrine insufficiency progressed.

Conclusions: Morphological changes in the head, body and tail of the pancreas have the same type in patients with CP. This is the baseline for revision of indications to resection operations. Patients with CP require parenchyma-preserving operation which prevents development of exo- and endocrine insufficiency.

Polymorphisms of CFTR Gene in Japanese Patients With Chronic Pancreatitis

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Background and Aim: Cystic fibrosis transmembrane conductance regulator (CFTR) anion channel plays a key role in HCO_3^- secretion in pancreatic duct cells. Loss of its function due to severe mutations in the CFTR gene causes cystic fibrosis. Mild dysfunction due to less severe mutations or polymorphisms is thought to be related to a certain cases of chronic pancreatitis. Although over 1,400 mutations and polymorphisms have been identified in the CFTR so far, only a few mutations and polymorphisms are well characterized in Asian population, except for sporadic reports on CFTR mutations of CF patients. In the present study, we analyzed mutations and polymorphisms of CFTR gene in Japanese patients with chronic pancreatitis.