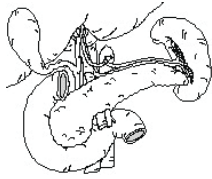


Pancreas Club, Inc.

42nd Annual Meeting
Sunday, May 18, 2008
University of San Diego
Atkinson Hall, CallT2, La Jolla

2008 Program

Jointly sponsored by the American College of Surgeons,
Division of Education and the Pancreas Club.



Welcome to the 42nd Annual Meeting of the Pancreas Club. The Mission of the Pancreas Club, since its founding in 1966, is to promote the interchange of ideas between pancreatologists throughout the world and to maintain

an informal "club" atmosphere. Thus there are no formal manuscript submissions and we encourage presentation and submission of your best ideas for our annual meeting held the Sunday before the start of Digestive Disease Week.

This year the Pancreas Club received over 140 abstracts which were reviewed by the Program Committee. We know that you will be fully engaged in both listening to the excellent presentations and in the discussions which follow. Poster authors will be available postside during the Poster Session.

For the first time, this meeting will offer continuing medical education credits through a joint sponsorship with the American College of Surgeons. We thank them for their support of this important meeting.

The abstracts selected for oral and poster presentation are included in this program book and will also be available on our website.

Pancreas Club Directors



Bill Traverso Bill Nealon Doug Evans



42nd Annual Pancreas Club Meeting

Location

University of San Diego
Atkinson Hall, CallT2,
Voigt Drive, LaJolla, CA

University Club
Symphony Towers
750 B St
San Diego, CA
(619) 234-5200

Registration

7:00 am – 4:00 pm CallT2 Pre Function Area
Registration includes continental breakfast and box lunch
2008 Pancreas Club Dues must be pre-paid to obtain member rate.

Scientific Session

8:00 am – 5:00 pm CallT2 Auditorium

Dinner

7:00 pm – 10:00 pm University Club

Shuttle Service

Shuttle service to and from the meeting and to and from the University Club for the dinner is provided by Coach America. Large buses will be used for the meeting and a smaller shuttle van for the evening transportation needs. Be sure there is a Pancreas Club sign in the window.

From Downtown to UCSD La Jolla, CallT2 Facility

Shuttle buses will pick up at the starting at the Omni and Westin Horton Plaza at 6:00 am, 7:00 am and approximately every hour after. The trip is approximately 45 minutes from last pick up.

To Downtown from UCSD La Jolla, CallT2 Facility

Attendees may take any return shuttle from CallT2 to downtown. The shuttles will make their final return trips from CallT2 at 5:15 and 5:45 pm.

To and From the University Club

Continuous pick up and delivery to and from the University Club with stops at the Omni and Westin Horton Plaza will begin at 6:30 pm and end at 10:15 pm.



42nd Annual Pancreas Club Meeting

Program Committee Members

William Nealon , Chair

Doug Evans

Michael Sarr

Gerard Aranha

Richard Bold

Matthew Walsh

John Christein

Thomas Howard

Sarah Thayer

Charles Vollmer

Kaye Reid Lombardo

William Traverso

Local Hosts: University of California San Diego

Mark Talamini

Mike Bouvet

Pancreas Club Executive Administrator

Beverlee Anderson

Continuing Medical Education

Meeting Objectives:

1. Elucidate the current clinical and basic science research in pancreatic cancer and pancreatitis
2. Discuss the European and North American perspective of clinical trials in pancreatology
3. Recognize the importance of new diagnostic and therapeutic modalities for diseases of the pancreas

Accreditation Statement:



This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the American College of Surgeons and the Pancreas Club. The American College Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

American College of Surgeons
Division of Education

AMA PRA Category 1 Credits™

The American College of Surgeons designates this educational activity for a maximum of 6.5 *AMA PRA*

Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Disclosure Statement

The Pancreas Club and the American College of Surgeons have a policy of disclosure of financial interests or possible conflicts of interest on the part of any presenters at the annual meeting. If such interests are present, they will be disclosed to the attendees via a handout distributed with the program book at the time of the scientific session.



42nd Annual Pancreas Club Meeting

Program At a Glance

7:00 am – 4:00 pm	Registration – CallT2 foyer
7:00 am – 5:00 pm	Exhibit Displays
7:00 am – 8:00 am	Continental Breakfast and poster viewing
7:55 am – 9:45 am	Scientific Session I
9:45 am – 10:00 am	Break and exhibit and poster viewing
10:00 am – 11:00 am	How I Do It Session
11:00am – 12 noon	Poster viewing & Professor Rounds
12 noon – 1:00 pm	Lunch on the patio
1:00 pm – 2:45 pm	Scientific Session II
2:45 pm – 3:00 pm	Break and exhibit and poster viewing
3:00 pm – 5:05 pm	Scientific Session III
5:05 pm – 5:15 pm	Business Meeting; 2009 Planning
5:15 pm	Adjourn Conference
7:00pm – 10:00pm	Cocktails and Dinner – University Club

Pancreas Club Dinner Dedication



This year we will dedicate the dinner in honor of Andy Warshaw and his many contributions to pancreatic surgery. Andy has had a tremendous impact, not only on the Pancreas Club for 35 years, but also in surgery.

Andy joined the surgical faculty at Massachusetts General Hospital in 1972. He is now the W. Gerald Austen Professor of Surgery, Harvard Medical School and Surgeon-in-Chief and Chairman, Department of Surgery, Massachusetts General Hospital.

His first attendance at the Pancreas Club was in 1973 when he presented nascent work on amylase isoenzymes. As he states: “the Club is pretty much what it always has been: a venue to present new ideas to a congregation of enthusiasts.”

Please join us to honor him at the annual Pancreas Club Dinner.



42nd Annual Pancreas Club Meeting

Program Schedule

- 7:55 am **Welcome and Introductory Remarks**
William H. Nealon, MD
University of Texas Medical Branch, Galveston, TX
- Mark Talamini, MD
Chairman, Department of Surgery
University of California San Diego

**SESSION I
PANCREATITIS
8:00 am – 9:45 am**

Moderators: Gerard Aranha, MD, Loyola University Medical Center, Chicago IL
Laureano Fernandez-Cruz, MD, University of Barcelona, Spain

- 8:00 am **TIMING OF CHOLECYSTECTOMY FOR BILIARY PANCREATITIS: DO THE DATA SUPPORT CURRENT GUIDELINES?**
*Kaori Ito, MD, Hiromichi Ito, M.D., Edward E. Whang, MD
Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA*
- 8:15 am **Five-Year Outcome of a Randomized Trial Comparing Pylorus- and Duodenum-Preserving Pancreatic Head Resection for Chronic Pancreatitis**
U. Adam, F. Makowiec, E. Fischer, T. Keck, H. Riediger, U.T. Hopt.
Department of Surgery, University of Freiburg, Germany
- 8:30 am **A UNIFYING CONCEPT: PANCREATIC DUCTAL ANATOMY BOTH PREDICTS AND DETERMINES THE MAJOR COMPLICATIONS RESULTING FROM PANCREATITIS**
William H Nealon¹, Manoop Bhutani², Taylor S. Riall¹, Gottumukkala Raju¹, Orhan Ozkan¹, Ryan Neilan¹
¹University of Texas Medical Branch, Galveston, TX; ²M.D. Anderson Cancer Center, Houston, TX
- 8:45 am **PROBIOTIC PROPHYLAXIS IN ACUTE PANCREATITIS; A PLACEBO CONTROLLED RANDOMIZED CLINICAL TRIAL**
Marc GH Besselink¹, Hjalmar C van Santvoort¹, Erik Buskens^{2,3}, Marja A Boermeester⁴, Harry van Goor⁵, Harro M Timmerman¹, et al; and the members of the Dutch Acute Pancreatitis Study Group
- 9:00 am **EARLY ERCP IS ONLY BENEFICIAL IN PREDICTED SEVERE ACUTE BILIARY PANCREATITIS IN PRESENCE OF CONCURRENT CHOLESTASIS**
H.C. van Santvoort¹, M.G. Besselink¹, A.C. de Vries², G. Cirkel¹, T.L. Bollen³, K. Fischer⁴, M.A. Boermeester⁵, B.L. Weusten⁶, A.F. Schaapherder⁷, P.D. Siersema⁸, B.J. Witteman⁹, V.B. Nieuwenhuijs¹⁰, H. van Goor¹¹, C.J. van Laarhoven¹², A.C. Tan¹³, M.P. Schwartz¹⁴, E. van der Harst¹⁵, P.J. Wahab¹⁶, C.H. van Eijck¹⁷, C.H. Dejong¹⁸, H.G. Gooszen¹, K.J. van Erpecum⁸ for the
Dutch Acute Pancreatitis Study Group

- 9:15 am **REPEATED INTERVENTION AGAINST ALCOHOL USE AT 6 MONTH INTERVALS IS BETTER THAN INITIAL INTERVENTION ALONE DURING HOSPITALIZATION IN REDUCING RECURRENT EPISODES OF ALCOHOLIC PANCREATITIS – PROSPECTIVE RANDOMIZED CONTROLLED TRIAL**
Nordback Isto, Lappalainen-Lehto Riitta, Pelli Hanna, Järvinen Satu, Rätty Sari, *Sand Juhani Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland*
- Short Oral Moderator:** William Nealon, MD
- 9:30 am **A COMPARISON OF DIRECT ENDOSCOPIC NECROSECTOMY AND USUAL TRANSMURAL ENDOSCOPIC TECHNIQUES FOR THE TREATMENT OF WALLED OFF PANCREATIC NECROSIS**
Short
Timothy B. Gardner, MD¹; Prabhleen Chahal, MBBS¹; Georgios I. Papachristou, MD²; Santhi Swaroop Vege, MD¹; Bret T Petersen, MD¹; Christopher J. Gostout, MD¹; Mark D. Topazian, MD¹; Naoki Takahashi, MD³; Michael G. Sarr, MD⁴; Todd H. Baron, MD¹
¹ *Miles and Shirley Fiterman Center for Digestive Diseases, Mayo Clinic Rochester, MN* ² *Department of Medicine, Division of Gastroenterology, Hepatology & Nutrition, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania,*
³ *Department of Radiology, Mayo Clinic, Rochester, MN*
⁴ *Department of Surgery, Mayo Clinic, Rochester, MN*
- 9:35 am **AUTOIMMUNE PANCREATITIS: APPLICATION OF CURRENT DIAGNOSTIC CRITERIA ARE SUBOPTIMAL**
Short
Giday, Samuel A.1; Buscaglia, Jonathan M.1; Mukkai Krishnamurty, Devi1; Chen, Terina2; Kalloo, Anthony N.1; Canto, Marcia I.1; Kantsevoy, Sergey V.1; Okolo, Patrick 1; Hruban, Ralph H.2; Jagannath, Sanjay B.1
1. *Medicine, Johns Hopkins Institute, Baltimore, MD,*
2. *Pathology, Johns Hopkins Hospital, Baltimore, MD.*
- 9:40 am **COMBINED RESECTION OF EXTRAPANCREATIC NERVE PLEXUS MAY IMPROVE THE SURVIVAL AFTER PANCREATICODUODENECTOMY FOR SMALL PANCREATIC CANCER**
Short
S. Egawa, F. Motoi, M. Unno
Hepato-Biliary-Pancreatic Surgery, Tohoku University, Sendai, JAPAN
- 9:45 am Break. Visit with exhibitors and view the posters

“HOW I DO IT” SESSION
Clinical Trials in Pancreatology:
An European and North American Perspective
10:00 am – 11:00 am

Moderator: Carlos Fernández-del Castillo, MD

William Traverso, MD
Virginia Mason Medical Center

Jakob Izbicki, MD
University Hospital, Hamburg, Germany

Keith Lillemoe, MD
Indiana University School of Medicine, Indianapolis, IN

- 11:00 am **POSTER SESSION.** Authors will be by their posters to discuss their research poster presentations. Abstracts identified in the program with ** will be part of the *Poster-side Professor Rounds*. Each invited Professor will discuss several posters.
- 12:00 pm **LUNCH** on the Patio with support from Thompson Surgical

SESSION II
BASIC SCIENCE AND CLINICAL STUDIES IN PANCREATIC CARCINOMA
1:00 pm – 2:45 pm

- Moderators:** John Hoffman, MD, Fox Chase Cancer Center, Philadelphia PA
Ernst Klar, MD, Universität Rostock, Rostock, Germany
- 1:00 pm **APPLYING PROTEOMIC BASED BIOMARKER TOOLS FOR THE ACCURATE DIAGNOSIS OF PANCREATIC CANCER**
John D. Christein¹, Kyoko Kojima², Senait Asmellash³, James A. Mobley⁴
Section of Gastrointestinal Surgery¹ and Division of Urology⁴, Department of Surgery; Department of Microbiology²; Department of Biochemistry and Molecular Genetics³; University of Alabama at Birmingham
- 1:15 pm **INDUCTION OF OSTEOPONTIN EXPRESSION BY NICOTINE AND CIGARETTE SMOKE IN THE PANCREAS AND PANCREATIC DUCTAL ADENOCARCINOMA CELLS**
Galina Chipitsyna¹, Qiaoke Gong¹, Rathai Anandanadesan¹, Akram Zaaqoq¹, Surinder K. Batra², David T. Denhardt³, Charles J. Yeo¹, Hwya A. Arafat¹
¹Department of Surgery, Thomas Jefferson University, Philadelphia, PA, ²Department of Biochemistry and Molecular Biology, Nebraska Medical Center, Omaha, NE, ³Department of Cell Biology and Neuroscience, Rutgers University, New Brunswick, NJ
- 1:30 pm **EPITHELIAL TO MESENCHYMAL TRANSITION IN PANCREATIC CANCER: EXPRESSION AND ROLE OF TRANSCRIPTION FACTORS SNAIL, SLUG, AND TWIST**
Hubert G. Hotz, Birgit Hotz, Elisabeth Schellhaas, Heinz J. Buhr
Dept. of Surgery I, Charité School of Medicine, Campus Benjamin Franklin, Berlin, Germany
- 1:45 pm **RECURRENT CHROMOSOMAL ABERRATIONS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMNS)**
S. Fritz¹, C. Fernandez-del Castillo¹, M. Mino-Kenudson², S. Crippa¹, J. M. Batten², A. T. Nguyen², S. P. Thayer¹, V. Deshpande², G. Y. Lauwers², A. L. Warshaw¹, and A. J. Iafrate²
¹Departments of Surgery and ²Molecular Diagnostics Laboratory, Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.
- 2:00 pm **PANCREATIC CANCER CELL GROWTH IS ATTENUATED BY THE EXPRESSION OF N-MYC DOWNREGULATED GENE**
E. Angst^{1,2}, S. Hasan¹, M. Kim¹, A. Li¹, B. Gloor², H. A. Reber¹, O. J. Hines¹, G. Eibl¹
¹Hirshberg Laboratories for Pancreatic Cancer Research, Department of Surgery, David Geffen School of Medicine at UCLA, ²Department of Visceral and Transplant Surgery, University Hospital, Berne, Switzerland

2:15 pm **PREOPERATIVE DETECTION OF FAMILIAL PANCREATIC NEOPLASMS BY ENDOSCOPIC ULTRASONOGRAPHY(EUS), MULTIDETECTOR COMPUTED TOMOGRAPHY (CT), AND/OR MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY (MRCP)**
Canto, Marcia I.^{1,3}; Schulick, Richard D.^{2,3}; Goggins, Michael G.^{1,5}; Yeo, Charles J.⁶; Cameron, John L.^{2,3}; Fishman, Elliot K.⁴; Kamel, Ihab R.⁴; Hruban, Ralph H.^{5,3}
1. Division of Gastroenterology, Johns Hopkins University, Baltimore, MD, 2. Surgery, Johns Hopkins Medical Institutions, Baltimore, MD, 3. Oncology, Johns Hopkins Medical Institutions, Baltimore, MD, 4. Radiology, Johns Hopkins Medical Institutions, Baltimore, MD, 5. Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, USA. 6. Surgery, Jefferson University, Philadelphia, PA, USA.

Short Oral Moderator: William Nealon, MD

2:30 pm **ASCORBATE-INDUCED CYTOTOXICITY IN PANCREATIC CANCER**
Short
Juan Du, Mark Levine, Brett Wagner, Garry R. Buettner, Joseph J. Cullen
Departments of Surgery and Radiation Oncology, University of Iowa College of Medicine and NIH/NIDDK

2:35 pm **TUMOR-DERIVED ICAM-1 MEDIATES TUMOR-ASSOCIATED LEUKOCYTE INFILTRATION.**
Short
C. L. Roland^{1,2}, S. P. Dineen^{1,2}, J. Toombs^{1,2}, J.G. Carbon^{1,2}, C. W. Smith³, R. A. Brekken^{1,2}, C. C. Barnett, Jr^{1,2}.
¹Division of Surgical Oncology, Department of Surgery, and the ²Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical School, Dallas, Texas and ³Baylor College of Medicine, Houston, Texas

2:40 pm **EFFECT OF HOSPITAL PANCREATECTOMY VOLUME ON MARGIN STATUS FOR PANCREATIC CANCER RESECTIONS IN THE UNITED STATES**
Short
Karl Y. Bilimoria^{1,2}; Mark S. Talamonti^{1,3}; Stephen F. Sener³; Malcolm M. Bilimoria³; Andrew K. Stewart²; David P. Winchester^{2,3}; Clifford Y. Ko^{2,4}; David J. Bentrem¹
1 Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL; 2 Cancer Programs, American College Surgeons, Chicago, IL; 3 Department of Surgery, Evanston Northwestern Healthcare, Chicago, IL 4 Department of Surgery, University of California, Los Angeles (UCLA) and VA Greater Los Angeles Healthcare System, Los Angeles, CA

2:45 pm Break: Visit with exhibitors and view the posters

**SESSION III
CLINICAL STUDIES IN PANCREATIC CARCINOMA
3:00 pm – 5:05 pm**

Moderators: William Traverso, MD, Virginia Mason Medical Center, Seattle WA
Massimo Falconi, MD, Policlinico GB Rossi, Verona Italy

3:00 pm **BENEFIT OF ADJUVANT THERAPY IN PATIENTS UNDERGOING SURGICAL RESECTION FOR PANCREATIC ADENOCARCINOMA**
¹Kimberly A Vanderveen, MD, MAS; ¹Steven L Chen, MD, MBA; ²Diaxin Yin, MS; ^{2,3}Rosemary D Cress, DrPH; and ¹Richard J Bold, MD
University of California, Davis¹ and California Cancer Registry²

- 3:15 pm **THE EFFECT OF OCCUPATIONAL AND ENVIRONMENTAL EXPOSURES IN CASES OF FAMILIAL AND SPORADIC PANCREATIC CANCER**
Theresa Pluth Yeo*, Ralph H. Hruban**, Kieran Brune**, Alison Klein** and Charles J. Yeo*
** Department of Surgery and School of Nursing, Thomas Jefferson University, Philadelphia, PA, and **Department of Pathology and Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD*
- 3:30 pm **FEASIBILITY AND SAFETY OF RADIOFREQUENCY ABLATION FOR LOCALLY ADVANCED PANCREATIC CANCER: RESULT OF A PILOT STUDY ON 27 CONSECUTIVE PATIENTS.**
Girelli R, Frigerio I, , Salvia R, Barbi E, Tinazzi Martini P and Bassi C
*HPB Unit, Pederzoli Clinic, Peschiera del Garda, Verona * Department of Surgery, GB Rossi Hospital University of Verona. ** Department of Radiology, Pederzoli Clinic, Peschiera del Garda, Verona - Italy*
- 3:45 pm **USING FLUOROPHORE-CONJUGATED ANTIBODIES TO IMPROVE SURGICAL NAVIGATION IN PANCREATIC CANCER**
Michele McElroy¹, Sharmeela Kaushal¹, A. R. Moossa¹, Mark A. Talamini¹, George A. Luiken², Robert M. Hoffman^{1,3}, Michael Bouvet¹
*¹Department of Surgery, University of California, San Diego, CA
²OncoFluor, Inc., San Diego, CA
³AntiCancer, Inc., San Diego, CA*
- 4:00 pm **MANAGEMENT OF SUSPECTED PANCREATIC CYSTIC NEOPLASMS BASED ON CYST SIZE.**
R.M. Walsh, D. Vogt, J.M. Henderson, K. Hirose, T. Mason, K. Bencsath, N Brown.
Digestive Disease Institute, Cleveland Clinic, Cleveland, Ohio
- 4:15 pm **PREDICTION OF MORBIDITY FOR PANCREATIC RESECTION: THE INFLUENCE OF SURGICAL PERFORMANCE ON BASELINE PHYSIOLOGY**
Wande B. Pratt, Mark P. Callery, Charles M. Vollmer, Jr.
Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School
- 4:30 pm **DELAYED GASTRIC EMPTYING (DGE) AFTER PANCREATODUODENECTOMY (PD) – THE INTERNATIONAL PANCREATIC STUDY GROUP (ISGPS) DEFINITION IS VERY USEFUL.**
Yasushi Hashimoto and L. William Traverso
Virginia Mason, Seattle WA
- Short Oral Moderators:** William Nealon, MD and William Traverso, MD
- 4:45 pm **FREQUENCY OF EXTRAPANCREATIC NEOPLASMS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS COMPARED TO PANCREATIC ADENOCARCINOMA AND REFERRAL PATIENTS**
Kellie L Mathis, MD¹, Kaye Reid Lombardo, MD¹, Michael G Sarr, MD¹
¹Division of GI and General Surgery, Mayo Clinic, Rochester, MN
- 4:50 pm **DOES LYMPH NODE RATIO (LNR) IMPACT SURVIVAL IN RESECTED PERIAMPULLARY MALIGNANCIES?**
M.G. Hurtuk¹, C. Hughes², M. Shoup¹, G.V.Aranha¹
¹Loyola University Medical Center, Division of Surgical Oncology, Maywood, IL, ²Stritch School of Medicine, Loyola University Chicago, Maywood, IL

- 4:55 pm Short **ADJUVANT CHEMORADIATION THERAPY AFTER SURGICAL RESECTION FOR 1092 CASES OF PANCREATIC ADENOCARCINOMA: THE JOHNS HOPKINS HOSPITAL - MAYO CLINIC COLLABORATIVE STUDY OF PANCREATIC CANCER**
Charles C Hsu¹, Joseph M Herman¹, Michele M Corsini², Jordan M Winter³, Matthew D Callister⁴, Michael G Haddock², John L Cameron³, Timothy M Pawlik³, Richard D Schulick³, Michael J Swartz¹, Leonard L Gunderson⁴, Robert C Miller²
The Departments of Radiation Oncology & Molecular Radiation Sciences¹, and Surgery³; The Johns Hopkins Hospital, Baltimore, Maryland
The Department of Radiation Oncology², The Mayo Clinic, Rochester, MN
The Department of Radiation Oncology⁴, The Mayo Clinic, Scottsdale, AZ
- 5:00 pm Short **DIAGNOSTIC LAPAROSCOPY AND PERITONEAL CYTOLOGY IN THE STAGING OF UNRESECTABLE PANCREATIC CANCER**
Clark, C, Traverso LW
Department of General, Thoracic, and Vascular Surgery, Virginia Mason Medical Center, Seattle, WA
- 5:05 pm **Pancreas Club Business Meeting and Planning for 2009**
- 7:00 pm **Pancreas Club Dinner at University Club**

Please take a minute to visit with our exhibitors who have provided educational grants and support to make this activity possible.

AXCAN Pharma, Inc.
Digestive Care, Inc.
Ethicon Endo Surgery
Genzyme Biosurgery
Solvay Pharmaceuticals
Surgrx
Thompson Surgical

Please return your Pancreas Club Meeting evaluation to the registration desk before you leave.
CME certificates will be available in return for the evaluation.

Session I: 8:00 am

TIMING OF CHOLECYSTECTOMY FOR BILIARY PANCREATITIS: DO THE DATA SUPPORT CURRENT GUIDELINES?

Kaori Ito, MD, Hiromichi Ito, M.D., Edward E. Whang, MD

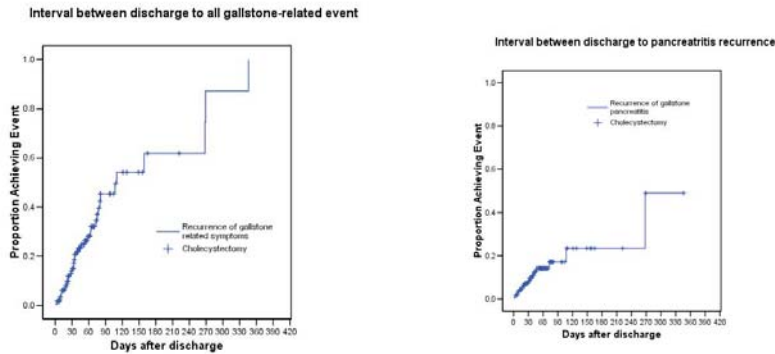
Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

BACKGROUND: Current guidelines suggest that cholecystectomy should be performed within 2 weeks after resolution of an episode of biliary pancreatitis (BP). We hypothesized that there is a high incidence of gallstone-related events within 2 weeks after discharge from index admission for BP in the absence of cholecystectomy.

METHODS: Medical records of 891 consecutive patients diagnosed with acute pancreatitis at our institution (1/199 –12/2005) were analyzed. Of 436 patients who had pancreatitis of biliary etiology, 281 patients underwent cholecystectomy following an episode of BP. These patients were allocated in the two groups: group A patients underwent cholecystectomy during index admission (during which pancreatitis was diagnosed, n=162). Group B patients underwent cholecystectomy following discharge from index admission (n=119). Incidence of gallstone-related events including recurrent pancreatitis, total length of hospital stay (index admission + admissions for recurrences and cholecystectomy), and postoperative morbidity and mortality rates were analyzed.

RESULTS: Groups were comparable in demographic variables, comorbidity rates, and disease severity. Thirty-nine (32.8%) group B patients experienced gallstone-related events (including 16 cases of recurrent pancreatitis) following discharge from index admission but prior to cholecystectomy. 12.5% of recurrences occurred within 1 week, 31.3% occurred within 2 weeks and 50% occurred within 4 weeks after discharge. Endoscopic sphincterotomy (ES) protected against preoperative recurrent pancreatitis but was associated with higher rates of other biliary events. Median total length of hospital stay was greater for group B than for group A (7 [range, 2-37] days vs. 5 [1-45] days, p=0.00). Postoperative recurrence and reoperation were more frequent for group B than for group A (10.1% vs. 3.1%, p=0.02 and 0% vs. 3.4%, p=0.02, respectively).

CONCLUSION: Current guidelines suggesting the appropriateness of waiting up to 2 weeks for cholecystectomy for BP may place patients at unacceptably high risk for recurrence. ES does not eliminate the need for cholecystectomy in these patients.



Session I: 8:15 am

Five-Year Outcome of a Randomized Trial Comparing Pylorus- and Duodenum-Preserving Pancreatic Head Resection for Chronic Pancreatitis

U. Adam, F. Makowiec, E. Fischer, T. Keck, H. Riediger, U.T. Hopt.

Department of Surgery, University of Freiburg, Germany

The 'ideal' technique of pancreatic head resection (PHR) for chronic pancreatitis (CP) is still discussed controversially. Although few trials have shown advantages for duodenum-preserving (DPPHR) techniques many centres continue to perform pancreaticoduodenectomies either as Whipple or pylorus-preserving (PPPD) procedures. After presentation of our initial results to the Society in 2004 we have performed further follow-up evaluations and can now report the five-year outcomes after randomization of patients to either DPPHR or PPPD. Our initial evaluations (perioperative course and three-year outcome) showed comparable results between the groups including quality of life.

Methods: We re-evaluated the outcome in 85 patients who were randomly assigned to DPPHR (n=42) or PPPD (n=43) between 1997 and 2001. After randomization for DPPHR the surgeon could decide, depending upon the morphology of CP, to perform either a FREY- (n=22) or a BEGER-procedure (n=20). Follow-up evaluations were performed by standardized questionnaires, supplemented by phone contacts with the home physicians. Median postoperative follow-up was now 61 months.

Results: Preoperatively, demographic and CP-related data showed no difference between the groups. After a median of 61 months following surgery 63% (PPPD) and 57% (DPPHR) of the patients were completely free of pain, respectively (n.s.).

Among the patients still suffering from pain (PPPD vs. DPPHR) 2% / 4% had pain every day, 7% / 7% had pain at least once per week, 7% / 14% at least once per month and 20% / 17% complained of pain less frequently (no difference between the groups). The pain scores as well showed no differences. Diabetes was documented in 44% (PPPD) and 45% (DPPHR), respectively, postoperative de novo-diabetes in 19% (PPPD) and 26% (DPPHR; n.s.). The frequencies of exocrine insufficiency (61% vs. 76%, p=0.12) and postoperative de-novo exocrine insufficiency (21% vs. 26%; p=0.57) were also comparable. Median gain in body weight was three kg after PPPD and two kg after DPPHR; n.s.). Further subgroup comparisons in the patients undergoing DPPHR (FREY vs. BEGER) did not reveal any differences in outcome.

Up to now 15 of the 85 patients died a median of 3.5 years after surgery, in most cases as a consequence of alcohol and/or tobacco use. Actuarial survival was 82% after five and 70% after ten years, without differences between the two randomized groups.

Conclusions: The late results of our randomized study demonstrate a comparable outcome after PPPD or DPPHR even five years after surgery. The type of PHR for CP might, therefore, be adapted to the morphology of CP and its local complications.

Session I: 8:30 am

A UNIFYING CONCEPT: PANCREATIC DUCTAL ANATOMY BOTH PREDICTS AND DETERMINES THE MAJOR COMPLICATIONS RESULTING FROM PANCREATITIS

William H Nealon¹, Manoop Bhutani², Taylor S. Riall¹, Gottumukkala Raju¹, Orhan Ozkan¹, Ryan Neilan¹

¹University of Texas Medical Branch, Galveston, TX;²M.D. Anderson Cancer Center, Houston, TX

Objective: We have long explored the relationship between pancreatic ductal abnormalities and the behavior of pseudocysts (PS) and in all aspects of pancreatitis. We have established a system to categorize ductal anatomy (ANN Surg 2002) Based upon this premise we obtained ERCP/MRCP in patients with chronic pancreatitis (CP) acute pancreatitis (AP) and necrotizing pancreatitis (NP). **Methods** From 1985 to 2006 we imaged and monitored patients with PS for persistence or complications during a period of observation and monitored for failure of percutaneous drainage (PD). NP was evaluated for subsequent episodes of recurrent AP after the initial event, for sepsis or persistent fistula after operative (OD) or PD. Each of these variables were correlated with the stratification system for ductal injuries. Our revised system defines Type I as normal duct, Type II as ductal stricture, Type III as occlusion/disconnected duct and Type IV as CP. **Results:** Summarized in the Table. Duct drainage alone was sufficient treatment of PS in CP confirming the significance of ductal dynamics in that disease. Pain, weight loss, recurrent pancreatitis and sepsis after NP correlated with Types II and III. 85% of pancreatic ascites/ruptured PS had type II or III. **Summary** Persistence, complications and failed PD of pseudocysts as well as major complications after NP all correlated with duct stricture or occlusion. Persistent fistula after debridement for NP as well as recurrent AP after NP are similarly correlated with duct injury. **Conclusion** Duct injury should be considered as one chooses the best modality to treat PS, and suspected when one encounters major complications or persistent pain, weight loss, pancreatitis, sepsis or fistula after NP. Therapy will be dictated in both AP and NP by the

Pancreatic Ductal Anatomy In Acute Pancreatitis (AP) Necrotizing Pancreatitis (NP) or Chronic Pancreatitis				
Pancreatic Duct Status	Type I	Type II	Type III	Type IV
Initial Dx PS (N=563)	152 (27%)	168 (30%)	90 (16%)	153(27%)
Spontaneous Resolution PS (N=142)	132 (96%)	6 (4%)	0	4 (3%)
Persistent PS (N=421)	20 (5%)	122 (29%)	130 (31%)	149 (35%)
PD Attempted	18/20	53/122	71/130	20/149
Persistent Fistula after PD (N=147)	3/18	27/53(21%)	71/71 (100%)	20/20 (100%)
Necrotizing Pancreatitis (N=174)	56 (32%)	47 (27%)	71 (41%)	n/a
Percutaneous Drainage (N=63)	22/56(39%)	21/47(45%)	20/71(28%)	n/a
Failed Percutaneous Drainage(41/63)	8/22(36%)	13/21(62%)	20/20(100%)	n/a
Operative Debridement 121/174(70%)	22/56(39%)	39/47(83%)	60/71(85%)	n/a
Persistent Fistula after OD 78/121(64%)	6/22(27%)	21/39(54%)	51/60(85%)	n/a
Recurrent Sepsis after Resolved Necrotizing Pancreatitis 44/174 (25%)	0/56 (0%)	17/47(36%)	27/71 (38%)	N/A
Recurrent Pancreatitis after Resolved Necrotizing Pancreatitis 96/174 (55%)	4/56 (7%)	29/47 (62%)	63/71 (89%)	n/a

Session I : 8:45 am

PROBIOTIC PROPHYLAXIS IN ACUTE PANCREATITIS; A PLACEBO CONTROLLED RANDOMIZED CLINICAL TRIAL

Marc GH Besselink¹, Hjalmar C van Santvoort¹, Erik Buskens^{2,3}, Marja A Boermeester⁴, Harry van Goor⁵, Harro M Timmerman¹, Vincent B Nieuwenhuijs⁶, Thomas L Bollen⁷, Bert van Ramshorst⁸, Ben JM Witteman⁹, Camiel Rosman¹⁰, Rutger J Ploeg⁶, Menno A Brink¹¹, Alexander FM Schaapherder¹², Cornelis HC Dejong¹³, Peter J Wahab¹⁴, Cees JHM van Laarhoven¹⁵, Erwin van der Harst¹⁶, Casper HJ van Eijck¹⁷, Miguel A Guesta¹⁸, Louis MA Akkermans¹, Hein G Gooszen¹ and the members of the Dutch Acute Pancreatitis Study Group

¹Dept of Surgery, University Medical Center Utrecht, Utrecht, ²Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, ³Dept of Epidemiology, University Medical Center Groningen, Groningen, ⁴Dept of Surgery, Academic Medical Center, Amsterdam, ⁵Dept of Surgery, Radboud University Nijmegen Medical Center, Nijmegen, ⁶Dept of Surgery, University Medical Center Groningen, Groningen, ⁷Depts of ¹Radiology and ²Surgery, St. Antonius Hospital, Nieuwegein, ⁹Dept of Gastroenterology, Gelderse Vallei Hospital, Ede, ¹⁰Dept of Surgery, Canisius Wilhelmina Hospital, Nijmegen, ¹¹Dept of Gastroenterology, Meander Medical Center, Amersfoort, ¹²Dept of Surgery, Leiden University Medical Center, Leiden, ¹³Dept of Surgery and NUTRIM, University Hospital Maastricht, Maastricht, ¹⁴Dept of Gastroenterology, Rijnstate Hospital, Arnhem, ¹⁵Dept of Surgery, St. Elisabeth Hospital, Tilburg, ¹⁶Dept of Surgery, Medical Center Rijnmond Zuid, Rotterdam, ¹⁷Dept of Surgery, Erasmus Medical Center, Rotterdam, ¹⁸Dept of Surgery, Vrije Universiteit Medical Center, Amsterdam, the Netherlands.

Background

Infectious complications and associated mortality are a major concern in acute pancreatitis. Enteral administration of probiotics allegedly prevents infectious complications, but convincing evidence based on a randomized comparison is lacking.

Methods

We conducted a multicenter, double-blind, placebo-controlled trial in 298 patients with predicted severe acute pancreatitis as defined by an Acute Physiology and Chronic Health Evaluation [APACHE II] score ≥ 8 , or Imrie score ≥ 3 , or C-reactive protein >150 mg/L. Within 72 hours after onset of symptoms a multispecies probiotic preparation or placebo was administered enterally twice daily for 28 days. The primary endpoint was the composite of infectious complications, *i.e.*, infected pancreatic necrosis, bacteremia, pneumonia, urosepsis, or infected ascites, during admission and a 90-day follow-up. Secondary endpoints included mortality and adverse events.

Results

Groups were comparable at baseline for patient characteristics and disease severity. Infectious complications occurred in 30 percent in the probiotics group (46 of 152 patients) and 29 percent in the placebo group (41 of 144 patients), resulting in a relative risk of 1.1 (95 percent confidence interval (CI) 0.8-1.5). Mortality was 16 percent in the probiotics group (24 of 152 patients) and 6 percent in the placebo group (9 of 144 patients), resulting in a relative risk of 2.5 (95 percent CI 1.2-5.3). In the probiotics group 9 patients developed bowel ischemia (8 with fatal outcome), whereas none did in the placebo group ($P = 0.004$). No additional differences in adverse events were found. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN38327949.

Conclusions

In patients with predicted severe acute pancreatitis, probiotic prophylaxis with this composition did not reduce the risk of infectious complications. Probiotic prophylaxis was moreover associated with an over two-fold increased mortality, and should therefore not be administered in this category of patients.

Session I: 9:00 am

EARLY ERCP IS ONLY BENEFICIAL IN PREDICTED SEVERE ACUTE BILIARY PANCREATITIS IN PRESENCE OF CONCURRENT CHOLESTASIS

H.C. van Santvoort¹, M.G. Besselink¹, A.C. de Vries², G. Cirkel¹, T.L. Bollen³, K. Fischer⁴, M.A. Boermeester⁵, B.L. Weusten⁶, A.F. Schaapherder⁷, P.D. Siersema⁸, B.J. Witteman⁹, V.B. Nieuwenhuijs¹⁰, H. van Goor¹¹, C.J. van Laarhoven¹², A.C. Tan¹³, M.P. Schwartz¹⁴, E. van der Harst¹⁵, P.J. Wahab¹⁶, C.H. van Eijck¹⁷, C.H. Dejong¹⁸, H.G. Gooszen¹, K.J. van Erpecum³ for the Dutch Acute Pancreatitis Study Group¹ Dept of Surgery, University Medical Center Utrecht, ²Dept of Gastroenterology, Erasmus Medical Center, Rotterdam, Dept of ³Radiology St. Antonius Hospital, Nieuwegein, ⁴Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, ⁵Dept of Surgery, Amsterdam Medical Center, Dept of ⁶Gastroenterology, St. Antonius Hospital, Nieuwegein, ⁷Dept of Surgery, Leiden University Medical Center, ⁸Dept of Gastroenterology, University Medical Center Utrecht, ⁹Dept of Gastroenterology, Gelderse Vallei Hospital, Ede, ¹⁰Dept of Surgery, University Medical Center Groningen, ¹¹Dept of Surgery, Radboud University Nijmegen Medical Centre, ¹²Dept of Surgery, St. Elisabeth Hospital, Tilburg, ¹³Dept of Gastroenterology, Canisius Wilhelmina Hospital, Nijmegen, ¹⁴Dept of Gastroenterology, Meander Medical Center, Amersfoort, ¹⁵Dept of Surgery, Medical Center Rijnmond Zuid, Rotterdam, ¹⁶Dept of Gastroenterology, Rijnstate Hospital, Arnhem, ¹⁷Dept of Surgery, Erasmus Medical Center, Rotterdam, ¹⁸Dept of Surgery and NUTRIM, University Hospital Maastricht

Introduction: It is controversial whether early ERCP is beneficial in patients with predicted severe acute biliary pancreatitis (ABP), in absence of cholangitis. Moreover, the effect of concurrent cholestasis on the potential benefits of ERCP in these patients is unclear. We therefore performed a prospective, observational multicenter study in parallel with the PRObiotics in PANcreatitis TRIal (PROPATRIA). Study aim was to investigate if early ERCP, as compared to conservative treatment, is associated with less complications and mortality in patients with predicted severe ABP without cholangitis.

Methods: During 2003-2007, all patients with predicted severe ABP (APACHE-II score ≥ 8 , or Imrie/modified Glasgow score ≥ 3 , or C-reactive protein >150 mg/L) were prospectively included in 15 Dutch hospitals. We excluded patients with potential cholangitis (bilirubin >20 $\mu\text{m/L}$ and/ or bile duct >8 mm with temperature $>38.5^\circ\text{C}$) and separately analyzed patients with and without cholestasis (bilirubin >40 $\mu\text{m/L}$ and/ or bile duct >8 mm with temperature $<38.5^\circ\text{C}$). The decision to perform ERCP was left to the treating physician, and varied between hospitals from 0% to 100%. Patients were assigned to the 'early ERCP group' (<72 hrs after onset of symptoms, usually on day of admission) or 'conservative group'. Logistic regression was applied to adjust for differences at baseline ($p < 0.2$) and disease severity (APACHE-II score). Overall complications included pancreatic necrosis, organ failure, pneumonia, bacteraemia, infected ascites and infected necrosis.

Results: 176 patients with predicted severe ABP were included, 13% (23/176) suffered from potential cholangitis and were excluded. From the remaining 153 patients, 51% (78/153) exhibited cholestasis and 49% (75/153) did not exhibit cholestasis. Of the patients with cholestasis, 67% (52/78) underwent early ERCP and 33% (26/78) underwent conservative treatment. At baseline, there were no significant differences between groups for patient characteristics and disease severity. Overall complication rate was significantly lower in the ERCP group than in the conservative group (25% vs 45%, $P=0.020$, adjusted relative risk [RR] 0.35, 95% confidence interval [CI] 0.13-0.99, $P=0.049$), including a significant reduction in the rate of $>30\%$ pancreatic necrosis (8% vs 31%, $P=0.010$). Mortality was non-significantly reduced in the ERCP group, as compared to the conservative group (6% vs 15%, $P=0.210$, adjusted RR 0.44, 95% CI 0.08-2.28, $P=0.330$). Of the patients without cholestasis, 39% (29/75) underwent early ERCP and 61% (46/75) conservative treatment. ASA-class was slightly greater in the conservative group ($P=0.016$), this was corrected by logistic regression. Groups were comparable for all other baseline characteristics. Overall complication rate and mortality were not significantly different between the early ERCP and conservative group (overall complications: 45% vs 41%, $P=0.81$ adjusted RR 0.73, 95% CI 0.19-3.12, $P=0.730$, mortality: 14% vs 17%, $P=0.750$, adjusted RR 1.36, 95% CI 0.49-3.76, $P=0.554$). Bile duct stones were detected in 51% (41/81) of patients undergoing early ERCP. In the conservative group, 10% (7/72) of patients underwent ERCP at later stages because of persistent or recurrent cholestasis.

Conclusion: In patients with predicted severe APB with cholestasis (but without cholangitis), early ERCP was associated with reduced complication rates, including extensive pancreas necrosis. Patients without cholestasis had no benefit from early ERCP.

Session I: 9:15 am

REPEATED INTERVENTION AGAINST ALCOHOL USE AT 6 MONTH INTERVALS IS BETTER THAN INITIAL INTERVENTION ALONE DURING HOSPITALIZATION IN REDUCING RECURRENT EPISODES OF ALCOHOLIC PANCREATITIS – PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Nordback Isto, Lappalainen-Lehto Riitta, Pelli Hanna, Järvinen Satu, Rätty Sari, *Sand Juhani* Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland

Introduction/Background The etiology of acute pancreatitis is considered as probably alcoholic, when associated with high alcohol consumption independent on the method of measurement (1). The continuing dependence on alcohol is the main determinant of a recurrent attack (2). Alcohol associated trauma recurs less often when an intervention against alcohol use has been given during a trauma admission (3). Such an initial intervention has been used also in alcoholic pancreatitis for years. This study was performed to investigate whether additional interventions further reduce the number of acute recurrent pancreatitis episodes.

Methods After written informed consent and before discharge from hospital, 120 patients recovering from their first acute alcoholic pancreatitis were randomized either to repeated intervention (n=59) or initial intervention (n=61) alone. The patients in the two groups did not differ from each other in demography, alcohol use or pancreatitis severity. The intervention, given by a trained specialist against substance abuse, contained parts of education, motivation and stressing of self-responsibility. Social problems were also focused on. Similar intervention was carried out in the study group at 6 month intervals, compared with initial intervention alone in the control group. Follow-up was 2 years, when the patients were re-checked for recurrent episodes. Hospital records were also scrutinized to confirm the diagnosis of recurrent pancreatitis. Additional 39 patients who did not enter the randomized study were separately analyzed retrospectively at 2 years for recurrent pancreatitis.

Results There were 9 recurrent episodes of pancreatitis in 5 patients in the repeated intervention group compared with 20 episodes ($p=0.02$) in 13 patients ($p=0.04$) in the initial intervention group. The recurrences were similar in number during the first 6 months (4 vs. 5, $p=0.67$), where after the repeated intervention group had fewer recurrences than the control group (5 vs. 15, $p=0.02$). Eleven out of the 39 non-randomized patients (28 %) had developed recurrent pancreatitis compared with 18 out of 120 patients (15%) in the randomized study ($p=0.07$). In the retrospective cohort more patients developed recurrent pancreatitis than in the repeated intervention arm of the prospective cohort ($p=0.01$). Such difference was not found between the non-randomized cohort and the randomized initial intervention arm of the prospective cohort ($p=0.14$).

Discussion/Conclusion The repeated intervention program against alcohol consumption appears to be more efficient than a single intervention during hospitalization in reducing the development of recurrent alcoholic pancreatitis.

Session I: 9:30 am Short

A COMPARISON OF DIRECT ENDOSCOPIC NECROSECTOMY AND USUAL TRANSMURAL ENDOSCOPIC TECHNIQUES FOR THE TREATMENT OF WALLED OFF PANCREATIC NECROSIS Timothy B. Gardner, MD¹; Prabheen Chahal, MBBS¹; Georgios I. Papachristou, MD²; Santhi Swaroop Vege, MD¹; Bret T Petersen, MD¹; Christopher J. Gostout, MD¹; Mark D. Topazian, MD¹; Naoki Takahashi, MD³; Michael G. Sarr, MD⁴; Todd H. Baron, MD¹

¹ *Miles and Shirley Fiterman Center for Digestive Diseases, Mayo Clinic Rochester, MN*

² *Department of Medicine, Division of Gastroenterology, Hepatology & Nutrition, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA.*

³ *Department of Radiology, Mayo Clinic, Rochester, MN*

⁴ *Department of Surgery, Mayo Clinic, Rochester, MN*

BACKGROUND & AIMS: Endoscopic therapy of symptomatic or infected pancreatic necrosis continues to evolve. We sought to compare direct endoscopic necrosectomy with conventional transmural endoscopic drainage for the treatment of organized pancreatic necrosis (walled-off pancreatic necrosis, WOPN).

METHODS: All patients referred to Mayo Clinic, Rochester since April 1998 for endoscopic drainage of WOPN were retrospectively identified. Each patient underwent standard endoscopic drainage consisting of transgastric or transduodenal cavity puncture, dilatation of the fistula tract, and large-bore stent placement. Patients were stratified into the direct endoscopic necrosectomy group if during any of their endoscopic procedures, the necrotic cavity was directly entered with an endoscope and necrosectomy was performed - all others were in the standard debridement group. Success was defined as resolution of the necrotic cavity without surgical or percutaneous intervention.

RESULTS: 45 patients were identified who met study criteria – 25 underwent direct endoscopic necrosectomy and 20 underwent standard endoscopic drainage. There were no differences in baseline patient characteristics. Successful cavity drainage was accomplished in 88% of those who underwent direct endoscopic necrosectomy vs. 45% for those receiving standard drainage ($p < 0.01$) without an increase in the total number of procedures. The maximum size of tract dilatation was larger in the direct endoscopic necrosectomy group (16.8 mm vs. 14.2 mm, $p < 0.02$). Complications were limited to mild peri-procedural bleeding with equivalent rates between groups.

CONCLUSIONS: Direct endoscopic necrosectomy achieves higher rates of successful resolution of walled-off pancreatic necrosis without a concomitant increase in the number of endoscopic procedures, complication rate or time to resolution compared with standard endoscopic drainage.

Session I : 9:35 am Short

AUTOIMMUNE PANCREATITIS: APPLICATION OF CURRENT DIAGNOSTIC CRITERIA ARE SUBOPTIMAL

Giday, Samuel A.1; Buscaglia, Jonathan M.1; Mukkai Krishnamurty, Devi1; Chen, Terina2; Kalloo, Anthony N.1; Canto, Marcia I.1; Kantsevov, Sergey V.1; Okolo, Patrick 1; Hruban, Ralph H.2; Jagannath, Sanjay B.1

1. *Medicine, Johns Hopkins Institute, Baltimore, MD, USA.*

2. *Pathology, Johns Hopkins Hospital, Baltimore, MD, USA.*

Autoimmune pancreatitis (AIP) is a clinical entity that is being recognized with increasing prevalence. However, the pre-operative diagnosis of AIP is difficult given its similar clinical presentation to pancreatic cancer. Several diagnostic criteria have been proposed, but most widely utilized is the revised criteria proposed in June 2006 by the Japanese Research Committee of Intractable Diseases of the Pancreas which requires the presence of diffuse or segmental pancreatic ductal irregularity and diffuse or localized pancreatic enlargement on imaging along with one of the following; high serum level of γ -globulin, IgG or IgG4, positive autoantibodies and marked interlobular fibrosis and prominent infiltration of lymphocytes and plasma cells in the periductal area on biopsy .

AIM: To correlate the revised Japanese diagnostic criteria for AIP to a cohort of patients with resected histologically proven autoimmune pancreatitis **METHODS:** Prospective pathology databases were queried for autoimmune pancreatitis that were evaluated and/or treated at Johns Hopkins Hospital from 2002-2007. AIP histology was defined as the presence of lymphoplasmacytic infiltration, periductal inflammation, fibrosis and periphlebitis. Radiographic imaging (CT, EUS, MRI) and clinical data was analyzed.

RESULTS: 30 patients (18 males, mean age 64.1 years, 80% Caucasian) had pancreatic resection with pathologic confirmation of AIP. Imaging revealed the following findings: pancreatic mass (45%), focal prominence without mass lesion (24%), diffuse enlargement (17%), and normal pancreas (14%). 24 patients underwent an ERCP and/or MRCP, and 4/24 (17%) had demonstrable pancreatic ductal narrowing or irregularity. Extrapancreaticobiliary organ involvement was found in 6% (N=2) of patients. Biliary strictures were present in 87% of the patients. Of the 16 patients who underwent preoperative tissue biopsy, N=10 had non diagnostic pathology, N=5 had cellular atypia, N=1 had AIP. Serum IgG4 levels were elevated in 12/29 (41%) of patients. When applying the revised Japanese Research Committee of Intractable Diseases of the Pancreas diagnostic criteria to the 27 patients that had serum IgG4 determination, preoperative biopsy and cross-sectional abdominal imaging, only 44% of the patients would have been diagnosed accurately.

CONCLUSIONS: When applied to a highly selected single center referral population in the United States, current Japanese guideline on the diagnosis of autoimmune pancreatitis leads to suboptimal diagnosis.

Session I: 9:40 am Short

COMBINED RESECTION OF EXTRAPANCREATIC NERVE PLEXUS MAY IMPROVE THE SURVIVAL AFTER PANCREATODUODENECTOMY FOR SMALL PANCREATIC CANCER

S. Egawa, F. Motoi, M. Unno

Hepato-Biliary-Pancreatic Surgery, Tohoku University, Sendai, JAPAN

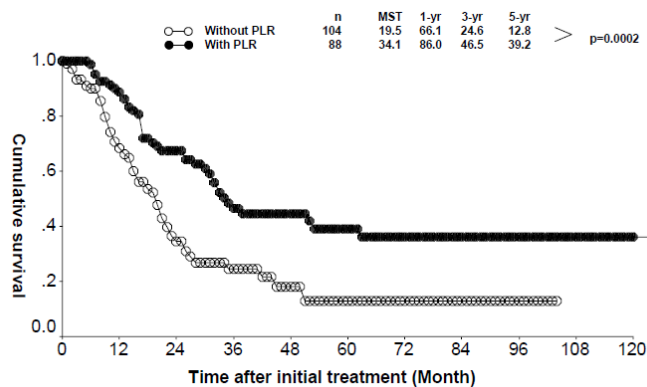
Background: Japan Pancreas Society (JPS) has been hosting the nationwide pancreatic cancer registry and published the accumulated data on-line with English subtitles (http://www.jstage.jst.go.jp/browse/suizo/22/1/_contents/-char/ja/). Several randomized studies showed that extended lymph node dissection should not be performed in pancreatic cancer, and that adjuvant chemotherapy improves disease free survival. In order to find the role of surgery, the combined resection of extrapancreatic nerve plexus was investigated

Methods: Patients with invasive pancreatic cancer were registered according to the latest JPS and UICC classifications. The survival rate was calculated by actuarial method and tested by generalized Wilcoxon method. The data based on published PDF files are indicated as (e-page).

Results: Out of 11407 patients with invasive cancer, 1049 patients (9.1%) had tumor less than 2 cm (TS1) (e239). 94.3% of patients with TS1 tumor underwent pancreatectomy. R0 resection was performed in 66% of patients and the 5-year survival rate was 37.5% (e240). The extent of lymph node dissection (D0-D3) and combined resection of portal vein did not correlate with survival of patients with TS1 tumor in the pancreatic head (e241, 242). Amazingly, combined resection of peripancreatic nerve plexus significantly ($p=0.0002$) improved the survival of same cohort of patients ($n=88$) (Figure, e243). Combined resection of plexus did not improve the patients with TS2 (2-4 cm) tumor ($n=410$) and larger ones.

Discussion:

Surgeons in most Japanese leading institutions are aware of extended lymph node and retroperitoneal dissection is no longer helpful for patients with pancreatic cancer. JPS classification recognizes plexus invasion as a prognostic factor independent of SMA or CA invasion, while UICC classification has no precise description. The data from JPS database suggest that we should perform sufficient resection especially in small pancreatic cancer and may warrant multi-institutional control study to investigate the significance of plexus resection for TS1 tumor together with standardization of procedures.



Session II: 1:00 pm

APPLYING PROTEOMIC BASED BIOMARKER TOOLS FOR THE ACCURATE DIAGNOSIS OF PANCREATIC CANCER

John D. Christein¹, Kyoko Kojima², Senait Asmellash³, James A. Mobley⁴
*Section of Gastrointestinal Surgery¹ and Division of Urology², Department of Surgery;
Department of Microbiology²; Department of Biochemistry and Molecular Genetics³;
University of Alabama at Birmingham*

BACKGROUND The proteome is the biologic protein signature produced by the genome and varies with physiologic and disease states. No proteomic studies have attempted to differentiate the proteome of those with pancreatic cancer from those without malignant disease.

AIM To apply proteomic technology to body fluids and accurately differentiate those with from those without pancreatic disease.

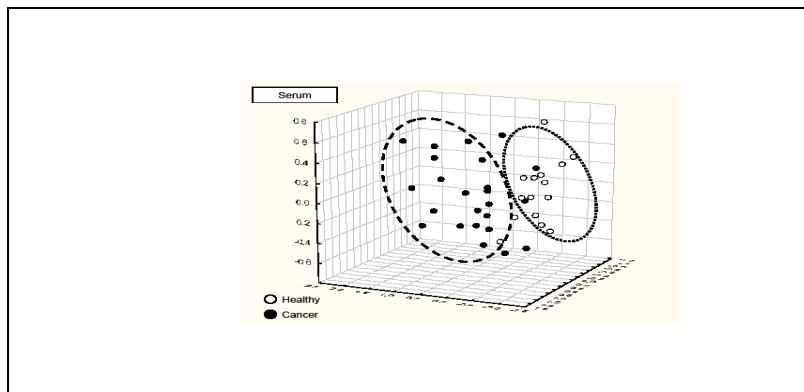
METHODS

Serum, plasma, and urine samples were prospectively collected from patients with and without pancreatic disease. Endoscopic ultrasound biopsy was used to determine normal (N), cancer (CA), or chronic pancreatitis (CP). A high throughput method, using high affinity solid lipophilic extraction resins, enriched low molecular weight protein for extraction with a high speed 200Hz matrix-assisted laser desorption/ionization-time of flight mass spectrometer (Bruker Ultraflex III). Samples from N, CA, and CP groups underwent software processing with FlexAnalysis, Clinprot, MatLab, and Statistica to align and normalize spectra. Non-parametric pairwise, multidimensional scaling, hierarchical analysis, and leave one out cross validation using a k-means based approach completed the analysis. Sensitivity (sn) and specificity (sp) of group comparisons were determined.

RESULTS Fifty serum samples (15 N, 24 CA, 11 CP) underwent analysis. Using 6 serum features, we accurately differentiated CA from N (sn 89%, sp 94%) (see Figure 1), CA from CP (sn 89%, sp 61%), and N from both CA and CP combined (sn 89%, sp 76%). When combined with 14 urine features, we differentiated CA from N and CP combined with a sensitivity of 94%. Interestingly, the plasma samples (considered by the Human Proteome Organization to be the preferred biological fluid) did not show significant differences between patient groups.

CONCLUSIONS Proteomic analysis of human serum and urine can provide a high level of predictability for diagnosing pancreatic cancer. The proteomic analysis of biologic fluids may be used to screen individuals for pancreatic cancer or differentiate benign from malignant disease.

Figure 1. Multidimensional scaling plot of serum protein features of those with pancreatic cancer (●) and those without disease (○)



Session II: 1:15 pm

Induction of Osteopontin Expression by Nicotine and Cigarette Smoke in the Pancreas and Pancreatic Ductal Adenocarcinoma Cells

Galina Chipitsyna¹, Qiaoke Gong¹, Rathai Anandanadesan¹, Akram Zaaqoq¹, Surinder K. Batra², David T. Denhardt³, Charles J. Yeo¹, Hwya A. Arafat¹

¹*Department of Surgery, Thomas Jefferson University, Philadelphia, PA,* ²*Department of Biochemistry and Molecular Biology, Nebraska Medical Center, Omaha, NE,* ³*Department of Cell Biology and Neuroscience, Rutgers University, New Brunswick, NJ*

Background: Pancreatic ductal adenocarcinoma (PDA) is a lethal disease with etiological association with cigarette smoking. Nicotine, an important component of cigarettes, exists at high concentrations in the bloodstream of smokers. Osteopontin (OPN) is a secreted phosphoprotein that confers on cancer cells a migratory phenotype and activates signaling pathways that induce cell survival, proliferation, invasion, and metastasis. Here, we investigated the potential molecular basis of nicotine role in PDA through studying its effect on OPN.

Methods: OPN mRNA and protein expression in nicotine-treated AsPC PDA cells was analyzed by real time PCR and ELISA, OPN promoter activity by Luciferase Reporter Assay System, and MAPkinase phosphorylation by Western immunoblotting. Pancreatic OPN was analyzed by real time PCR and immunofluorescence staining in Sprague Dawley rats exposed to tobacco smoke. OPN in human PDA tissue was analyzed by immunohistochemistry.

Results: Nicotine significantly increased OPN mRNA and protein secretion in AsPC cells and activated OPN transcription. Nicotine-OPN mRNA induction was inhibited by a nicotine acetylcholine receptor antagonist, mecamylamine. Nicotine activated the phosphorylation of ERK1/2, but not p38 or c-Jun NH2-terminal MAP kinases. Inhibition of ERK1/2 activation reduced the nicotine-induced OPN synthesis. Rats exposed to cigarette smoke showed a dose-dependent increase in pancreatic OPN. In human PDA, intense OPN immunoreactivity was seen in the malignant ducts and the surrounding pancreatic acini.

Conclusion: Our data suggest that nicotine may contribute to PDA through upregulation of OPN; they provide the first insight into a nicotine-initiated signal transduction pathway that regulates OPN as a possible tumorigenic mechanism in PDA.

Session II: 1:30 pm

EPITHELIAL TO MESENCHYMAL TRANSITION IN PANCREATIC CANCER: EXPRESSION AND ROLE OF TRANSCRIPTION FACTORS SNAIL, SLUG, AND TWIST

Hubert G. Hotz, Birgit Hotz, Elisabeth Schellhaas, Heinz J. Buhr

Dept. of Surgery I, Charité School of Medicine, Campus Benjamin Franklin, Berlin, Germany

Background: Epithelial to mesenchymal transitions (EMT) are vital for tumor progression and metastasis. Several inducers of EMT are transcription factors that repress E-Cadherin expression such as Snail, Slug and Twist. This study examined expression and role of these transcription factors in pancreatic cancer.

Methods: Expression of Snail, Slug, Twist, and E-Cadherin was detected by immunohistochemistry in tissue samples from 36 patients with pancreatic ductal adenocarcinoma. Four human pancreatic cancer cell lines (Capan-1, HPAF-2, MIAPaCa-2, Panc-1) and human endothelial cells (HUVEC; control) were analyzed by RT-PCR, real-time PCR and western blotting. A nude mouse model was applied for in vivo experiments: tumors were derived from the four human pancreatic cancer cell lines and animals (12 per group) observed for 14 weeks. Expression of transcription factors and E-Cadherin was correlated with tumor spread and metastasis (dissemination score).

Results: 78% of human pancreatic cancer tissues expressed Snail, 50% displayed positive expression of Slug. Twist showed no or only weak expression. A strong Snail expression in undifferentiated cancer cell lines (MIAPaCa-2, Panc-1) was associated with low E-Cadherin and extensive metastasis in mice. In contrast, low Snail and strong E-Cadherin expression in more differentiated cells lines (Capan-1, HPAF-2) corresponded with a significantly reduced tumor spread in animals (table). Snail mRNA expression correlated positively with metastatic potential of the cancer cells ($r = 0.8$), whereas a negative correlation was found between E-Cadherin and metastasis ($r = -0.9$).

$p < 0.05$: * vs. MIAPaCa-2 / Panc-1

Conclusions: The transcription factors and EMT-regulators Snail and Slug are expressed in pancreatic cancer but not in normal tissue. The upregulation of Snail is associated with low expression of the adhesion molecule E-Cadherin, suggesting a role for Snail in the progression and metastasis of human pancreatic carcinomas.

Cell line	Relative mRNA concentration		Metastasis (Dissemination-Score)
	Snail	E-Cadherin	
Capan-1	0,39	7,64	5,9 ± 0,6*
HPAF-2	1,03	5,58	6,9 ± 0,5*
MIAPaCa-2	7,17	0,10	14,3 ± 0,9
Panc-1	11,42	0,69	10,8 ± 0,7
HUVEC (control)	1	1	

Session II: 1:45 pm

RECURRENT CHROMOSOMAL ABERRATIONS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMNS)

S. Fritz.¹, C. Fernandez-del Castillo.¹, M. Mino-Kenudson.², S. Crippa.¹, J. M. Batten.², A. T. Nguyen.², S. P. Thayer.¹, V. Deshpande.², G. Y. Lauwers.², A. L. Warshaw.¹, and A. J. Iafrate.²

¹*Departments of Surgery and* ²*Molecular Diagnostics Laboratory, Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.*

Introduction/Background: The biological behavior of IPMNs and IPMN-associated adenocarcinoma is different from pancreatic ductal adenocarcinoma in having a less aggressive tumor growth and significant improved survival after surgical resection. Although a number of shared genetic mutations have been identified, the molecular mechanisms underlying the clinical behavior of IPMNs are poorly understood. Array-based comparative genetic hybridization (array CGH) allows identification of recurrent genetic imbalances and global changes and consequently localization of genes that may contribute to the progression of normal epithelium to pre-malignant and then invasive cancer.

Methods: A series of 20 IPMN specimens (6 females and 14 males) was prospectively identified and subdivided by histology criteria into those with low-grade dysplasia (n=7), moderate dysplasia (n=5), and malignant IPMN (high-grade dysplasia and invasive cancer) (n=8). DNA was isolated from fresh frozen tissue, and array CGH was performed using high-resolution oligonucleotide arrays (Agilent Technologies, Santa Clara, CA). In addition, the *KRAS* locus on exon 2 was determined by PCR amplification and bi-directional sequencing. To confirm our findings based on array CGH, we evaluated chromosome 6q, 6p, and 18q copy numbers by fluorescence in situ hybridization (FISH).

Results: While none of the IPMNs with low-grade dysplasia (IPM adenomas) displayed detectable chromosomal aberrations, IPMNs with moderate dysplasia (borderline IPMNs) showed an average of 3.6 gains (range 1-7) and 6.4 losses (range 2-14), and malignant IPMNs (specimens with carcinoma in situ and invasive carcinoma) had an average of 7.1 gains (range 1-16) and 10.3 losses (range 6-14). In IPMNs with moderate dysplasia and malignant IPMNs, loss of 6q occurred in 80% and 75% respectively, while a gain of chromosome 7 was found in 61.5% overall. Other commonly lost regions were located on chromosome 5q, 10q, 11q, 13q, 18q, and 22. Distinct high-level amplifications were seen on 11q13.2 and 12p13.2. FISH analysis using 6q and 18q probes confirmed copy number loss in IPMNs specimens with moderate dysplasia and malignant features. The overall incidence of *KRAS* mutations at codon 12 was 40.0% (4/7 IPMNs with low-grade dysplasia, 2/5 IPMNs with moderate dysplasia, and 2/8 malignant IPMNs, P = ns).

Conclusions: These data provide evidence for a number of cytogenetically defined recurrent aberrations that are characteristic for IPMNs. While some are similar to ductal adenocarcinoma, some are distinct. The observations may provide a basis for understanding the unique biologic and clinical behavior of IPMNs and help to identify potential oncogenes and tumor suppressor genes that may be involved in the multistep tumorigenesis of these neoplasms.

Session II: 2:00 pm

PANCREATIC CANCER CELL GROWTH IS ATTENUATED BY THE EXPRESSION OF N-MYC DOWNREGULATED GENE

E. Angst^{1,2}, S. Hasan¹, M. Kim¹, A. Li¹, B. Gloor², H. A. Reber¹, O. J. Hines¹, G. Eibl¹

¹Hirshberg Laboratories for Pancreatic Cancer Research, Department of Surgery, David Geffen School of Medicine at UCLA, ²Department of Visceral and Transplant Surgery, University Hospital, Berne, Switzerland

Introduction: The study of N-myc downregulated gene-1 (NDRG1, Cap43, RIT42), a 43 kDa protein, in tumor growth and metastasis has recently gained interest as a potential therapeutic target. Although its function and molecular signals are largely unknown, loss of NDRG1 expression in colon cancer is associated with a more aggressive tumor phenotype and more metastatic spread. In human pancreatic cancers the expression of NDRG1 is correlated with better differentiated tumors and improved clinical outcome. The aim of the present study was to elucidate the functional role of NDRG1 in human pancreatic cancer cells *in vitro*.

Methods and Results: Six human pancreatic cancer cells lines (AsPC-1, BxPC-3, Capan-2, HPAF-II, MiaPaCa-2, and Panc-1) with varying degree of differentiation were screened for NDRG1 mRNA and protein expression by real time PCR and Western blotting. NDRG1 transcripts and proteins were detected in all cell lines with a strongest expression in the moderately differentiated cell line BxPC-3. To clearly delineate the functional role of NDRG1 in pancreatic cancer cells, HPAF-II cells, displaying weak NDRG1 expression, were transfected with the full-length *NDRG1* cDNA cloned into the pcDNA3.1+ vector. Stable cell clones were selected with neomycin. Successful transfection was confirmed by real-time PCR and Western blotting, which demonstrated marked over-expression of NDRG1. Stable expression of NDRG1 was verified by repeated protein measurements of cell clones growing in culture for up to four weeks. Three separate clones expressing either NDRG1 or the control vector were analyzed for cell growth using cell count and MTT assay for 24 to 96 hours. While HPAF-II clones stably expressing the empty vector showed a 457±44% increase in cell count at 96 hours, NDRG1-expressing HPAF-II cells demonstrated a 241±57% increase ($p<0.01$). The MTT assay confirmed these results with a 227±4% and 154±13% increase ($p<0.01$) in absorbance in control and NDRG1-expressing HPAF-II cells, respectively. To elucidate potential molecular targets of NDRG1, a Tumor Metastasis PCR Array comprising of 84 different metastasis-related genes, was performed. Compared to control clones, NDRG1 expressing HPAF-II cells displayed a significant (>2-fold decrease or increase in gene expression) difference in 14 genes, most of them with known functions in intercellular adhesion (e.g. *CD44*, *E-cadherin*, *ITGB3*) and matrix degradation (e.g. *MMP10*, *MMP11*).

Conclusion: In summary we found that expression of NDRG1 correlated with reduced cell growth in human pancreatic cancer cells. In addition, gene array analysis detected differences in several metastasis-related genes, suggesting a functional role for NDRG1 in pancreatic cancer cell adhesion and invasion.

Session II : 2:15 pm

PREOPERATIVE DETECTION OF FAMILIAL PANCREATIC NEOPLASMS BY ENDOSCOPIC ULTRASONOGRAPHY(EUS), MULTIDETECTOR COMPUTED TOMOGRAPHY (CT), AND/OR MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY (MRCP)

Canto, Marcia I.^{1,3}; Schulick, Richard D.^{2,3}; Goggins, Michael G.^{1,5}; Yeo, Charles J.⁶; Cameron, John L.^{2,3}; Fishman, Elliot K.⁴; Kamel, Ihab R.⁴; Hruban, Ralph H.^{5,3}

1. Division of Gastroenterology, Johns Hopkins University, Baltimore, MD, USA.
2. Surgery, Johns Hopkins Medical Institutions, Baltimore, MD, USA.
3. Oncology, Johns Hopkins Medical Institutions, Baltimore, MD, USA.
4. Radiology, Johns Hopkins Medical Institutions, Baltimore, MD, USA.
5. Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, USA.
6. Surgery, Jefferson University, Philadelphia, PA, USA.

Lives can be saved if high grade dysplasia (HGD) and early familial ductal adenocarcinoma (FPC) can be detected in high-risk individuals (HRI) before these lesions progress to advanced disease. AIM: 1) To characterize pancreatic neoplastic lesions detected by imaging tests in HRI. 2) To compare the diagnostic yield and incremental benefit of EUS over CT/MRCP for detection of pancreatic neoplasms in HRI. 3) To determine the incremental benefit of FNA over EUS alone.

METHODS: We analyzed data prospectively collected(1998-2007) from 2 screening studies and our clinical screening program. Adult HRI with Peutz-Jeghers syndrome (PJS) or first-degree relatives from FPC kindreds with at least 2 affected had either multi-detector CT (1998-2004) and/or MRI/MRCP (2004-2007), and EUS. Radiologic and EUS features of each preoperatively detected lesion were compared with the pathologic findings. The diagnostic yield of each imaging modality was calculated on a per lesion basis.

RESULTS: Of 165 patients who had EUS and CT/MRCP, 19 asymptomatic HRI (16 FPC relatives, 2 PJS) underwent partial resection (15), partial followed by completion pancreatectomy (3), or total pancreatectomy (1) for 44 pancreatic lesions (size range 2.6-21 mm) detected by EUS, CT, and/or MRCP. There were 32 cysts: branch-duct intraductal papillary mucinous neoplasm (IPMN) (n=21), incipient IPMN (n=2), or large PanIN (n=4). 2 IPMNs with HGD were small (15 and 20 mm)with no mural nodules; the rest of the IPMNs had low or moderate grade dysplasia. EUS visualized 4 cysts that were "large" PanIN-3 (3-4 mm). There were 4 masses > 10 mm: invasive ductal CA (1), serous cystadenoma (1), chronic pancreatitis (1), and a pancreatic endocrine neoplasm (PEN). There were 8 nodules < 10 mm: PEN (2), incipient IPMNs (2), and acinar nodules (4) associated with pancreatic intraepithelial neoplasia (PanIN). All 7 neoplasms with HGD/CA were 3-21 mm in size. CT, MRI/MRCP, and EUS detected 10/34 (29%), 13/26 (50%), and 43/44 (98%) of all lesions, respectively. MRCP was superior to CT for detection of cystic neoplasms (71% vs. 14%, p<001). The overall incremental benefit of EUS over MRCP and/or CT for detection of proven pancreatic neoplasia was 21/43 (49%) and was independent of lesion size - (12/31 (39%) for IPMNs or PanINs, 2/4 (50%) for masses, and 7/8 (88%) for nodules). EUS-FNA was suggestive of neoplasia in only 51% of lesions and did not change the EUS diagnosis in all cases.

CONCLUSION: Most pancreatic neoplasms detected by screening tests are small and low-grade, but 6% of IPMNs < 3 cm may contain HGD. EUS detects almost twice as many neoplastic lesions as CT/MRCP, regardless of size. FNA adds little to EUS.

Session II: 2:30 pm Short

ASCORBATE-INDUCED CYTOTOXICITY IN PANCREATIC CANCER

Juan Du, Mark Levine, Brett Wagner, Garry R. Buettner, Joseph J. Cullen
Departments of Surgery and Radiation Oncology, University of Iowa College of Medicine and NIH/NIDDK.

Background: Pharmacological concentrations of ascorbate easily achieved in humans may be effective in cancer therapeutics (PNAS, 104:8749, 2007). We hypothesized that ascorbate concentrations achievable with intravenous dosing may be cytotoxic in pancreatic cancer where the five year survival is < 3%.

Methods: Pancreatic cancer cell lines were treated with ascorbate (0, 5, and 10 mM) for one hour and viability and clonogenic survival were determined. In addition, the immortal H6c7 cell line (pancreatic ductal epithelial cell) and its derivatives, H6c7eR-pBp (retroviral vector control), H6c7eR-Kras (H6c7 cells expressing K-ras oncogene), and H6c7eR-KrasT (tumorigenic H6c7 cells expressing K-ras oncogene) (Cancer Res., 65:5045, 2005) were treated with ascorbate (0, 5, and 10 mM) and viability were determined. MIA PaCa-2 pancreatic cancer cell lines with functional mitochondria (ρ^+) and the same lines without functional mitochondria (ρ^0) (J. Biol. Chem. 281:37416, 2006), were treated with ascorbate and clonogenic survival determined. The oxygen electrode method was used to determine H_2O_2 production. MIA PaCa-2 tumor cells (2×10^6) were delivered subcutaneously into the flank region of nude mice and allowed to grow until they reached 3 mm in greatest dimension at which time they were randomized to receive either ascorbate (4g/kg) or osmotically equivalent i.p. saline as a control (1 M) given to mice i.p. every day for two weeks.

Results: There was a time and dose-dependent increase in measured H_2O_2 production with increased concentrations of ascorbate. Ascorbate decreased clonogenic survival and viability in pancreatic cancer cell lines in a dose-dependent manner. Ascorbate had no effect on the H6c7 cell line, but decreased viability in the H6c7 cell lines that express K-ras oncogene. Ascorbate (5 and 10 mM) decreased viability in all human pancreatic cancer cell lines tested. In ρ^+ cells, ascorbate resulted in a dose-dependent decrease in clonogenic survival, but no cytotoxicity in the ρ^0 cells. The group of animals that received ascorbate had significantly slower tumor growth when compared to the controls receiving osmotically equivalent saline ($P < 0.0001$, $n = 5-8$ /group). On day 15 of treatment, there was a 3.5-fold decrease in tumor growth in animals receiving ascorbate when compared to controls.

Conclusions: Pharmacological doses of ascorbate, achievable in humans when given intravenously, may have potential for therapy in pancreatic cancer. The ascorbate-induced cytotoxicity in pancreatic cancer cells may be mediated by a mitochondrial mechanism. Support: NIH grants CA115785, CA66081, the Medical Research Service, Department of Veterans Affairs, and the Susan L. Bader Foundation of Hope.

TUMOR-DERIVED ICAM-1 MEDIATES TUMOR-ASSOCIATED LEUKOCYTE INFILTRATION.

C. L. Roland^{1,2}, S. P. Dineen^{1,2}, J. Toombs^{1,2}, J.G. Carbon^{1,2}, C. W. Smith³, R. A. Brekken^{1,2}, C. C. Barnett, Jr^{1,2}.

¹*Division of Surgical Oncology, Department of Surgery, and the* ²*Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical School, Dallas, Texas and* ³*Baylor College of Medicine, Houston, Texas*

Introduction: Intercellular adhesion molecule-1 (ICAM-1) is a cell surface glycoprotein that mediates cell-cell and cell-matrix adhesion through homotypic and heterotypic interaction with LFA-1 and MAC-1 on neutrophils (PMNs) and macrophages facilitating tight adhesion and transendothelial migration. In the setting of locally advanced pancreatic cancer increased expression of ICAM-1 on the tumor correlates with poor prognosis. It is postulated that TNF- α , IL-1 and IFN- γ released by tumor cells increase tumor ICAM-1 expression. In vitro studies have demonstrated increased adhesion of human pancreatic carcinoma cells to microvascular endothelium in the presence of PMNs, suggesting that PMNs participate in tumor adhesion and metastasis. The aim of this study was to investigate the function of host versus tumor derived ICAM-1 in pancreatic cancer progression and metastasis using ICAM-1-null (ICAM-1^{-/-}) mice.

Methods: Murine pancreatic tumor cells (Pan02) were found to be positive for ICAM-1. 2.5 x 10⁵ Pan02 cells were injected into the tail of the pancreas of wild-type (WT) or ICAM-1^{-/-} mice. Tumors were established for 6 weeks and the animals were then sacrificed. Liver, lymph node, GI and peritoneal metastases were evaluated by visual inspection. Tumor weights were calculated in conjunction with residual pancreas. Tissues were snap frozen in liquid nitrogen. Frozen tumor sections were stained with rat anti-mouse ICAM-1 and rabbit anti-myeloperoxidase (MPO, a marker of PMNs) and incubated with the appropriate fluorescently-labeled secondary antibody. Nuclei were stained with DAPI and sections were examined on a Nikon E600 microscope and analyzed with NIS Elements.

Results: At sacrifice, there was no difference in final combined tumor/pancreas weights between WT and ICAM-1^{-/-} mice (0.52g vs. 0.35g; p=0.28). There was also no difference in the metastatic incidence or the number of metastatic events between the two groups. Taken together, these data indicate that loss of host ICAM-1 does not effect pancreatic cancer progression and metastasis. To further investigate the interaction PMNs and tumor cells via ICAM-1 expression; colocalization of ICAM-1 and PMNs was performed on frozen sections of tumor tissue harvested from WT and ICAM-1^{-/-} animals. In tumors from WT and ICAM-1^{-/-} animals, ICAM-1 and MPO co-localized at the invasion front, indicating a role for ICAM-1-mediated PMN activity at the zone of tumor invasion. Interestingly, we found an increase in the number of PMNs in tumors from ICAM-1^{-/-} mice compared to WT animals, indicating that tumor derived ICAM-1 is sufficient for PMN infiltration of pancreatic tumors.

Discussion: Using an ICAM-1 null background, we investigated the function of host and tumor cell-derived ICAM-1 in pancreatic cancer progression and PMN infiltration. Our data demonstrates that host ICAM-1 is not necessary for pancreatic cancer progression and that tumor-derived ICAM-1 is sufficient as a docking site for PMNs at the tumor invasion front. Further, these findings suggest that PMNs in this location participate in the progression of pancreatic cancer.

Session II: 2:40 pm Short

EFFECT OF HOSPITAL PANCREATECTOMY VOLUME ON MARGIN STATUS FOR PANCREATIC CANCER RESECTIONS IN THE UNITED STATES

Karl Y. Bilimoria^{1,2}; Mark S. Talamonti^{1,3}; Stephen F. Sener³; Malcolm M. Bilimora³; Andrew K. Stewart²; David P. Winchester^{2,3}; Clifford Y. Ko^{2,4}; David J. Bentrem¹

1 Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL; 2 Cancer Programs, American College Surgeons, Chicago, IL; 3 Department of Surgery, Evanston Northwestern Healthcare, Chicago, IL 4 Department of Surgery, University of California, Los Angeles (UCLA) and VA Greater Los Angeles Healthcare System, Los Angeles, CA

BACKGROUND: The volume-outcome relationship has been repeatedly demonstrated for pancreatectomy; however, identifying reasons for this association has been challenging. Margin status is associated with pancreatic cancer outcomes; however, it is unknown whether margin-negative resection rates vary by hospital volume. Our objective was to evaluate the impact of hospital pancreatectomy volume on margin status.

METHODS: Patients who underwent resection for localized pancreatic adenocarcinoma were identified from the National Cancer Data Base (1998-2004). Multivariable regression modeling adjusting for patient, tumor, and hospital factors was used to assess predictors of margin involvement and to evaluate the effect of margin status on survival.

RESULTS: Of 15,507 patients, 23.3% had positive resection margins (13.3% microscopic; 10% gross). From 1998 to 2004, there was not a significant change in margin-positive resection rates. On multivariable analysis, increasing T stage and nodal involvement were associated with a higher likelihood of margin involvement ($P<0.0001$). Patients treated at lowest-volume hospitals (based on average annual hospital pancreatectomy volume) were more likely to have positive margins than patients undergoing surgery at highest-volume hospitals (27.4% vs. 20.2%; Odds Ratio 1.60, 95% CI 1.26 - 2.04; $P<0.0001$), despite low-volume hospitals operating on a lower proportion of T3 tumors compared to high-volume centers (58.7% vs. 63.3%). On multivariate analysis, margin involvement was associated with a 28% higher risk of death compared to margin-negative resections (5-year observed survival: 11.7% vs. 5.0; Hazard Ratio 1.42, 95% CI 1.24-1.64; $P<0.0001$). Margin status accounts for ~5% of the volume-based variation in long-term pancreatectomy outcomes.

CONCLUSIONS: Patients undergoing pancreatectomy at high-volume centers are more likely to have a margin-negative resection. Volume-based differences in margin status have a small impact on outcomes for pancreatic surgery; however, standardized pathologic evaluation at low-volume centers would likely augment the differences in margin-positive resection rates between high and low-volume hospitals.

Continued with table on next page

Table. Factors associated with a margin-positive resection (microscopic/gross vs. clear).

	Unadjusted Positive Resection Margin Rate	Adjusted Odds Ratio (95% Confidence Interval)
All patients	23.3%	
Age (continuous)		1.01 (1.00- 1.02)
T Stage		
T1	11.5%	1.0 (Referent)
T2	16.8%	1.41 (0.99 - 2.01)
T3	29.2%	2.74 (1.97 - 3.82)
Nodal Status		
N0	17.3%	1.0 (Referent)
N1	28.7%	1.54 (1.31 - 1.80)
Surgical Procedure		
Pancreaticoduodenectomy	24.8%	1.51 (1.20 - 1.90)
Distal Pancreatectomy	21.2%	1.63 (1.18 - 2.25)
Total Pancreatectomy	18.8%	1.0 (Referent)
Pancreatectomy NOS	28.8%	1.66 (0.96 - 2.87)
Hospital Volume Quintiles		
Highest	20.2%	1.0 (Referent)
High	22.7%	1.23 (0.96 - 1.57)
Moderate	24.8%	1.42 (1.12 - 1.81)
Low	23.3%	1.30 (1.02 - 1.67)
Lowest	27.4%	1.60 (1.26 - 2.04)

*Factors not significant in the model include gender, race, grade, insurance status, median income, and year of diagnosis.

Odds ratios greater than 1.0 indicate a higher likelihood of involved resection margins.

BENEFIT OF ADJUVANT THERAPY IN PATIENTS UNDERGOING SURGICAL RESECTION FOR PANCREATIC ADENOCARCINOMA

¹Kimberly A Vanderveen, MD, MAS; ¹Steven L Chen, MD, MBA; ²Diaxis Yin, MS; ^{2,3}Rosemary D Cress, DrPH; and ¹Richard J Bold, MD
University of California, Davis¹ and California Cancer Registry²

BACKGROUND: The benefit of postoperative adjuvant therapy after resection for pancreatic adenocarcinoma remains controversial. Despite the lack of definitive benefit, many patients undergo adjuvant therapy.

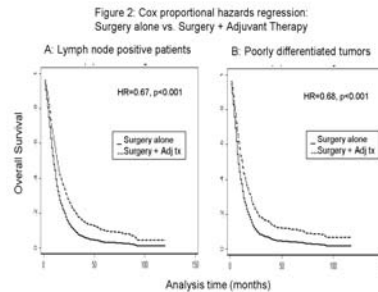
OBJECTIVE: We sought to identify the impact of adjuvant therapy and factors associated with any improvement in survival after pancreatic adenocarcinoma resection.

METHODS: Through the California Cancer Registry, we identified all California residents diagnosed with invasive pancreatic adenocarcinoma between 1994 and 2002. The study population consisted of those undergoing potentially curative resections. Factors potentially impacting survival including age, gender, tumor characteristics, lymph node status, stage, and type of adjuvant therapy were analyzed. Univariate survival analysis was performed by the Kaplan-Meier method. Multivariate analysis was performed using Cox regression analysis.

RESULTS: 26,518 patients were identified, of which 3,196 (12.1%) underwent resection as their primary treatment. Of these, 58% received some form of adjuvant therapy. The median overall survival was 16 months for resected patients. On multivariate analysis, after adjusting for patient demographics and tumor characteristics, adjuvant therapy demonstrated a statistically significant, though modest, impact on survival with a hazard ratio of 0.79 (95% CI 0.75 – 0.90, $p < 0.001$). Adjuvant therapy was most beneficial in patients with:

Positive lymph nodes (HR 0.67, 95% CI: 0.59 - 0.76) and poorly differentiated tumors (HR 0.68, 95% CI: 0.58 – 0.78). Adjuvant therapy did not benefit patients with negative lymph nodes or well-differentiated tumors (Figure).

CONCLUSIONS: Adjuvant therapy provides for a modest improvement in overall survival following surgical resection of pancreatic adenocarcinoma. The absolute effect is most pronounced in those with poor prognostic indicators. In order to identify effective systemic therapy for this deadly cancer, future clinical trials of adjuvant therapy should focus on these groups of patients.



Session III : 3:15 pm

THE EFFECT OF OCCUPATIONAL AND ENVIRONMENTAL EXPOSURES IN CASES OF FAMILIAL AND SPORADIC PANCREATIC CANCER

Theresa Pluth Yeo*, Ralph H. Hruban**, Kieran Brune**, Alison Klein** and Charles J. Yeo*

* *Department of Surgery and School of Nursing, Thomas Jefferson University, Philadelphia, PA, and **Department of Pathology and Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD*

Introduction: Pancreatic cancer (PC) is the fifth leading cause of cancer death in the United States. This study characterizes one of the largest national registries of familial PC (FPC) and sporadic PC (SPC), focusing on demographics, clinical factors, self-reported environmental and occupational lifetime exposures and survival status.

Background: Reported risk factors for PC include: advancing age, a family history of PC, high-risk inherited syndromes, cigarette smoking, exposure to occupational and environmental carcinogens, African-American race, high fat/high cholesterol diet, obesity, chronic pancreatitis, and diabetes mellitus.

Methods: This retrospective cross-sectional, case-only analysis includes cases of FPC (n = 569) and SPC (n = 689) from the Johns Hopkins National Familial Pancreas Tumor Registry (NFPTR) enrolled between 1994 and 2005.

Results: Significant findings include:

- 1) Mild, multiplicative interaction between family history of PC and exposure to asbestos, environmental radon, and environmental tobacco smoke (ETS) (Odds Ratios > 1.0).
- 2) Non-smoker ETS exposed cases were diagnosed at a significantly younger mean age (64.0 years) than non-smoker non-ETS exposed cases (66.5 years) ($p < 0.0004$).
- 3) FPC smokers with ETS exposure were diagnosed at a significantly ($p = 0.05$) younger mean age (63.7 years) compared to FPC non-smokers without ETS exposure (66.6 years).
- 4) Mean age at diagnosis for Ashkenazi Jewish SPC subjects was significantly younger (by 2.1 years) than Ashkenazi Jewish FPC cases ($p = 0.05$).
- 5) Ashkenazi Jewish FPC subjects who smoked were diagnosed 5.9 years earlier than Ashkenazi Jewish FPC non-smokers ($p = 0.05$).
- 6) Median survival for unresected FPC cases was significantly shorter (168 days) compared to unresected SPC cases (200 days) ($p = 0.04$), survival significantly improved to 713 days for FPC cases and 727 days for SPC cases after surgical resection.

Conclusions/Discussion: These are the first data to show that occupational and environmental exposures may act synergistically with inherited or acquired genetic polymorphisms, resulting in earlier occurrence of PC. Exposure to cigarette smoking and ETS is associated with a younger mean age of diagnosis in FPC and SPC cases and those with an Ashkenazi Jewish heritage, compared to non-exposed cases. These results imply that unaffected individuals from families with a history of PC who smoke, have had early life ETS exposure, or have certain occupational and environmental exposures may benefit from screening and early identification of pre-malignant lesions.

Session III : 3:30 pm

FEASIBILITY AND SAFETY OF RADIOFREQUENCY ABLATION FOR LOCALLY ADVANCED PANCREATIC CANCER: RESULT OF A PILOT STUDY ON 27 CONSECUTIVE PATIENTS.

Girelli R, Frigerio I, Salvia R, Barbi E, Tinazzi Martini P and Bassi C.
HPB Unit, Pederzoli Clinic, Peschiera del Garda, Verona * Department of Surgery, GB Rossi Hospital University of Verona. ** Department of Radiology, Pederzoli Clinic, Peschiera del Garda, Verona - Italy

Background Efficacy and safety of tumour ablation with radiofrequency (RFA) is widely accepted for the treatment of primary and metastatic solid tumors but feasibility, safety and standard technique for pancreatic cancer (PC) is still lacking. Previous published studies describe case report or small number of patients with frequently liver metastatic disease. Treating PC in Stage III or IVa with RFA for debulking neoplastic tissue could make the following chemo-radiotherapy more effective. Aim of this study is to evaluate short term morbidity and mortality and to define a safe and standardised technique of RFA in locally advanced PC.

Methods: Patients with documented locally advanced PC were enrolled for this study after informed consensus. They received prophylaxis for acute pancreatitis, pancreatic infection, thrombosis and duodenal bleeding. RFA was performed during laparotomy under US vision and associated to palliative surgery when needed. Times and depth of heating were depending on tumour size. Postoperative care included routine blood tests, PCR and amylase content in abdominal drain. Abdominal CT scan was done 7 days after surgery to check the coagulative effect on the PC. The impact of the procedure on abdominal pain was also evaluated at discharge using a 0-10 Pain Score System. Short term follow up after 30 days included interview and clinical examination, serum CEA, Ca19.9 and abdominal MRI.

Results Between February 2007 and January 2008, 27 patients with histologically proven PC were prospectively enrolled. The M:F ratio was 12:15 and average age 65,8 (range 53-80). All patients were studied with contrast US and CT scan or MRI. Tumour site was the pancreatic head in 17 pts (63%), uncinata process in 2 pts (7%) and body-tail in 8pts (30%) and the average size was 38,6mm (range 12mm-65mm). Twelve patients received RFA alone (44,5%), in 9 pts RFA was associated to digestive and biliary by pass (33,5%), for 2 pts only biliary by pass was done (7,3%) and in one case a cystopancreatic-jejunostomy was necessary (3,7%). There was no mortality up to one month after the procedure. Postoperative course was uneventful in 14 pts (52%) whereas 12 pts (44,3%) had abdominal complications: for 7 pts (26%) strictly related to RFA (1 pancreatic fistula, 2 mesenteric vein thrombosis, 1 thrombosis and acute pancreatitis, 1 thrombosis and duodenal bleeding, 2 anemia). One patient was reoperated on for a severe bleeding from a pseudoaneurism of the splenic artery after 21 days from RFA procedure and one patient for a duodenal stenosis; surprisingly, this particular patient, at first not resectable, was radically treated by pancreaticoduodenectomy after one month from RFA. All the other complications were conservatively treated. Average value of Ca19.9 dropped from 434 U/mL to 218 U/mL seven days after RFA. Fifteen patients with abdominal pain (75%) gained significant benefit.

Conclusions RFA of locally advanced PC with cytoreductive intent is feasible and safe. Palliative surgery has to be associated if needed and to prevent digestive or biliary stenosis. RFA management, carried out in order to reduce as much as possible the volume of vital neoplastic tissue, must be performed in high volume and experienced centre to treat possible severe complications. Because of the systemic nature of PC, RFA has to be followed by chemo and/or radiotherapy. Further studies are necessary to evaluate the effect on long term survival.

Session III : 3:45 pm

USING FLUOROPHORE-CONJUGATED ANTIBODIES TO IMPROVE SURGICAL NAVIGATION IN PANCREATIC CANCER

Michele McElroy¹, Sharmeela Kaushal¹, A. R. Moossa¹, Mark A. Talamini¹, George A. Luiken², Robert M. Hoffman^{1,3}, Michael Bouvet¹

¹*Department of Surgery, University of California, San Diego, CA*

²*OncoFluor, Inc., San Diego, CA*

³*AntiCancer, Inc., San Diego, CA*

Introduction/Background:

Despite its relatively rare presentation pancreatic cancers remains the fourth most common causes of cancer-related death in the United States. The lethality of this disease is related to the late stage at diagnosis and limitations in available operative and medical management. Surgery remains the only chance for cure in these patients, and strategies to improve intraoperative localization and resection of tumor tissue are vitally important to patient care. We have investigated the use of fluorophore-labeled anti-CA19-9 and anti-CEA monoclonal antibodies to aid in cancer visualization in nude mouse models of human pancreatic cancer.

Methods:

Monoclonal antibodies including anti-CA19-9, anti-CEA and control IgG were conjugated to a green fluorophore using the AlexaFluor 488 labeling system. In vitro staining demonstrated positive CA19-9 expression in three (CFPAC, Panc-1 and BxPC-3), and positive CEA expression in five (ASPC-1, BxPC-3, Panc-1, CFPAC and CAPAN-1) human pancreatic cancer cell lines. The BxPC3 and ASPC-1 cell lines were chosen for in vivo studies due to their high CA19-9 and CEA expression as well as their reliable growth kinetics in mice. Tumors were implanted subcutaneously in nude mice and imaged after systemic delivery of either anti-CEA or anti-CA19-9 antibody. Subcutaneous and orthotopic pancreatic tumors as well as experimentally generated metastases to the liver, spleen and peritoneum were imaged following administration of anti-CA19-9. After tumor implantation into nude mice the animals were given a single intravenous dose of conjugated antibody and were imaged using the OV-100 Small Animal Imaging System.

Results:

Small (1-2 mm diameter) subcutaneous tumors were clearly visible with bright green fluorescence both through the skin itself and via skin-flap elevation 24 hours after administration of either labeled anti-CEA or anti-CA19-9 antibody. The signal remained present within the cancer tissue for over one week in the case of anti-CEA and over 3 weeks in the case of anti-CA19-9. Dosing experiments revealed increasing tumor fluorescence with increasing antibody dose, and metastatic implants were clearly visible when stained with the conjugated anti-CA19-9 delivered systemically.

Discussion/Conclusions:

Monoclonal antibodies have been used safely in clinical medicine for years, and several small studies in human subjects have demonstrated the potential advantages of using fluorescence imaging in staging laparoscopy. Tumor cells bound to fluorescent proteins can be imaged either via fluorescence laparoscopy or using a handheld LED light source during laparotomy. Fluorophore-labeled anti-CA19-9 and anti-CEA offer a novel potential intra-operative imaging technique for the enhanced visualization of tumor in

Session III : 4:00 pm

MANAGEMENT OF SUSPECTED PANCREATIC CYSTIC NEOPLASMS BASED ON CYST SIZE.

R.M. Walsh, D. Vogt, J.M. Henderson, K. Hirose, T. Mason, K. Bencsath, N Brown.
Digestive Disease Institute, Cleveland Clinic, Cleveland, Ohio

Background: Evaluation and management of cystic pancreatic neoplasms remain problematic. One approach is to select patients for resection based on cyst size. An international consensus symposium has advised resection only for lesions > 3cm.

Methods: We reviewed our prospective pancreatic cystic neoplasm database for outcomes based on cyst size of 3cm. Resection is advised for symptoms, results of cyst aspiration and imaging.

Results: A total of 500 patients have been evaluated from 1999-2006. One hundred and twenty four (25%) were operated with a mortality of 1.6%. There were 349 patients (70%) with cysts \leq 3cm: 292 (84%) were not operated and included 243 that were considered nonmucinous by cyst aspiration. At a mean follow up of 24 months, 2 failed observation: a 1.4cm cyst became invasive IPMN at 26 months and a 2.5cm MCN was resected at 27 months. Fifty patients had mucinous aspirate results but were not operated, including 27 that were asymptomatic. After a mean follow-up of 24 months, 2 developed unresectable carcinoma, and no others were operated. Fifty-six patients with cysts \leq 3cm were initially operated (16%) including 23 asymptomatic patients. Final pathology showed IPMN in 20, MCN in 18, carcinoma in 7, and serous cystadenoma in 5. A total of 151 patients (30%) had cysts >3cm. Eighty four (55%) were not operated and had a median cyst size of 4.7cm. At a mean follow up of 42 months, two serous cystadenoma became symptomatic and were operated. Nineteen non-operated patients had mucin or carcinoma at aspiration, none came to operation, but 8 died during a mean follow up of 32 months. Sixty-four patients with cysts >3cm (42%) were initially operated and final pathology showed MCN in 27, serous cystadenoma in 11, carcinoma in 13, IPMN in 7, and pseudocyst in 7. Patients with cysts \leq 3cm were less likely to be operated (16 vs. 42%, $p<0.001$), less often symptomatic (39 vs. 50%, $p=0.017$) while older (mean age 65 vs. 61 years, $p=0.03$). Had patients been managed by size alone, up to 20% would have received inappropriate treatment. Management based on aspiration was significantly better in predicting mucinous neoplasms compared to size (75% vs. 57%, $p<0.001$), including asymptomatic patients \leq 3 cm (78% vs. 65%, $p=0.003$).

Conclusion: Size of pancreatic cystic lesions alone is not a reasonable basis for determining management. Cyst aspiration should be done to assist the management of asymptomatic cysts.

Session III: 4:15 pm

PREDICTION OF MORBIDITY FOR PANCREATIC RESECTION: THE INFLUENCE OF SURGICAL PERFORMANCE ON BASELINE PHYSIOLOGY

Wanda B. Pratt1, Mark P. Callery1, Charles M. Vollmer, Jr.1

1 Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School

Background: The interplay between baseline physiology, operative performance and postoperative recovery is poorly defined. We describe the beneficial effect of a successful operation on outcomes across the full spectrum of physiologic risk.

Methods: 379 consecutive pancreatic resections, performed between 2001 and 2007, were analyzed according to the Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM). This previously validated scoring system estimates the risk of morbidity in major operations based on preoperative physiology and surgical performance. Baseline physiology is classified according to the Physiologic severity score: *Minor* (≤ 15); *Moderate* (16 to 24); *Severe* (≥ 25). Surgical performance is assigned by the Operative severity component: Class I (≤ 15) and Class II (≥ 16). Physiologic and operative predictions were independently correlated with actual clinical and economic outcomes, and then merged to measure the influence of surgical performance beyond baseline physiology.

Results: As baseline physiology declines, patients suffer more complications, and require more therapeutic and invasive interventions (Table). More severe (Class II) operations similarly portend worse outcomes. Within each physiologic risk grade, Class I operations (improved surgical performance) were associated with lower rates of morbidity, shorter hospital stays, and improved cost-efficiency. Deeper analysis reveals that intraoperative blood loss is the most variable and influential factor affecting physiologic risk. Each additional unit (375 ml) of blood loss raises the operative severity score 2.5 points, increases the odds of morbidity by 45%, prolongs hospital stay by one day, and costs an additional \$3,700 per patient.

Conclusion: Predictive risk assessment accurately demonstrates that escalating physiologic risk worsens postoperative morbidity, prolongs hospital duration, and increases costs after high-acuity surgery. However, these effects are attenuated by improved operative performance.

Table. The impact of surgical performance on baseline physiology.

Baseline Physiology	Minor		Moderate		Severe		p Value
Patients (% overall)	118 (31)		174 (47)		81 (22)		—
Complications (%)	46 (39)		95 (55)		54 (67)		< .001
ICU Utilization (%)	0 (0)		7 (4)		9 (11)		.001
Duration of Stay (days)	7		8		9		.001
Total Hospital Costs	\$16,934		\$18,235		\$19,829		.013
Surgical Performance	Class I	Class II	Class I	Class II	Class I	Class II	p Value
Patients (%physiology grade)	75 (64)	43 (36)	90 (52)	84 (48)	39 (48)	42 (52)	—
Complications (%)	24 (32)	22 (51)	44 (49)	51 (61)	24 (62)	30 (71)	< .001
ICU Utilization (%)	0 (0)	0 (0)	3 (3)	4 (5)	3 (8)	6 (14)	< .001
Duration of Stay (days)	7	8	8	8	8	9	< .001
Total Hospital Costs	\$16,933	\$16,767	\$17,232	\$19,667	\$18,346	\$21,497	.008
All continuous variables are represented by the median value.							

Session III: 4:30 pm

**DELAYED GASTRIC EMPTYING (DGE) AFTER PANCREATOCODUODENECTOMY (PD)
– THE INTERNATIONAL PANCREATIC STUDY GROUP (ISGPS) DEFINITION IS VERY
USEFUL.**

Yasushi Hashimoto and L. William Traverso
Virginia Mason, Seattle WA

Introduction: The ISGPS definition for DGE has recently been published (Surgery 2007; 142:761-8). For the first time we can avoid the Tower of Babel and use the same definition to compare results. Since the definition is based on expert opinion we decided to test the grading system. Were the grades clinically useful or was a modification required?

Methods: Between 1997 and 2007, 416 consecutive cases by a single surgeon were analyzed. Only cases with pancreaticojejunostomy (PJ) were included (duct-to-mucosa, two-layer, internally-stented, n=398) of which 377 were pylorus preserving. We calculated DGE, pancreatic anastomotic leak (LEAK) and median length of stay (LOS) in postoperative days (POD). DGE definitions per ISGPS are listed below:

Data in POD	No DGE	Grade A	Grade B	Grade C
NG removed	<4	4 to 7	8 to 14	>14
NG reinsert	none	>3	>7	>14
Intolerant of oral intake until	none	7	14	21

LEAK per ISGPS was defined as none, Grade A (any drain amylase >3X upper limit of serum, any volume), Grade B (neither A or C), and Grade C (reoperation, sepsis, death).

Results: For all years the rate of DGE and the LOS was:

	No DGE	Grade A	Grade B	Grade C
Rate	42%	46%	8%	4%
LOS (median)	8	9	13	17

After 2002 when microsurgery for the PJ became routine we observed an abrupt decrease in Grade A (70% to 26%) and an increase in No DGE (16% to 66%, $p<0.0001$). The rate of DGE Grades B/C decreased from 14.4% to 7.5% ($p<0.0001$). ISGPS LEAK rate – After 2002 the rate of Grade B leak decreased from 14.4% to 7.9% ($p<0.05$) while we did not observe any Grade C leaks.

Conclusion: The ISGPS DGE definition nicely separated PD cases into useful spectrum of DGE categories. Based on LOS, Grade A was similar to No DGE. However Grade A was useful as it allowed the observation that, with use of microsurgery for PJ, the rate of Grade A markedly decreased as the No DGE category increased. Similarly DGE Grades B and C were noted to decrease as PJ LEAK rates declined. Without modification this DGE definition allowed detection of improved results with microsurgery and should be useful for future collaboration.

FREQUENCY OF EXTRAPANCREATIC NEOPLASMS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS COMPARED TO PANCREATIC ADENOCARCINOMA AND REFERRAL PATIENTS

Kellie L Mathis, MD¹, Kaye Reid Lombardo, MD¹, Michael G Sarr, MD¹

¹*Division of GI and General Surgery, Mayo Clinic, Rochester, MN*

Introduction: Our aim was to estimate the frequency of extra-pancreatic benign and malignant neoplasms in patients with intraductal papillary mucinous neoplasm (IPMN) of the pancreas and compare the derived frequency to two, matched, control groups.

Methods: We identified all cases of IPMN diagnosed from 1994-2006 using 4 institutional registries. For matched groups, we used control Group 1 consisting of patients diagnosed with pancreatic adenocarcinoma during the same time period matched for sex and age at diagnosis (± 2 years). Control Group 2 was a random selection of referral patients seen at our institution during the time period matched 3:1 for sex, birth date (± 5 years), year of registration at our clinic (± 5 years), and geographic location of primary address. We compared the proportions of patients with any extra-pancreatic benign or malignant neoplasm diagnosed before and/or coincident with the diagnosis of IPMN or pancreatic adenocarcinoma between the IPMN cases and each control group separately using the Chi-square test. We calculated the risk of new benign or malignant neoplasms diagnosed after the diagnosis of IPMN or adenocarcinoma between groups using Cox proportional hazards regression.

Results: The IPMN group consisted of 477 patients, pancreatic adenocarcinoma group 471, and general referral group 1431. The proportion of patients in the IPMN group having any extra-pancreatic neoplasm (benign or malignant) diagnosed before or coincident to the index date was 52% (95% CI 47-56%), compared with 36% (95% CI 32-41%) in Group 1 ($p < 0.001$), and 43% (95% CI 41-46%) in Group 2 ($p = 0.002$). Most common benign neoplasms in the IPMN group were adenomatous colon polyps ($n = 116$), Barrett's neoplasia ($n = 18$), and carcinoid neoplasms ($n = 6$). The most common malignant neoplasms were non-melanoma skin ($n = 36$), breast ($n = 24$), prostate ($n = 24$), and colorectal cancers ($n = 19$). The hazard ratio of diagnosis of any neoplasm *after* the index date was 3.8 (95% CI 2.0-7.3, $p < 0.001$) for the IPMN group compared to Group 1, and 1.4 (95% CI 0.9-2.1, $p = 0.09$) for the IPMN group compared to the Group 2. In the IPMN group, 47 patients had a new neoplasm diagnosed after the index date.

Conclusions: Patients with IPMN are at greater risk of benign or malignant extra-pancreatic neoplasms compared to both control groups. The majority of neoplasms were diagnosed prior to or coincident with the IPMN diagnosis; however, the risk of developing neoplasms after the diagnosis of IPMN remains increased. Based on the frequency of colonic polyps, screening colonoscopy should be considered in all patients with IPMN.

DOES LYMPH NODE RATIO (LNR) IMPACT SURVIVAL IN RESECTED PERIAMPULLARY MALIGNANCIES?

M.G. Hurtuk¹, C. Hughes², M. Shoup¹, G.V.Aranha¹

¹Loyola University Medical Center, Division of Surgical Oncology, Maywood, IL, ²Stritch School of Medicine, Loyola University Chicago, Maywood, IL

Background: Previous studies show that lymph node ratio (LNR), or the ratio of positive lymph nodes to total lymph nodes resected, is associated with long-term survival in patients with pancreatic adenocarcinoma. This has not been shown in other periampullary malignancies. The purpose of this study is to determine if LNR is associated with long-term survival of other periampullary malignancies.

Methods: A retrospective review of a single institution's prospective database of 522 pancreaticoduodenectomies (PDs) performed between 1988 to 2007 was performed. Patients with pancreatic adenocarcinoma (PA), ampullary adenocarcinoma (AA), duodenal adenocarcinoma (DA) and cholangiocarcinoma (CA) were identified. Patients in whom pathological data was missing or died of causes not related to malignancy were excluded. Clinicopathological data was collected and LNR was calculated. Patients with positive LN status were grouped into the following: LNR=0, 0<LNR≤0.2, 0.2<LNR≤0.4, and LNR>0.4. All statistics were calculated using SPSS 16.0 (Chicago, IL), with p≤0.05 being considered statistically significant.

Results: Of the 522 PDs performed, 341(65%) were for periampullary malignancies. The pathological and survival data are summarized in the table below. Positive LN status was found to significantly affect survival in PA (p=0.035), DA (p=0.016), and AA (p=0.003), but the absolute number of positive LNs obtained during resection did not significantly change prognosis (data not shown).

	All Patients	LNR =0	0<LNR≤0.2	0.2<LNR≤0.4	LNR >0.4	p value
Pancreatic Adenocarcinoma n (%)	200 (59)	53 (27)	86 (43)	34 (17)	27 (13)	-
<i>Median number of LN studied (range)</i>	18 (1-45)	16 (1-39)	19 (5-45)	19 (5-37)	14 (1-28)	-
<i>Median survival (range)</i>	17 (1-160)	22 (3-131)	17 (2-160)	14 (2-160)	12 (-122)	0.024
Duodenal Adenocarcinoma n (%)	35 (10)	19 (54)	7 (20)	4 (11)	5 (14)	-
<i>Median number of LN studied (range)</i>	16 (3-46)	13 (3-20)	20 (9-29)	20 (18-46)	18 (10-26)	-
<i>Median survival (range)</i>	42 (2-212)	72 (2-201)	15 (5-212)	23 (4-33)	39 (8-117)	0.066
Ampullary Adenocarcinoma n (%)	71 (21)	40 (56)	17 (24)	8 (11)	6 (8)	-
<i>Median number of LN studied (range)</i>	15 (2-38)	14 (2-38)	18 (9-35)	14 (6-28)	11 (4-23)	-
<i>Median survival (range)</i>	67 (2-165)	56 (2-165)	34 (12-161)	20 (6-90)	14 (6-73)	<0.001
Cholangiocarcinoma n (%)	35 (10)	17 (49)	14 (40)	2 (6)	2 (6)	-
<i>Median number of LN studied (range)</i>	14 (2-36)	12 (3-31)	20 (10-36)	7 (3-11)	2 (2-2)	-
<i>Median survival (range)</i>	29 (6-145)	25 (1-145)	12 (7-145)	19 (1-38)	13 (6-18)	0.405

Session III : 4:55 pm Short

ADJUVANT CHEMORADIATION THERAPY AFTER SURGICAL RESECTION FOR 1092 CASES OF PANCREATIC ADENOCARCINOMA: THE JOHNS HOPKINS HOSPITAL - MAYO CLINIC COLLABORATIVE STUDY OF PANCREATIC CANCER

Charles C Hsu¹, Joseph M Herman¹, Michele M Corsini², Jordan M Winter³, Matthew D Callister⁴, Michael G Haddock², John L Cameron³, Timothy M Pawlik³, Richard D Schulick³, Michael J Swartz¹, Leonard L Gunderson⁴, Robert C Miller²

The Departments of Radiation Oncology & Molecular Radiation Sciences¹ and Surgery³; The Johns Hopkins Hospital, Baltimore, Maryland

The Department of Radiation Oncology², The Mayo Clinic, Rochester, MN

The Department of Radiation Oncology⁴, The Mayo Clinic, Scottsdale, AZ

Purpose: Long-term survival after pancreaticoduodenectomy (PD) for pancreatic ductal adenocarcinoma is uncommon, with 5-year survival rates of 10-25% commonly reported. PD remains the primary modality for cure; however, the role of adjuvant chemoradiation therapy has remained controversial. The purpose of this study was to combine the collective experience of the Mayo Clinic and the Johns Hopkins Hospital to examine the efficacy of adjuvant therapy, particularly, to determine if treatment effect differed by margin positivity, nodal status, tumor size, and tumor differentiation.

Methods: All patients who underwent PD for pancreatic adenocarcinoma at the Johns Hopkins Hospital (n=794) between 8/30/93 and 2/28/05 were reviewed in a prospectively collected database. A retrospective review of 478 consecutive resections for pancreatic adenocarcinoma between 1985 and 2005 was conducted at the Mayo Clinic, Rochester, MN. Exclusion included death within 60-days of surgery, unresectable disease, intra-operative RT, vaccine recipients, distal pancreatectomies, and single modality adjuvant treatment (n=85). The study consisted of N=1092 patients treated with curative intent (N=618 JHH, n=474 Mayo), with 583 receiving adjuvant 5-FU based CRT (median RT dose 50.4 Gy). Median follow-up was 18.2 months. The study consisted of N=1092 patients treated with curative intent (N=618 JHH, n=474 Mayo), with 583 receiving adjuvant 5-FU based CRT (median RT dose 50.4 Gy). Median follow-up was 18.2 months. Cox proportional hazards analysis was performed to evaluate survival by adjuvant treatment. Propensity score and matched-pair analyses accounted for biases associated with nonrandom allocation of patients to adjuvant CRT or surgery alone. Propensity score analysis was generated with 16 variables, and the ROC area under the curve for association with treatment was 0.74 and was used in Cox regression analyses. We also performed 1:1 matching by treatment group based on institution, age, sex, tumor size/stage, differentiation, margin, and node positivity with N=496 (n=248 per treatment arm)

Results: Median survival was 18.8 months overall. Patients with adjuvant CRT tended to be younger, from the Mayo Clinic, had worse histologic tumor grade, and positive margins (P<0.05). Overall survival was significantly longer among those who received adjuvant CRT versus PD alone (mOS 21.1 vs. 15.5 months, P<0.001; 2-y OS 44.7% vs. 34.6%, 5-y OS 22.3% vs 16.1%, P<0.001). When stratified by age≥70, margin status, node status, primary tumor size, and tumor differentiation, overall survival was significantly associated with adjuvant CRT in all sub-groups (P<0.05) after adjusting for covariates. Propensity score analysis attempted to account for biases associated with nonrandom allocation of patients to treatment and had similar results. Matched-pair analysis demonstrated overall survival was longer with adjuvant CRT versus PD alone (21.9mo vs. 14.3 mo mOS, P<0.001).

Conclusions: Adjuvant CRT is significantly associated with improved survival after PD, regardless of age, tumor size, margin status, node status, and tumor differentiation. The status of operative resection (R0, R1, R2) should not significantly alter adjuvant chemoradiation treatment recommendations.

Session III: 5:00 pm Short

DIAGNOSTIC LAPAROSCOPY AND PERITONEAL CYTOLOGY IN THE STAGING OF UNRESECTABLE PANCREATIC CANCER

C.J. Clark¹, F. Bahiraei¹, V. Picozzi², L.W. Traverso¹.

¹Department of General Surgery, Virginia Mason Medical Center, Seattle

²Department of Hematology & Oncology, Virginia Mason Medical Center, Seattle

Background: Precise staging of pancreatic cancer is essential for determining patient prognosis, identification of surgical candidates, and selection of the optimal therapeutic approach. In unresectable locally-advanced Stage III pancreatic cancer, diagnostic laparoscopy and peritoneal cytology may provide more accurate staging. The purpose of this study was to calculate the incidence of occult metastatic pancreatic cancer (Stage IV) found at staging laparoscopy in patients with computed tomography (CT) findings of locally-advanced disease (CT stage III).

Methods: Between April 2000 and February 2008, 183 consecutive patients with locally-advanced unresectable pancreatic cancer determined by thin-cut, contrast-enhanced pancreas protocol CT underwent diagnostic laparoscopy and collection of peritoneal washings for cytology (DLPLC). All cases ultimately had a tissue diagnosis of pancreatic cancer.

Results: DLPLC upstaged 43 of 183 patients (23.5%).

Predictor of Cytology Results	Peritoneal Lavage Cytology (n = 183)		
	Positive (n=36)	Negative (n=147)	Chi-Square
Tumor Size > 4.5 cm	15 (41.7%)	28 (19.3%)	p < 0.05
Peritoneal Metastasis Visible during Laparoscopy	3 (8.3%)	0 (0.0%)	p < 0.05
Hepatic Metastasis Visible during Laparoscopy	6 (16.7%)	10 (6.8%)	p = 0.06
Indeterminate Hepatic Lesion(s) Visible on High Resolution CT	8 (22.2%)	29 (19.7%)	p = 0.82
Primary Tumor in Body/Tail	9 (25.0%)	30 (20.4%)	p = 0.36

Sixty-eight patients (37.2%) had liver lesions that were biopsied at laparoscopy but less than a quarter (23.5%) represented metastatic disease (8.7% of all patients). Metastatic peritoneal deposits were uncommon and identified in 3 patients (1.6%). Thirty-six patients (19.7%) had positive peritoneal lavage cytology. Head vs. body/tail lesions did not predict the presence of malignant cells in the peritoneal washing. Positive cytology had a significant association with large tumor size (> 4.5 cm) and laparoscopically visible peritoneal lesions.

Discussion: Despite advancements in the sensitivity of high-resolution CT, the use of diagnostic laparoscopy and peritoneal lavage cytology in selected patients provides for additional accuracy by upstaging 23.5%. Whether this information is useful to the oncologist in designing chemotherapeutic or chemoradiation regimens remains to be answered. Also, yet to be addressed is the therapeutic and prognostic implication of a positive peritoneal washing in locally-advanced pancreatic cancer.