

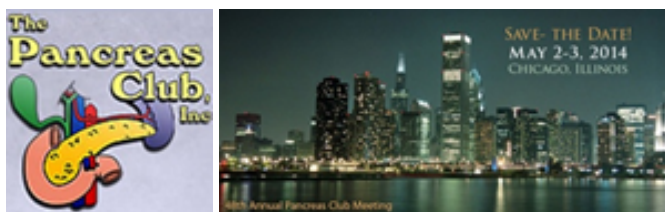
HIGHLIGHT ARTICLE

Updates on Pancreatic Cancer

Highlights from the "48th Annual Pancreas Club Meeting" Chicago, IL, USA. May 2-3, 2014

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Pancreatic adenocarcinoma remains a therapeutic challenge. The American Cancer Society estimates that in 2014 about 46,420 people will be diagnosed with pancreatic cancer and about 39,590 people will die of pancreatic cancer in the United States [1]. The incidence of pancreatic carcinoma has markedly increased over the past several decades and it now ranks as the fourth leading cause of cancer-related death in the United States. Despite the high mortality rate associated with pancreatic cancer, its etiology is poorly understood. Although progress in the development of new cytotoxic and biological drugs for the treatment of pancreatic cancer continues, the outcome remains grim.

Many organizations and associations have taken an effort to improve knowledge, understanding and outcome of patients with pancreatic cancer. Pancreas Club, since its founding in 1966, is aimed to promote the interchange of ideas between physicians and scientists focused on pancreas throughout the world in an informal "club" atmosphere. We attended the 48th Annual Meeting of Pancreas Club in Chicago and reviewed many interesting posters and oral presentations. Here we discuss a few selected abstracts.

Preliminary Results of a Swedish, MR Based, Screening Program for Individuals at Risk for Pancreas Cancer [2]

Del Chiaro et al. presented preliminary results of an

Keywords Carcinoma; Pancreas; Pancreatic Neoplasms; Therapeutics/toxicity

Abbreviations MIPD: Minimally Invasive Pancreaticoduodenectomy; NCDB: National Cancer Database; SDL: Staging Diagnostic Laparoscopy

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MR-based screening program for pancreatic cancer in individuals at risk. These patients were identified based on personal and family history. Forty patients were enrolled between 2010 and 2013. They were screened for genetic mutations associated with pancreatic cancer development. A p16 mutation was noted in 4 (10%) patients, BRCA2 mutation in 3 (8%) and BRCA1 mutation in 1 patient (3%). The mean length of follow-up was 12.9 months and patients underwent MR at time of enrollment and intervals were determined based on findings. Sixteen (40%) of patients had positive findings on MR surveillance. Fourteen (35%) patients were found to have an IPMN and 2 (5%) were found to have pancreatic cancer. Five (13%) of patients underwent surgical intervention. Interestingly, the number of family members with pancreatic cancer did not correlate with the likelihood of development of abnormal findings. This study, though limited by current follow-up of approximately one year, suggests that, in a well-defined population, an MR-based screening program could be effective in pancreatic cancer.

Diagnostic Laparoscopy to Detect Occult Metastatic Disease Prior to Neoadjuvant Chemoradiation in Borderline Resectable Pancreatic Ductal Adenocarcinoma. A Cost Analysis [3]

Peng et al. assessed the cost-effectiveness of staging diagnostic laparoscopy (SDL) in borderline resectable pancreatic cancer. Data was retrospectively collected from a single institution. A total of 116 patients were identified, of which 102 (88%) were candidates for neoadjuvant therapy. Seventy-six (75%) of these patients underwent SDL, while 26 (25%) were planned for neoadjuvant chemotherapy without SDL. Tumors in the two groups had similar characteristics including size and arterial or venous involvement. Nineteen of the 75 (25%) patients who underwent SDL were found to have evidence of metastatic disease due to metastatic implants or cytology findings. While no significant difference was found in the overall costs to patients who undergo SDL prior to treatment. However, 25% of patients undergoing SDL had a change in their treatment pathway due to positive SDL findings, suggesting SDL may merit further study.

A Comprehensive Assessment of Neoadjuvant Therapy for Pancreatic Adenocarcinoma: Results from the National Cancer Database (NCDB) [4]

Lewis et al. addressed the benefit of neoadjuvant therapy

for pancreatic adenocarcinoma based on data from the NCDB. They found the frequency of use of neoadjuvant therapy doubled from 6 to 12% of surgical patients from 2006 to 2012. Patients who received neoadjuvant therapy were more likely to be treated at academic centers than those who received surgery first. Those receiving neoadjuvant therapy had statistically significant reductions in post-operative stay (11 vs. 12 days) and 30-day surgical mortality (2.8% vs. 4.9%). Median survival from diagnosis was longer in neoadjuvant therapy group (19.9 months) vs. surgery first group (15.3 months; $P < 0.001$). This benefit was not observed in patients with stage I disease. Long-term survival at 5 years did not differ between the two groups (14% in both groups). This demonstrates that neoadjuvant therapy is becoming increasingly more utilized in clinical practice and may have some benefits in short-term survival and patient selection for surgery, particularly in those with advanced stage disease.

Minimally Invasive Pancreaticoduodenectomy: Is the Learning Curve Surmountable? [5]

Data from multiple institutions performing minimally invasive pancreaticoduodenectomy (MIPD) and participating in the National Surgical Quality Improvement Program (ACS-NSQIP) Pancreatectomy Demonstration Project was analyzed by Nakeeb *et al.* A total of 1,781 patients underwent pancreaticoduodenectomy at 43 institutions. MIPD was initiated on 131 (7.4%) of these patients at 21 institutions. Patients who underwent open pancreaticoduodenectomy and MIPD were similar in age, gender, race, cardiopulmonary disease and other comorbidities. Half of the attempted MIPD were converted to open procedures. Analysis showed MIPD was associated with statistically significant increase in operative time (7.5 vs. 6.1 h), septic shock (11.5 vs. 3.5%), reoperation (11.0 vs. 3.5%), major morbidity (55.0 vs. 44.4%) and mortality (4.7 vs. 1.8%). This data suggests that, at the present time, MIPD is associated with higher complication, morbidity and mortality. Before this procedure becomes generalizable, further training paradigms may be required.

Clinical Outcomes in Pancreatic Adenocarcinoma Associated with BRCA2 Mutation [6]

Our group presented outcomes in patients with pancreatic adenocarcinoma associated with BRCA2 mutations with a focus on benefits of chemotherapeutic agents targeting the DNA repair deficits in BRCA2 mutation. Patients with a known BRCA mutation and pancreatic adenocarcinoma were identified in a retrospective chart review. Ten patients were identified of which 4 (40%) were of Ashkenazi heritage and 4 (40%) had a personal history of malignancy. Seven patients (70%) received platinum-based therapy, two (20%) received mitomycin-C, one (10%) received PARP inhibitor, and seven (70%) received a topoisomerase-I inhibitor. One patient receiving gemcitabine and irinotecan demonstrated a complete response after 6 months of therapy. She received an 8-month course before recurrence 4 months afterwards. Another patient received irinotecan as second-line therapy for 81 weeks. Cetuximab was added to irinotecan with stable disease for 52 weeks (for

a combined duration of 133 weeks). Overall, clinical and radiologic responses were seen with various cytotoxic agents all targeting DNA repair deficiencies in BRCA2 mutation. These data highlights that BRCA2 patients may have a unique biology underlying their malignancies and that genetic testing may guide therapeutic choices in the future.

Discussion

Pancreatic cancer is the fourth-leading cause of cancer-related death in the United States and continues to carry a grim prognosis, but progress continues to be made regarding optimal diagnosis and therapy. Individuals with genetic predisposition of pancreatic adenocarcinoma are at significantly increased risk of developing pancreatic adenocarcinoma [7, 8]. Screening protocols based on history and genetic testing may allow for earlier diagnosis of this devastating disease. The role of staging laparoscopy to identify those with metastatic disease is still developing as well. In those with disease amenable to surgical resection, the role of neoadjuvant therapy remains controversial though it is being more increasingly adopted. Evidence suggests it may improve surgical and oncologic outcomes. Advances in surgical techniques mean minimally invasive techniques may develop into a viable, frequently used alternative to open approaches; although the field is still developing. In terms of chemotherapeutics for advanced malignancies, tailored therapy targeting underlying genetic mutations such as BRCA1 and BRCA2 may improve clinical outcomes.

Conflicts of Interest

The authors have no potential conflicts of interest.

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