AHPBA
Americas Hepato-Pancreato-Biliary Association
Advancing HPB care to improve patient lives

The Best of AHPBA 2019

March 20-24, 2019

The Best of AHPBA 2019 includes reviews selected and submitted by the Professional Development Committee. Recordings of named lectures will be available in the Members Only section of the AHPBA website.

Presidential Plenary Session

Submitted by Patrick J. Worth, MD

The Presidential Plenary Session at this year's AHPBA Meeting not only highlighted some of the finest academic work being carried out by members, but also served to underscore the Association's commitment to patient advocacy. The first presentation was by Dr. Gementezis and showcased the thorough work that Dr. Wolfgang and the Hopkins group is doing with their study of circulating tumor cells in pancreatic cancer (CLUSTER Trial). This study is the first prospective, longitudinal analysis of CTCs in PDAc. The investigators have identified epithelial (eCTC, cytokeratin + and vimentin -) and mesenchymal (mCTC, cytokeratin + and vimentin +) subtypes of circulating tumor cells in peripheral blood of patients diagnosed with PDAc. These cells are present at higher levels in patients with occult metastatic disease diagnosed at resection, they decrease with neoadjuvant therapy, and high levels preoperatively (in treatment naïve and neoadjuvant patients) were the only factor predictive of <12-month recurrence in multivariate analysis. The authors also reported that patients who experienced a recurrence had a "disproportionate increase in mCTCs", offering both a predictive and possibly mechanistic explanation for early metastatic recurrence after resection. Further, increase in CTCs was seen on average three months before imaging recurrence. Dr. Schirmer was the discussant and raised the question of cost; the investigators noted that the per-sample cost was around $300 and that most patients had on average four samples taken. Dr. Pitt raised the question of correlation with CA19-9 levels, which the investigators recognized as a limitation of the trial in that not all study patients had well-recorded CA 19-9 levels, however for the patients who did, preliminary analysis demonstrated improved sensitivity and specificity for CTCs.

The second plenary talk was given by Mrs. Bachini, a patient advocate and survivor of cholangiocarcinoma who presented a heartfelt account of her first-hand experience with this disease and with making change at a state- and national-level. Her experience has also motivated her to become deeply involved with the Cholangiocarcinoma Foundation (CCF). She dovetailed her moving story with the results of a survey that was recently co-sponsored by CCF and

Presidential Plenary Session

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the Pancreatic Cancer Action Network (PANCAN), aimed at elucidating the patient experience of coming to and living with a diagnosis of hepatobiliary or pancreatic malignancy. The survey, which had over 1,000 respondents highlighted patients' willingness to go to great lengths (both geographically and bodily) to have treatments which may only offer a narrow possibility of cure. Interestingly, the authors found that over 80% of respondents would be willing to "try lines of therapy that had no guarantee of helping", a fact that clinicians should keep in mind considering the relatively low level of enrollment of HPB patients in clinical trials. Mrs. Bachini and the survey further highlighted the importance of physical and online resources as well as the importance of reiteration for patients who have just been "hit" with a diagnosis of one of these malignancies.

Guillame Martel and his colleagues at the University of Ottowa presented the final plenary talk on their randomized controlled trial examining the role of hypovolemic phlebotomy (HP) in patients undergoing liver resections. The technique is aimed at reducing central venous pressure and theoretically reducing hemorrhagic volume during parenchymal transection in liver surgery. It involves intentional phlebotomy of 7-10mL/kg of whole blood into an autotransfusion bag 30-60 minutes before the transection, which is then re-transfused at the conclusion of the transection, effectively simulating a class I hemorrhage. While it has been utilized in various centers, and makes some physiologic and theoretical sense, there is a paucity of prospective literature on the topic. The surgeon was blinded to the treatment arm, as was the anesthesiologist before the case, and a larger drape was utilized to prevent unblinding of the surgeon, who was subjected to a survey following the case. Meticulous measurement of blood loss intraoperatively was critical. Though there was no difference in blood loss volumes across treatments, there was a tendency of the surgeons to report increased ease of transection in the HP patients ($p = 0.06$). Surgeons were unable to reliably identify patient treatment group and no differences in rates of postoperative transfusion, or major/minor complications were noted.

While the trial presented overall negative results, Dr. Jarnagin (the discussant) applauded the authors for taking on a randomized controlled trial that aimed to settle this question, adding: "surgeons infrequently know what's going on behind the ether screen and estimates of blood loss are usually …bad, so you confirmed that for us." The authors have initiated a second trial where they aim to recruit >400 patients. This study will be conducted at multiple centers across Canada, powered to identify smaller differences in overall transfusion rates and outcomes.

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March 5 – 8, 2020

Loews Miami Beach Hotel, Miami Beach, FL

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State of the Art Lecture 1
Safe Cholecystectomy and Bile Duct Injury- Where Do We Go From Here?
Steven Strasberg MD | Washington University, Saint Louis

Submitted by Erin Baker, MD

Dr. Steven Strasberg from Washington University provided the first State of the Art Lecture of the conference on Friday morning. His talk entitled "Safe Cholecystectomy and Bile Duct Injury- Where do we go from here", is presented in conjunction with his recent work from the SAGES Safe Cholecystectomy project. He highlighted for us the importance of this topic acknowledging that bile duct injury following cholecystectomy is a highly morbid complication with significant long-term impact on the quality of life of the patient with compounding psychologic effects. In surgical education, we should be teaching trainees techniques for completion of cholecystectomy to avoid bile duct injury.

Dr. Strasberg proposes a three-step conceptual roadmap to avoid common bile duct injury. **Step1** defines the importance in getting secure anatomic identification. He highlighted the fallacy of the infundibular technique which is frequently taught and can be extremely difficult to use correctly. The critical view of safety, while heralded as an excellent technique for securing anatomic identification, is largely unproven with high levels of evidence due to the overall low incidence of major common bile duct injury. **Step 2** highlights the surgeon's ability to recognize danger and know when to stop. Here Dr. Strasberg discussed the inflection point of the laparoscopic cholecystectomy procedure at which point proceeding forward may lead to danger for the patient and risk of injury to critical structures. He emphasized indicators of difficult gallbladder operations including acute cholecystitis and the pucker sign of the liver on CT scan whereby the small contracted gallbladder can make the operation exceedingly more difficult. **Step 3** describes the importance of bail out options, knowing how to complete the operation safely when things are difficult. Here the situation may change depending on the surgeon's level of experience. For situations in which the gallbladder can't be found, typically patients should be referred to a tertiary care facility. A cholecystostomy tube can be place for temporary drainage but ultimately may not fix the need for completion cholecystectomy later. Finally, if the hepatocystic triangle cannot be dissected then options for subtotal cholecystectomy exist. These include the fenestrating cholecystectomy where a portion of the gallbladder wall is removed, and the remaining mucosa ablated or a reconstituting subtotal cholecystectomy whereby the stump of the gallbladder is closed. These three steps when combined represent a safe approach to cholecystectomy and hopefully will lead to avoidance of biliary injury and improved patient outcomes.

Oral Presentations 4 – Pancreas

Submitted by Mustafa Raoof MD

Several new research findings were presented at the 2019 AHPBA pertinent to pancreatic cancer:

A study by Lyman and colleagues applied deep learning methods (artificial intelligence) with the goal of identifying high risk pancreatic cysts. In 27 patients that underwent pre-operative CT scans, 9 had evidence of advance neoplasia. The machine algorithm was trained on 18 patients and applied to the remaining 9 for validation. The authors demonstrated that all patients with advanced neoplasia and 83% of benign lesions were correctly identified by this machine learning algorithm. This was superior to Fukuoka guidelines. The results although preliminary are encouraging and will shape future work in this area.

The work presented by Janjua and colleagues from Tampa General Hospital focused on reducing cost after pancreaticoduodenectomy by optimizing the length of hospitalization and minimizing readmissions. They used data from Healthcare Cost and Utilization Project for 8 states and merged it to American Hospital Association Survey data. They used a multivariable regression model to predict ideal length of stay for each patient. In their analysis they showed that those patients that were discharged 2 days prior to their ideal hospitalization stay accounted for 44% of all readmissions and greater than $50,00 excess average costs per patient. This work suggests that an ideal length of stay can be predicted based on pre-operative factors and can be used to guide discharge planning and patient expectations.

A paper from University of Pittsburgh sought to utilize video review to identify technical factors predictive of adverse outcomes from hepaticojejunostomy (bile leak, cholangitis, anastomotic stricture) during performance of a robotic whipple. The authors demonstrated that a detailed video review encompassing 20 technical variables identified fewer posterior row stitches and longer distance between hepaticojejunostomy and hilar plate as independent risk factors for adverse hepaticojejunostomy outcomes.

Using data from Dutch pancreatic cancer audit, S van Roessel and colleagues propose a new pancreatic cancer quality measure – "textbook outcome". This was defined on the basis of an international survey of experts as absence of: 1) pancreatic fistula (ISPGS grade B/C); 2) bile leak; 3) hemorrhage; 4) severe complications (Grade 3 or higher); 5) readmission; or 6) Mortality. The authors demonstrated that the observed to expected ratio of this outcome between Dutch pancreatic centers varied from 0.7 to 1.5 and can help identify underperforming hospitals.

A paper from Columbia University used a survey design to perform long-term follow up on survivors after pancreatic surgery. The goal was to identify quality of life issues pertinent to long-term survivors. They demonstrated that new-onset diabetes and pancreatic insufficiency are more common than previously appreciated. These findings will have high relevance as more patients live longer with advancement in cancer therapies.

Jie et. al presented their work on molecular characterization of pancreatic neuroendocrine tumors. They used whole exome sequencing to identify genetic variants and performed validation using Sanger sequencing and immunohistochemistry. On average each pancreatic neuroendocrine tumor had 102 variants and paired liver samples showed 124 variants. Primary tumors had enrichment of PI3K/ Akt pathway while the liver metastases had mutations involving MAPK and ErbB signaling pathway. They demonstrated that a third of patients with liver metastases had an FGFR3 mutation. These intriguing findings are hypothesis generating and encourage ongoing studies in a larger cohort of patients.

Powers et. al. form Moffit Cancer Center asked the question if surgery improves survival in patients with AJCC Stage 1 pancreatic neuroendocrine tumors. They used data from SEER registry 2007-2015. The median follow-up was 24 months. They found that surgery improved overall survival but not cancer-specific survival. While these findings are pro-surgery, there were only 38 deaths in their cohort. Few events and a short follow up limit the validity of these findings. The authors propose an individualized approach to patients with Stage 1 pancreatic neuroendocrine tumors and ongoing work in this area.

Leslie Blumgart Historical Lecture
Hilar Cholangicarcinoma. Reflections and Perspectives
David Nagorney MD | Mayo Clinic
Submitted by Kerri Simo MD

Dr. David Nagorney from Mayo Clinic, Rochester, tackled the surgical enigma that is hilar cholangiocarcinoma in the annual Leslie H Blumgart Historical Lecture entitled "Hilar Cholangicarcinoma. Reflections and Perspectives" given on Saturday afternoon of this year's AHPBA meeting.

Despite being first recognized in 1840, hilar cholangiocarcinoma remains one of the most intellectually and technologically challenging diseases to treat. Early Mayo Clinical reports can be found to describe hilar cholangiocarcinoma and pathologically it was often misdiagnosed as focal sclerosing cholangitis up until as late as 1960. This eventually led to the recogniziation of primary sclerosing cholangitis as a predisposing factor for cholangiocarcinoma in the 1990s. As we are all aware, accessibility to the tumor has historically been problematic leading to its technical and diagnostic challenges.

Surgical treatment in the 1960's was for the most part palliative and offered few cures, mostly for small lesions. Then in the mid 1970's Dr. Bismuth published an operative series of 45 patients with hilar cholangiocarcinoma with a 4% mortality. He noted that intrahepatic ductal anatomy, use of intraoperative cholangiogram and location of anastomosis were critical. Of course he also established the Bismuth classification (now Bismuth Corlette) as a descriptor, not a staging system for this cancer.

Surgical approaches continued to evolve from biliary bypass and rare resection until 1984 when Dr. Blumgart published a standardization of the approach to surgery for hilar cholangiocarcinoma. The median survival with resection was 30 months in this series. Moving forward from the 1990's until now ERCP and Interventional radiology have continued to have a great impact on the diagnosis and management of these patients. Particularly, hepatic lobe embolization has proven to be paradigm shifting and frankly invaluable.

"Criteria of unresectability" from the Expert Consensus Conference were reviewed and included: 1. Bilateral segmental ductal extension, 2. Unilateral atrophy with either contralateral segment ductal extension or vascular inflow involvement, and 3. Unilateral segmental ductal extension with contralateral inflow involvement (Mansour HPB 2015).

Dr. Nagorney was also very clear that "Crowded anatomy and margins are the responsibility of the surgeon with the optimal margin length for resection on a bile duct being 10mm". He also postulated that regarding the caudate lobe, he would take the whole lobe as it is technically an easier resection. However, he notes that this is drive more by practice paradigm and not hard data.

To summarize, resection for this tumor has come a long way and will likely become even more complex moving toward adapting the liver resection to the individual patient. The road to liver transplant for cholangiocarcinoma has been a rocky one with current success related to the neoadjuvant protocols of the 1990s, Mayo Clinic's being most recognized and externally validated. Dr. Nagorney concluded that the answer is still out for cholangiocarcinoma de novo and that as s survival for resection continues to increase, the use of liver transplant was likely only be for a very select patients.

Finally, looking forward Dr. Nagorney believes the treatment of hilar cholangiocarcinoma will continue to be advanced by:

1. Continued improvement in the safety of resection with preoperative preparation and technical refinement,
2. 2. Tumor profiling becoming routine to guide concurrent treatments,
3. 3. Improvements in resolution of imaging with dimensional imaging for staging and endoscopic imaging for ductal mapping, and
4. 4. Multimodality therapy with refinement of neoadjuvant and adjuvant regimes as well as chemo-irradiation.

Education & Training Committee Symposium

Submitted by Ken Lee MD

The Education and Training Committee sponsored a symposium on Sunday March 24, 2019 moderated by committee chair Dr. Tara S. Kent of the Beth Israel Deaconess Medical Center and Dr. Melissa E. Hogg of the Northshore University Health System.

The first presentation entitled "Inclusion of Non-Operative Modalities in HPB Training" was given by Dr. Ellen Hagopian of the Hackensack University Medical Center. While noting the importance of non-operative modalities such as professionalism and multidisciplinary collaboration, Dr. Hagopian focused on training in ultrasound and ultrasound-guided ablation. She noted that in HPB surgery, ultrasound confirms the known, detects the unknown, and guides operative execution. Ultrasound optimizes clinical outcomes and improves survival by aiding in detection of all disease, enhancing completeness of resection, and decreasing local recurrence after ablative procedures.

A study of HPB, surgical oncology, and transplant fellows found that many felt deficient in their training in ultrasound and tumor ablation. Informal observations and interviews also found that fellows are not consistently trained in ultrasound during their training. These concerns have resulted in efforts to provide standardized ultrasound training consisting of incorporation of a full-day HPB ultrasound course into the Fellows' Course, a hands on HPB ultrasound skills practicum testing key elements of diagnostic ultrasound, and an online post-test taken after completion of the practicum. Core components of the curriculum and evaluation include (1) a pretest prior to didactic and hands-on course (2) a didactic (lecture) component (3) hands on skills sessions (4) self-assessments (5) mentored practical experience (6) a hands-on ultrasound skills practicum and (7) a written post-test. The goal of the standardized curriculum is to ensure that graduating fellows are well-prepared for future clinical practice.

The second presentation entitled "How Much is Enough/Too Much? MIS Training and Metrics of Proficiency" was given by Dr. Melissa Hogg. In this presentation Dr. Hogg used the robot platform to focus on how to teach trainees new technical skills. She began by emphasizing that successful introduction of new technical skills into a training program requires that trainees be interested and motivated. This in turn is dependent upon trainees having clinical opportunities to apply their new technical skills. At the same time, such opportunities are more apt to be provided to trainees who have acquired sufficient skills through dedicated practice. Ideally, participation in training programs should be mandatory and coordinated with progressive clinical opportunities.

Dr. Hogg then outlined the robust robotic curriculum that she has developed. This curriculum is widely regarded as the most effective for structured training in robotic pancreatic surgery, and as a model for teaching new technical skills. This curriculum consists of several components matched to specific training objections: (1) mastery of the robotic console using a simulation curriculum comprised of virtual exercises (2) mastery of loss of haptic feedback using a biotissue inanimate curriculum (3) mastery of the operative procedures though review of a video library (4) mastery of psychomotor function using a structured clinical surgical curriculum and (5) development of decision making and judgment through ongoing quality assessment and improvement. Dr. Hogg provided data validating the simulation and biotissue curricula and demonstrating that biotissue curriculum improves the technical performance of surgical oncology fellows. She also described strategies for development of a video library to be used for education and research. This might include videos created by attending surgeons

illustrating their "text book" procedures, and video portfolios created by trainees from their personal experiences. Dr. Hogg then shared data showing that fellow participation in robotic Whipple procedures, the percentage of robotic Whipple procedure steps performed by fellows, and the percentage of robotic Whipple procedures performed by fellows have annually increased since the established of this structured curriculum.

Finally, metrics for evaluation at the different stages of the curriculum were reviewed. These include scores generated by the virtual simulator, measures such as time to completion and number of errors during the inanimate curriculum exercises, and time to completion of individual steps in the Whipple procedures.

Dr. Hogg summarized by emphasizing that involvement as primary surgeon is critical, mandatory training is better, a step by step approach is recommended, and metrics should be measured as possible.

Dr. Rebecca Minter of the University of Wisconsin School of Medicine and Public Health gave the third presentation entitled "What are EPAs and How Do They Fit Into Fellowship?" She began by explaining that an entrustable professional activity (EPA) defines a discrete element of surgical care that assessors can relate to and more objectively evaluate, and that EPAs start with the end in mind – what do we expect a graduating trainee to be able to do independently. Dr. Minter also explained that an EPA is not a narrow slice of surgical care, and that EPAs are assessed iteratively in the workplace, rather than as a single final exam-like assessment. Collectively EPAs represent the core of a profession and are measured in the workplace. Dr. Minter then discussed the following levels of entrustment as they relate to the progression of trainees towards independent practice:

•Level 0 – Trusted to observe only (deficient fellow)
•Level 1 – Trusted to diagnose and manage with direct supervision and coaching (entering fellow)
•Level 2 – Trusted to diagnosed and manage with indirect supervision for simple cases (developing fellow)
•Level 3 –Trusted to diagnose and manage with indirect supervision for more complex cases (developing fellow)
•Level 4 – Trusted to execute without supervision, but with availability for clinical oversight as needed (practice ready fellow)

Thus far the following 11 HPB EPAs have been developed:

- Multidisciplinary evaluation and management of a patient with benign and malignant HPB disease
- Evaluation and management of
- A patient with a solid pancreatic mass
- A patient with a cystic pancreatic mass
- A patient with severe acute pancreatitis
- A patient with chronic pancreatitis
- A patient with biliary obstruction
- A patient with a hilar biliary stricture
- A patient with a gallbladder or liver mass
- A surgical patient with cirrhosis and portal hypertension
- A patient with duodenal and periampullary disease

Finally, Dr. Minter noted that EPAs can provide a blueprint for fellows and can be used as a measure of the effectiveness of a training program. The goal for a training program and its fellows will be to reach the highest levels of entrustment at the conclusion of training.

Dr Tara Kent gave the next presentation entitled "HPB trainees – what are their needs." She summarized the current HPB requirements for general surgery residents in the United States (5 pancreas, 5 liver, and 85 biliary cases) and showed the average HPB experience for graduates of US surgical residency programs. There is great variability in HPB experience both across and within individual residency programs. Experience in HPB surgery tends to be greatest in high volume centers and among residents interested in pursuing careers in HPB surgery. She noted, however, that HPB operative experience for many residents is steady but modest and that many residents finishing general surgery residencies do not feel comfortable performing major liver, major pancreas, and complex biliary operations. Dr. Kent suggested that flexibility in surgical training as permitted by the American Board of Surgery may allow residents who are interested in pursuing careers in HPB to increase their experience in HPB surgery during residency. This increased experience will then better prepare them fellowship training in HPB surgery, complex general surgery (surgical oncology), GI surgery, or transplantation and future independent practice of HPB surgery.

The final talk entitled "Training in Latin America – How Does It Look" was given by Dr. I Ismael Dominguez Rosado from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiráne. He noted the advantages (high volume, early exposure to operating experience, complete autonomy in the last year of training, learning to practice with limited resources) and disadvantages (lack of standardized curriculum and evaluation, limited laparoscopic experience, absence of laboratories for skills training) of a typical Latin American surgical training experience. He reviewed the challenges faced by international applicants seeking training in accredited US HPB fellowship programs and the obstacles that they encounter when returning to their home countries after completion of training in the United States.

Finally, Dr. Dominguez Rosado discussed efforts and strategies to improve HPB training in Central and South America. A survey of HPB fellowship directors from these regions found high levels of interest in participating in AHPBA certification of fellowship programs and a strong belief that certification by the AHPBA would impact favorably on fellowship programs. The leading perceived barriers to meeting AHPBA accreditation standards were research and case volumes. Strategies to overcome the research and case volume limitations include collaboration among programs and countries, fellow exchanges, and identification of funding sources to support research.