



ABSTRACTS

** Denotes Resident/Fellow Research Award Competition Paper*

ABSTRACTS

*Paper 1 (3:15pm - 3:30pm)

ADRENOCORTICAL CARCINOMA: THE INFLUENCE OF LARGE VESSEL EXTENSION

Harma K. Turbendian, Meier Hsu

New York Presbyterian Hospital - Weill Cornell, Memorial Sloan Kettering Cancer Center

Background: Adrenocortical carcinoma (ACC) portends a poor prognosis and a high recurrence rate. Surgical resection is the only potentially curative treatment. Prognostic factors for survival and recurrence are well documented, but the importance of large vessel extension (LVE) is not commonly evaluated. This study aims to assess outcome of ACC in the presence and absence of LVE.

Methods: Dual-institution, retrospective review of 57 patients who underwent curative intent resection for ACC between 1988 and 2008 allowed comparison of patients with and without LVE. LVE was defined as the presence of vascular wall invasion or intraluminal extension of tumor in the inferior vena cava or renal vein. Preoperative diagnostics, operative details, pathology, overall survival (OS), and recurrence free survival (RFS) were analyzed.

Results: Twenty-two patients had LVE (39%) and 35 patients (61%) had no LVE. Patients with LVE were more likely to have functional tumors (70% vs. 37%, $p=0.03$) and higher preoperative serum hormone levels (74% vs. 34%, $p=0.01$). There were no significant differences in patient characteristics, operative details, tumor size, presence of metastases, or pathology. Patients with LVE were more likely to have positive margins (55% vs. 15%, $p=0.005$). Survival analysis was performed on 55 of 57 patients with a median follow up time of 3 years, a median OS time of 6 years (95% CI 3-15), and a median RFS time of 3 years (95% CI 1-5). Kaplan-Meier analysis demonstrated a significant reduction in OS ($p=0.0006$) and RFS ($p=0.001$) in patients with LVE. Median OS with and without LVE were 17.8 and 111.4 months respectively and median RFS were 10.7 and 63.6 months. Three year OS with and without LVE were 29% and 93% respectively and 3 year RFS were 15% and 67%. LVE, Stage III disease, Stage IV disease, Weiss score, positive margins, positive lymph nodes, adjacent organ invasion, metastatic disease, elevated preoperative hormone levels, and functional tumors were all significantly associated with OS and RFS on univariate analysis. Multivariable regression analysis showed a significant association for only LVE, Stage III disease, and Stage IV disease.

Conclusions: LVE in ACC is associated with poorer OS and RFS when compared to patients without LVE. In addition to systemic and lymph node metastases, LVE is a significant prognosticator for outcome in ACC.

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*Paper 2 (3:30pm - 3:45pm)

RESIDENT/FELLOW ASSISTANCE IN THE OPERATING ROOM DURING THE ERA OF FELLOWSHIPS

Melanie Goldfarb, Richard A. Hodin, Sareh Parangi
Beth Israel Deaconess, Massachusetts General Hospital

Background: The role of surgical residents and fellows participating in endocrine surgical cases may be undergoing dynamic changes due to an increasing number of fellowships. We sought to see if we could identify the level of resident and fellow involvement in endocrine operations at hospitals participating in the National Surgical Quality Improvement Program (NSQIP). In addition, we studied the operative characteristics and patient outcomes after endocrine operations performed with the assistance of surgical residents and fellows compared to surgical attendings operating alone.

Methods: The NSQIP database was queried for all major endocrine operations (adrenal, parathyroid, and thyroid) performed during 2005-2008, which is approximately 20% of all endocrine operations at participating hospitals. Resident assistance in the operating room was classified as none, junior (PGY1-3), senior (PGY4,5) or fellow (PGY6 or higher).

Results: 24.9% of all endocrine operations were performed by an attending surgeon operating alone (17.3% adrenals, 27.7% thyroids, 20.8% parathyroids). Fellows assisted in 6.8% of the total cases (18.6% adrenals, 4.8% thyroids, 8.4% parathyroids; 586 in 2006, 629 in 2007, 720 in 2008). Senior residents assisted in 37.2% of the total cases (52.6% adrenals, 35.6% thyroids, 37.4% parathyroids). Junior residents assisted in 31.1% of the total cases (11.5% adrenals, 31.9% thyroids, 33.5% parathyroids). Operating with residents or fellows did not significantly increase wound infections, medical complications, return to the OR, or overall morbidity. Operating without residents led to shorter operative times ($p < .001$) but longer surgical lengths of stay for all operations (adrenal: 2.32 days, parathyroid: 1.79 days, thyroid: 1.81 days, $p < .001$). Their patients had similar risk factors except for a higher prevalence of obesity (BMI > 30) and octogenarians ($p = .03$).

Conclusions: Even with the increase in endocrine surgery fellowships, almost one fourth of all endocrine operations are still performed by attending surgeons operating alone. The percentage of fellow-assisted cases has not increased over the past few years despite an increase in the number of fellowships. There was no significant difference in patient outcomes if surgeons operated alone or with residents and fellows, though operations did last significantly longer.

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*Paper 3 (3:45pm - 4:00pm)

TRAINING OUR FUTURE ENDOCRINE SURGEONS: A LOOK AT THE ENDOCRINE SURGERY OPERATIVE EXPERIENCE OF U.S. SURGICAL RESIDENTS

Barbara Zarebczan, Victoria Rajamanickam, Glen Leverson, Herbert Chen, and Rebecca S Sippel

University of Wisconsin

Background: Previous studies have shown that the average number of endocrine cases performed by graduating chief residents in US general surgery programs is inadequate. In the last 10 years the number of endocrine procedures performed in the US has increased significantly. We sought to determine if that increase in endocrine procedures has led to an increase in operative case volume for general surgery and/or otolaryngology residents.

METHOD: We evaluated the records from the Resident Statistic Summaries of the Resident Review Committee (RRC) for US general surgery and otolaryngology residents for the years 2004-2008. We specifically examined data on thyroidectomies and parathyroidectomies for both groups.

Results: Between 2004 and 2008, the average endocrine case volume of both US general surgery and otolaryngology residents increased by approximately 15%. Although both saw a similar rate of growth, otolaryngology residents performed over twice as many operations as US general surgery residents. Otolaryngology increased their volume from 57.1 to 67.3 cases compared to general surgery residents who saw an increase from 26.4 to 30.9 cases ($p < 0.001$). The growth in case volume was mostly due to increases in the number of thyroidectomies performed by US general surgery residents and otolaryngology residents (17.9 to 21.8, $p = 0.007$ and 46.5 to 54.4, $p = 0.04$). When comparing the average number of thyroidectomies by resident level, as surgeon juniors otolaryngologists performed 14.8 cases compared to 11.6 done by general surgeons ($p = 0.02$). The most striking difference was seen in the significantly larger number of thyroidectomies done by otolaryngology chiefs (34.8 vs. 8.3, $p = 0.001$). Overall, otolaryngology residents performed more parathyroidectomies than their general surgery counterparts (11.6 vs. 8.8, $p = 0.007$). As junior residents, general surgeons performed more parathyroidectomies than otolaryngologists (5.1 vs. 3.6, $p = 0.001$). However, otolaryngology chiefs performed significantly more parathyroidectomies than general surgery chiefs (8.0 vs. 3.7, $p = 0.002$).

Conclusion: Although there has been an increase in the number of endocrine cases performed by graduating US general surgery residents, this is still significantly smaller than the number being done by otolaryngology residents. In order to remain competitive, general surgery residents wishing to practice endocrine surgery may need to pursue additional fellowship training.

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*Paper 4 (4:00pm - 4:15pm)

PET-CT SCANS IN RECURRENT OR PERSISTENT DIFFERENTIATED THYROID CANCER - IS THERE ADDED UTILITY BEYOND CONVENTIONAL IMAGING

Tricia Fairchild, Yusuf Menda, James R. Howe, Ronald J. Weigel, Sonia L. Sugg, Geeta Lal
University of Iowa, Department of Surgery and Radiology

Background: Integrated PET-CT may have advantages over conventional imaging in accurately locating disease in patients with recurrent or persistent differentiated thyroid cancer. Our study aims to 1) evaluate the settings in which PET-CT scans are obtained for differentiated thyroid cancers at our institution, 2) assess the utility of PET-CT in localizing disease and 3) assess the additive value of PET-CT over conventional imaging studies.

Methods: A retrospective review of all patients with differentiated thyroid cancer who underwent a PET-CT scan between January 2003 and June 2008 was performed. PET-CT results were compared to conventional imaging including contrast CT/MRI, neck ultrasound and Radioactive Iodine (RAI) scans. The performance characteristics of PET-CT were evaluated with histological confirmation or follow-up.

Results: 30 patients (11 male, 19 female) with a mean age of 49.9+/-17 years with prior thyroidectomy and RAI ablation for thyroid cancer (Papillary or Follicular variant of Papillary 25, Follicular 1, Hurthle cell 2 and Mixed Papillary and Follicular 2) underwent 36 PET-CT scans. Initial stage at presentation was Stage I in 11, Stage II in 1, Stage III in 8, and Stage 4 in 9 patients. Indications for PET-CT were: Elevated thyroglobulin (Tg) level and negative RAI scan in 30, positive Tg antibodies in 3, and re-staging in 3 patients. Median unstimulated and stimulated Tg levels prior to imaging were 4.9 and 136.9, respectively. 18/36 (50%) of PET-CT scans showed increased uptake in the neck, 11/36 (31%) in the lung, 3/36 (8.3%) in bone and 6/36 (16.6%) in other areas. PET-CT had an overall sensitivity of 73.9%, specificity of 61.5% and positive predictive value of 77.3%. To assess the added value of PET-CT, we focused on the 21 (58%) scans performed after conventional imaging in 20 patients. PET-CT provided additional information in 2 (10%) patients, both of whom were spared additional intervention. However, PET-CT also underestimated extent of disease when compared to conventional imaging in 3 (15%) patients, and led to unnecessary interventions (including surgery, RAI and antibiotics) in 3 (15%) additional patients.

Conclusion: PET-CT has reasonable sensitivity in the detection of recurrent differentiated thyroid cancer, however, the added value of PET-CT may be limited after good quality conventional imaging. Further studies are needed to determine the most cost-effective approach to managing these challenging patients.

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Paper 5 (4:15pm - 4:30pm)

AN ECONOMIC COMPARISON OF SURGICAL AND PHARMACEUTICAL THERAPY IN PATIENTS WITH SECONDARY HYPERPARATHYROIDISM IN GERMANY

Ralph Schneider, Georgios Kolios, Emilio Dominguez-Fernandez, Benjamin M. Koch, Detlef K. Bartsch, Katja Schlosser

Philipps University Marburg; Department of Visceral, Thoracic and Vascular Surgery

Background: Secondary hyperparathyroidism (sHPT) is a frequent complication in patients with chronic kidney disease leading to osteopathy, myopathy and an increased morbidity and mortality related to major vessel calcifications. Total parathyroidectomy (PTX) with autotransplantation and subtotal PTX are considered standard procedures in surgical treatment of sHPT. Conservative therapy was significantly amended with the introduction of Cinacalcet in 2004 and Paricalcitol in 2005 and led to a consecutive reduction in the frequency of surgical procedures performed for sHPT worldwide. Limitations of resources in public health systems demand detailed analyses of accruing costs. The aim of this study was to evaluate and compare the costs of surgical and medical therapy.

Methods: All patients with sHPT who underwent initial PTX at our hospital between 01/2003 and 01/2006 (n=91) and all patients treated with Cinacalcet or Paricalcitol at an ambulatory dialysis centre (n=100) were analyzed. The revenues of both therapies for the funding agencies were calculated by a cost-cost-analysis. The real arising costs of the supplier (hospital) were analyzed performing clinical pathways and compared to the revenues of the medical therapies.

Results: The annual costs of a therapy with Cinacalcet (60mg/day) were calculated with 5828.40€ and for Paricalcitol (15×g/week) with 4485.20€. Inpatient revenues were calculated using base-case-values, special relative weight and an average rate of reoperations of 5% leading to a total amount of 3755.38€. Additionally, the costs for postoperative ambulant therapy including blood examinations and calcium and calcitriol supplementation were calculated with 545.05€ for the first year and 384.97€ for the following year.

Conclusions: Due to linearly rising, expenses of medical treatment with Cinacalcet for more than 9 months or Paricalcitol for more than 12 months exceeded the costs of surgical therapy. The indication of these new medical therapies should therefore be restricted to patients as an interim solution ahead of surgery or in those who are considered unsuitable for surgery.

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*Paper 6 (5:00pm - 5:15pm)

ROUTINE CENTRAL LYMPH NODE DISSECTION FOR PAPILLARY THYROID CANCER

David T. Hughes, Matthew L. White, Paul G. Gauger, Barbra S. Miller, Richard E. Burney, and Gerard M. Doherty
University of Michigan

Background: Routine central lymph node dissection with total thyroidectomy is controversial in the treatment of papillary thyroid cancer due to the possibility of increased operative morbidity with uncertain clinical benefit.

Method: Retrospective cohort study from 2002 to 2009 of 144 patients undergoing total thyroidectomy (TT) (66) or total thyroidectomy with bilateral central lymph node dissection (TT+BCLND) (79) for treatment of papillary thyroid carcinoma larger than one centimeter without preoperative evidence of lymph node involvement.

Results: The groups were similar in age, sex, tumor size, multifocality, angioinvasion and MACIS score. There were more tumors with extrathyroidal extension in the TT+BCLND group (41% vs 17%; $p < 0.01$). Median follow up was also longer in TT group (27.5 months vs 19.1 months; $p = 0.05$) because of a trend toward TT+BCLND over the duration of the study.

The mean number of unintentional parathyroids in the pathologic specimen (TT 0.14 vs TT+BCLND 0.41; $p < 0.01$) and the mean number of parathyroid glands reimplemented (TT 0.1 vs TT+BCLND 0.7; $p < 0.01$) were higher in the TT+BCLND patients. The incidence of temporary symptomatic hypocalcemia was more frequent in TT+BCLND patients (7.6% vs. 25.6%; $p < 0.01$) while permanent hypoparathyroidism and recurrent laryngeal nerve injury rates were equivalent at 1.3%.

Patients undergoing TT+BCLND had positive nodes in 62% of cases. The presence of positive nodes upstaged 29% TT+BCLND patients over age 45 and the median dose of radioactive iodine ablation was higher (150 mCi vs 30 mCi) in TT+BCLND patients due to higher disease stage. Median stimulated serum thyroglobin levels before and 1 year after radioactive iodine ablation were equivalent. The number of patients with undetectable thyroglobin 1 year after radioactive iodine ablation was similar. Recurrence occurred in 3% of TT patients and in 5% of TT+BCLND patients.

Conclusion: The addition of routine central lymph node dissection to total thyroidectomy for the treatment of papillary thyroid cancer increases the rates of temporary hypocalcemia but does not change the rate of other complications. Routine level VI dissection upstaged 29% of patients over the age of 45 thereby changing adjuvant radioactive iodine ablative therapy dose. Stimulated thyroglobin levels were similar with or without central lymph node dissection. Short-term disease recurrence was unchanged in patients undergoing routine central lymph node dissection.

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*Paper 7 (5:15pm - 5:30pm)

COMORBIDITY-RELATED MEDICATION DISCONTINUATION AFTER PARATHYROIDECTOMY

Adrienne L. Melick, Michaele J. Armstrong, Michael T. Stang, Sally E. Carty, Linwah Yip
University of Pittsburgh Medical Center

Background: Primary hyperparathyroidism (PHPT) associated comorbidities and nonspecific neurobehavioral, musculoskeletal and gastrointestinal symptoms have been documented to improve after parathyroidectomy (Ptx). Whether symptom improvement translates into the discontinuation or dose-reduction of drugs used to treat these comorbidities is unknown.

Methods: All cases of sporadic PHPT treated by Ptx from 1/2007 to 4/2009 with biochemical cure at 6 months (normal calcium and parathormone levels) were retrieved from a prospective database and compared to a cohort of patients undergoing thyroidectomy (Tx) during the same time period. Tx patients who were not euthyroid at postoperative follow-up were excluded. We reviewed patient demographics, medical history, perioperative symptoms and medications (antidepressants, antihypertensives, antilipids, analgesics, antacids, stool softeners, and bisphosphonates). The Fisher's exact and t-tests were used for statistical comparisons.

Results: We compared 263 Ptx to 176 Tx patients. The Ptx patients were older compared to the Tx patients (mean age 63 v. 57 yrs, $p < .001$) and were more commonly men (26 v. 15%, $p = .004$). Preoperatively, Ptx patients had a higher prevalence of hypertension (53 v. 38%, $p = .002$), hyperlipidemia (51 v. 27%, $p < .001$), GERD (28 v. 10%, $p < .001$), constipation (22 v. 2%, $p < .001$), osteoporosis (21 v. 5%, $p < .001$), arthritis (62 v. 33%, $p < .001$), fatigue (63 v. 15%, $p < .001$), and/or depression (29 v. 15%, $p = .001$). After surgery, Ptx patients self-reported improvements in their preoperative nocturia (22%), arthritis (36%), fatigue (45%), and depression (23%). Discontinuation or dose-reduction of medications used to treat depression, osteoporosis, hypertension, hyperlipidemia, arthritis, GERD and constipation occurred in 33 (13%) Ptx patients compared to 8 (5%) Tx patients ($p = .004$). Analgesics (9/33, 27%) and antidepressants (6/33, 18%) were the most frequently discontinued medications.

Conclusion: Alleviation of PHPT-related symptoms after surgery has been demonstrated by several experts, but remains controversial. We confirm the improvement of these symptoms after Ptx and also show, for the first time, that patients can discontinue associated comorbidity medications. After Ptx, medications for PHPT-related comorbidities should be routinely reviewed and adjusted. Cost-effective analysis must now incorporate ongoing drug therapies for PHPT-related comorbidities.

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*Paper 8 (5:30pm - 5:45pm)

NOMOGRAM FOR PREDICTING MALIGNANCY IN THYROID NODULES USING CLINICAL, ULTRASOUND AND CYTOLOGY FEATURES

Iain J. Nixon, Lucy E. Hann, Oscar Lin, Debra A. Goldman, , Monica M. Witcher, BA, Changhong Yu, Frank L. Palmer, BA, Ashok Shaha, Jatin P. Shah, Ian Ganly, Michael W. Kattan, Snehal G. Patel

Memorial Sloan Kettering Cancer Center

Background: Ready access to high definition ultrasound, has resulted in an increase in the number of nodules detected. However, only around 10% of nodules are malignant and need surgical intervention. The judicious use of fine needle aspiration(FNA) can help identify those needing surgery, but the limitations of a non-diagnostic FNA in predicting malignancy are well recognized. The decision to recommend surgery is based on the clinician's assessment of malignancy risk. Experienced clinicians can predict the chance of malignancy within a nodule using clinical, ultrasound and cytologic features and provide treatment recommendations. However, accurate quantification of risk would be helpful in decision making and counseling patients. The aim of this study was therefore to create a predictive nomogram based on clinical, ultrasound and cytology features to accurately predict the chance of malignancy within a thyroid nodule in a tertiary care setting.

Methods: All patients who underwent ultrasound guided FNA and had surgery within our institution during 2007-2008 were identified. Clinical records and pathology reports were reviewed. Ultrasound images were reviewed by a radiologist and cytology slides were reviewed by a cytologist for a list of predetermined features. Data was entered into an electronic database for analysis. Multivariate logistic regression was used to quantify the predictive value of clinical, ultrasound and cytology variables in predicting the risk of malignant nodules. Eight variables with the highest predictive value were selected for the final nomogram. The nomogram was internally validated by assessing discrimination and calibration. Bootstrapping was used to correct for over-fitting bias.

Results: One hundred and fifty eight patients with 190 nodules were identified. Eighteen patients were excluded, leaving 172 nodules for analysis. Seventy seven of the 172 nodules were positive for malignancy on histopathology. The 8 variables with highest predictive value selected for the nomogram were: clinical (TSH), ultrasound (shape, echo texture, vascularity) and cytology (nuclear grooves, pseudo-inclusions, cellularity and presence of colloid). The nomogram had an excellent predictive accuracy with a concordance index of 91%.

Conclusion: We have produced a nomogram which is able to accurately quantify the risk of malignancy in a thyroid nodule in a tertiary care population based on a combination of clinical, ultrasound and cytology features.

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Paper 9 (5:45pm - 6:00pm)

ACCURACY OF 4D-CT IN POORLY-LOCALIZED PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

Carrie C. Lubitz, George J. Hunter, Leena M. Hamberg, Sareh Parangi, Daniel Ruan, Atul Gawande, Randall D. Gaz, Gregory W. Randolph, Francis D. Moore, Jr., Richard A. Hodin, and Antonia E. Stephen

Massachusetts General Hospital; Brigham & Women's Hospital

Background: 4D-CT is a new imaging modality that utilizes multi-planar images and perfusion characteristics to identify abnormal parathyroid glands. Although 4D-CT has been reported to show improved accuracy compared to sestamibi and ultrasound, the appropriate role for this novel imaging study remains to be determined. We aimed to assess the benefit of 4D-CT in patients with inconclusive pre-operative ultrasound and sestamibi localization studies.

Methods: The study population consisted of adult patients with primary hyperparathyroidism and non-confirmatory standard imaging (ultrasound and sestamibi) who underwent both localization with 4D-CT and surgery for curative intent by one of eight endocrine surgeons at two tertiary-care, academic hospitals from 5/08-9/09. Patient characteristics, 4D-CT scan results as compared to surgical and pathological findings, and curative proportion were assessed (means (SD), medians (IQR), Fisher exact test). Surgical findings were considered the gold standard for localization.

Results: Sixty patients met the inclusion criteria. Sixty-five percent of the patients had no previous neck surgery, whereas 35% had previous parathyroid or thyroid operations. Overall, 4D-CT accurately lateralized 72% and localized 60% of abnormal glands found at surgery. When the 4D-CT identified a single candidate lesion (46/60), findings were confirmed at surgery in 69%. When multiple lesions were identified on 4D-CT (14/60), accuracy dropped to 36%. Accuracy of 4D-CT was not significantly different between primary and re-operative cases (Fisher exact $p = 0.21$). The one case labeled four-gland hyperplasia on 4D-CT was confirmed at surgery. Of the eight patients with multi-gland disease (> one abnormal parathyroid) diagnosed at the time of surgery, five had multiple candidate lesions noted on 4D-CT. In 90% of patients, a greater than 50% drop in PTH level was achieved 10 minutes after resection and 83% were normocalcemic (8.5-10.4 mg/dL) following surgery (median follow-up 22 days, IQR 14-129). A single gland was found on 4D-CT and confirmed at surgery in 32 of the 60 cases; 96% had a 50% fall in intra-operative PTH level.

Conclusions: 4D-CT identifies the majority of abnormal parathyroids missed by traditional imaging and should be considered in cases with negative or discordant sestamibi and ultrasound. Multi-gland disease remains a challenging entity.

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*Paper 10 (7:45am - 8:00am)

BRAF MUTATION IS ASSOCIATED WITH AN INCREASED RISK OF LOCAL RECURRENCE REQUIRING RE-OPERATIVE SURGERY IN PATIENTS WITH PAPILLARY THYROID CANCER

Christine J. O'Neill, Martyn Bullock, Angela Chou, Stan B. Sidhu, Leigh W. Delbridge, Anthony Gill, Diana L. Learoyd, Roderick Clifton-Bligh, Mark S. Sywak
University of Sydney Endocrine Surgical Unit

Background: Mutation of the BRAF oncogene is the most common genetic alteration in papillary thyroid cancer (PTC) yet its role as an independent prognostic factor remains controversial. Some studies suggest that BRAF mutation is associated with poor radioactive iodine uptake and a higher risk of local recurrence. The aim of this study was to evaluate the relationship between BRAF mutation and disease-free survival particularly with regards to local recurrence requiring further surgery.

Methods: Paraffin embedded specimens from consecutive patients who underwent surgery for PTC prior to 2003 were retrieved and independently reviewed by an endocrine pathologist. DNA was extracted, amplified by polymerase chain reaction and BRAF V600E (valine to glutamic acid at codon 600) mutational status determined by restriction digest. These results were correlated with the clinicopathological features of the tumor and with long-term disease outcomes.

Results: The study group comprised 100 patients (81% female) with a median age of 43 years. BRAF mutation was present in 58% of thyroid tumors. At a median follow-up of 105 months (8.8 years) overall disease-free survival was 80% and disease related mortality was 4%. Local recurrence occurred in 14% of BRAF positive patients and all required further surgery with lateral neck dissection ($p=0.02$). In contrast local recurrence occurred in 7% of BRAF negative patients with none requiring further surgery as all were successfully ablated with radioactive iodine. All 4 disease-related deaths occurred in patients whose primary tumour contained the BRAF mutation, however this did not reach statistical significance ($p=0.09$). In patients with Stage III or IV disease there was a trend towards poorer disease-free survival ($p=0.05$) in those with BRAF mutation.

Conclusion: BRAF mutation is associated with an increased risk of local recurrence and the need for re-operative surgery.

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Paper 11 (8:00am - 8:15am)

ANALYSIS OF THE RISING INCIDENCE OF THYROID CANCER UTILIZING THE SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) NATIONAL CANCER DATA REGISTRY

John D. Cramer, Pingfu Fu, Karem C. Harth and Scott M. Wilhelm
University Hospitals/Case Western Reserve University, School of Medicine

Background: The incidence of thyroid cancer has more than doubled in recent decades. Debate continues if the rising incidence is due to an increased detection of small tumors or other factors. Our aims are to examine trends in thyroid cancer incidence and to analyze tumor histopathologic characteristics and treatment modalities.

Method: We evaluated a retrospective cohort of patients from 1973-2006 in the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute. All thyroid cancer diagnoses (Papillary, Follicular, Medullary, and Anaplastic) were extracted, yielding 50,212 cases. We examined the incidence of thyroid cancer and compared variations based on tumor size and stage, as well as the surgical and adjuvant therapy of the tumors. Incidence rates (Data available 1973-2006) were age adjusted based on the U.S. population in 2000 expressed per 100,000 individuals with the use of SEER Stat. The Cochran-Armitage (CA) trend test was then used to examine the trends for papillary thyroid cancer (Tumor pathology data available from 1983-2006). $P < 0.05$ was significant.

Results: Thyroid cancer (all types) increased from a rate of 4.5 per 100,000 in 1973 to 11.0 per 100,000 in 2006, a 2.4 fold increase. This change can be primarily attributed to a rise in papillary thyroid carcinoma (PTC), 2.67 to 8.78 per 100,000, a 3.3 fold increase ($P < 0.0001$). The rise in PTC was further examined based on tumor size. While the incidence of micropapillary thyroid cancer (microPTC), tumor ≤ 1 cm, increased the most at a total of 441% between 1983-2006 or 19.2% per year, the incidence of PTC also increased significantly in 1.1-2cm tumors, 12.3%/year, 10.3%/year in 2.1-5cm tumors, and 12.0%/year for >5 cm tumors (all $P < 0.0001$ by CA trend test). Tumors confined to the thyroid increased at 15.1%/year, while PTC with regional lymph node metastases increased 15.6%/year. Annual rates of distant metastatic disease did not increase. Treatment for thyroid cancer has also shifted with total thyroidectomy replacing partial thyroidectomy as the most common surgical therapy.

Conclusions: Contrary to other studies, our data indicates that the rising incidence of thyroid cancer cannot be fully accounted for by an increased detection of small tumors representing microPTC. Other possible explanations for the rise in clinically significant (>1 cm) well differentiated thyroid carcinoma should be explored.

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*Paper 12 (8:15am - 8:30am)

THYROIDECTOMY WITH NEOADJUVANT PLX4720 EXTENDS SURVIVAL AND DECREASES TUMOR BURDEN IN AN ORTHOTOPIC MOUSE MODEL OF ANAPLASTIC THYROID CANCER

Matthew A. Nehs, Sushruta Nagarkatti, Carmelo Nucera, Richard A. Hodin, and Sareh Parangi

Massachusetts General Hospital

Background: Anaplastic thyroid cancer is among the most lethal of all human cancers and has very few therapeutic options. BRAFV600E is a common mutation in these tumors and represents a novel therapeutic target. We hypothesized that PLX4720 (a selective inhibitor of BRAFV600E) and subsequent thyroidectomy would extend survival and decrease tumor burden in an orthotopic mouse model of anaplastic thyroid cancer.

Methods: Orthotopic thyroid tumors were induced in SCID mice using the human-derived anaplastic thyroid cancer cell line, 8505c. Three experimental conditions were used: Vehicle+Sham Surgery (Group 1, n=5), PLX4720+Sham Surgery (Group 2, n=6), and PLX4720+Thyroidectomy (Group 3, n=6). Either PLX4720 or vehicle was administered for three weeks after a one week period of tumor growth. Thyroidectomy or sham surgery was performed after two weeks of tumor growth. At 35 days, the neck space was re-explored and tumor volume was measured. Mice were sacrificed when they lost >25% of their initial weight or developed tracheal compression symptoms.

Results: All (five) mice in Group 1 had invasive, unresectable tumors at two weeks that developed into large thyroid tumors (average 61 mm³) at 35 days. All of these mice developed cachexia and met criteria to be sacrificed at 35 days. All (six) mice in Group 2 had small tumors (average 1.3 mm³) and maintained their weight. In Group 3, three of six mice had no evidence of tumor at 35 days; the other three mice had small tumors (average 1.4 mm³) and showed no signs of metastatic disease. All mice in groups 2 and 3 were alive and well-appearing at 50 days.

Conclusions: While orthotopic anaplastic thyroid cancer (8505c) is uniformly fatal in untreated mice, early treatment with PLX4720 and thyroidectomy dramatically reduces tumor volume and extends survival. Thyroidectomy with neoadjuvant PLX4720 could be an effective therapeutic strategy for early anaplastic thyroid cancers that harbor the BRAFV600E mutation and are refractory to conventional therapeutic modalities.

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*Paper 13 (8:30am - 8:45am)

IS DVT PROPHYLAXIS NECESSARY FOR THYROIDECTOMY AND PARATHYROIDECTOMY?

Madhu Roy, Victoria Rajamanickam, Herbert Chen, and Rebecca Sippel
University of Wisconsin

Background: Recent guidelines suggest pharmacologic DVT prophylaxis in all patients undergoing major surgical procedures to minimize the risk of post-operative DVT and PE. Pharmacologic DVT prophylaxis peri-operatively may increase the risk of bleeding complications. We hypothesized that the risk of DVT formation in patients undergoing thyroid and parathyroid surgeries is significantly lower than other surgical procedures. We also hypothesized that these patients are at a much higher risk of developing life-threatening bleeding complications. Therefore, the risk to benefit ratio of DVT prophylaxis in this group of patients may need to be reconsidered.

Methods: A review of the ACS NSQIP Database from 2005-2007 was performed. The incidence of DVT/PE complications in the entire cohort of 347,862 patients was compared to the 16,022 patients who underwent a thyroidectomy or parathyroidectomy. We identified risk factors for DVT/PE and developed a surrogate variable to determine the risk for post-operative bleeding.

Results: The risk of DVT/PE complication in the total surgical population was 0.96% while the incidence in the thyroidectomy and parathyroidectomy patients was only 0.16%, 6 fold less than the entire cohort ($p < 0.001$). In a univariate analysis, the variables associated with a higher risk of DVT formation were the 'duration the patient is in the room', 'the anesthesia time', 'length of total hospital stay', and 'history of CVA'. While bleeding, not requiring a transfusion, is not specifically tracked in NSQIP, return to the operating room is. After eliminating patients that had undergone a thyroid lobectomy who were found to have cancer, and eliminating patients with wound infections, we found that the remaining patients had a 1.6% incidence of returning to the operating room within the first 30 days. This suggests that the risk of bleeding requiring a return to the operating room may be as high as 1.6%, which is 10 fold higher than the risk of developing a DVT/PE ($p < 0.001$).

Conclusions: Patients undergoing thyroidectomy and parathyroidectomy have a very low incidence of developing DVT/PE complications and have a significantly higher risk of developing bleeding complications. Hence we believe that DVT prophylaxis should not be mandatory for thyroidectomy and parathyroidectomy cases and should be done at the discretion of the surgeon in select high-risk patients.

* Denotes Resident/Fellow Research Award Competition Paper

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Paper 14 (8:45am - 9:00am)

DO INTRA-OPERATIVE HORMONE ASSAYS GUIDE THE EXTENT OF SURGICAL RESECTION IN THE MANAGEMENT OF SPORADIC AND SYNDROMIC INSULINOMA?

James Kirkby-Bott, Robert Caiazza, Laurent Arnalsteen, Pascal Pigny, Emmanuelle Leteurtre, Guelareh Dezfoulian, Marie-Christine Vantyghem, Michele D'Herbomez, Rachel Desailoud, Odile Verrier Mine, Jean-Louis Wemeau, Bruno Carnaille, François Pattou

Dept Endocrine & Metabolic surgery, Hopital Huriez, CHU

Background: Surgery for insulinoma is sometimes complex, especially in certain cases: syndromic disease, equivocal imaging findings and when a laparoscopic approach is planned. Like in parathyroid surgery, intra-operative peptide assay has been proposed to guide the surgical management of insulinoma. In this study we assessed the performance of intra-operative insulin assay (IOIA) and its clinical usefulness in patients with sporadic and syndromic insulinoma.

Method: Patients operated on for insulinoma between 1998 and 2009 underwent intra-operative insulin measurement (IOIA). Insulin, proinsulin, C-peptide and insulin: glucose ratios were measured in portal and peripheral vein samples at 5 and 20 minutes post excision. At the end of the study the threshold of change in peptide levels needed to predict biochemical cure after surgery was determined using a receiver operating characteristic (ROC) curve. We assessed the performance of the test in sporadic and syndromic cases. IOIA was considered clinically useful when its results significantly affected the extent of surgery.

Results: A total of 33 patients (22 female, 11 male median age 44 years), including 21 with sporadic insulinomas and 12 syndromic cases (9 MEN-1, 2 carcinomas and 1 islet cell hyperplasia) were enrolled. Biochemical cure was achieved after surgery in 100% of sporadic cases and 11/12 (92%) of syndromic cases. ROC curve analysis showed that the most accurate parameter was an insulin drop greater than 50%, 20 minutes after excision. Portal sampling gave no advantage over peripheral sampling. In sporadic cases IOIA had a positive predictive value (PPV) of 100% and sensitivity of 91%; and determined the extent of surgery in 2 patients (10%) with equivocal imaging. In syndromic cases IOIA had a positive predictive value (PPV) of 90% and sensitivity of 90%; and determined the extent of surgery in 3 patients (25%) with multiple lesions on imaging.

Conclusion: We found that IOIA was clinically useful in the surgical treatment of insulinomas. A 50% drop in insulin levels in peripheral blood 20 minutes after excision confirmed biochemical cure after the excision of a seemingly unique lesion. IOIA guided the extent of resection in cases with multiple lesions.

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Paper 15 (9:00am - 9:15am)

A PROSPECTIVE TRIAL EVALUATING THE ACCURACY OF USING COMBINED CLINICAL FACTORS AND CANDIDATE DIAGNOSTIC MARKERS TO REFINE THE ACCURACY OF THYROID FINE NEEDLE ASPIRATION BIOPSY

Aarti Mathur, Julie Weng , Willieford Moses , Seth Steinberg, Quan-Yang Duh, Orlo H. Clark, Electron Kebebew

National Institutes of Health/NCI

Background: Although thyroid fine needle aspiration (FNA) biopsy is an accurate diagnostic test to evaluate for malignancy, approximately 30% will provide inconclusive Results (indeterminate, suspicious, or nondiagnostic). The development of adjunct diagnostic approaches to thyroid FNA biopsy has been an active area of thyroid cancer research with candidate markers identified. We conducted a prospective trial to determine if clinical, imaging, laboratory and molecular markers could be used in combination to improve the accuracy of thyroid FNA biopsy.

Methods: 423 patients were enrolled in a prospective trial. Demographic, clinical, imaging, tumor FNA genotype for common somatic mutations (BRAF V600E, NRAS, KRAS, RET/PTC1, RET/PTC3, NTRK1) and 6 candidate gene expression levels were analyzed to determine if they could reliably distinguish benign from malignant thyroid tumors. FNA cytologic interpretation was classified according to the NCI State of the Science recommendation. Univariate and multivariate analyses were performed to determine which factors predict malignancy.

Results: Out of 423 patients with a dominant thyroid nodule, 302 were benign and 121 were malignant. Univariate analysis revealed a significant difference in patient age, gender, greatest tumor diameter on ultrasound, presence of a somatic mutation, and 4 of 6 candidate gene expression levels ($p \leq 0.01$). By multivariate analysis age, gender, FNA cytology classification, and TIMP1 expression level were significant predictors of malignancy ($p \leq 0.03$). The overall accuracy of the scoring model to distinguish benign from malignant thyroid tumors was 89%. In the indeterminate FNA biopsies, 32% (21/66) were malignant. The scoring model, when applied was 65% accurate with a specificity of 93% and sensitivity of 5%. In the suspicious FNA group, 59% were malignant and increased to 82% using the scoring model with a sensitivity of 88% and specificity of 73%.

Conclusions: Age, classification of FNA cytology, and TIMP1 mRNA expression levels in combination have a high diagnostic accuracy to allow selection of more definitive initial surgical treatment but the sensitivity is not high enough to avoid the need for diagnostic thyroidectomies in patients with indeterminate FNA findings.

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*Paper 16 (10:00am - 10:15am)

ALDOSTERONE-SECRETING ADRENAL ADENOMAS - IS SURGERY TOO EXPENSIVE?

BethAnn Reimel, Mark J. Russo, Kyle Zanooco, Rasa Zarnegar, Cord Sturgeon, Orlo H. Clark, John D Allendorf, John A Chabot, Quan-Yang Duh, James A Lee
Columbia University Medical Center

Background: Primary hyperaldosteronism (PHA) is the disease characterized by excessive secretion of aldosterone by the adrenal glands. In the majority of cases, this is due to an aldosterone-secreting adrenal adenoma. Recently, there has been some controversy over the best management of patients with this problem. Some endocrinologists have suggested that long-term medical management with oral spironolactone is preferable to surgical resection via laparoscopic adrenalectomy, even in younger patients. In our current cultural and economic environment, the financial cost associated with treatment options should be one of the points considered as we make medical decisions. In this study, we sought to compare the cost of long-term medical management to surgical resection in patients with primary hyperaldosteronism.

Methods: Based on review of the literature and a series of 122 patients with primary hyperaldosteronism that underwent laparoscopic adrenalectomy at a tertiary medical center between 1994 and 2006, success rates were determined for the various medical and surgical treatment arms.

Medicare reimbursement rates and Agency for Healthcare Research and Quality database were used to obtain costs of treatment regimens. Cost analysis differentiated between one-time costs and those to be multiplied by years of life.

Decision analysis was performed by constructing a Markov state transition model comparing two strategies: (1) medical management of aldosteronomas (2) surgical resection of aldosteronomas. Extensive sensitivity analyses were performed. A threshold analysis was performed to determine the number of years from diagnosis when surgery becomes the less costly treatment strategy.

Results: Threshold analysis was performed to determine the time (from diagnosis to end-of-life) at which surgical treatment becomes a less costly option than medical treatment. Our analyses found that if, at the time of diagnosis, the patient has a life expectancy of 15.9 years or more, surgery is less costly than medical management, and is the optimal strategy from a cost perspective. The discounted average cost of the surgical strategy was \$33,437 vs \$54,946 in a 40-year-old with a 48 year life expectancy.

Conclusions: For patients with PHA due to an adrenal aldosteronoma, surgery is the optimal strategy from a cost-perspective if, at the time of diagnosis, the patient has a life expectancy of 15.9 years or more.

* Denotes Resident/Fellow Research Award Competition Paper

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Paper 17 (10:15am - 10:30am)

DIFFERENTIATING HUMAN STEM CELLS INTO PARATHYROID FOR TREATMENT OF HYPOPARATHYROIDISM

Kathleen M. Woods Ignatoski, Eve L. Bingham and Gerard M. Doherty
University of Michigan

Background: Loss of parathyroid gland function (hypoparathyroidism) is the most frequent permanent complication of thyroid and parathyroid surgery. Hypoparathyroidism is poorly managed by currently available replacement methods which require the patient to take multiple daily oral doses of vitamin D and calcium supplements to avoid neuromuscular symptoms, but do not alleviate chronic bone problems; therefore, new therapies are needed.

Parathyroid glands are optimal for cellular replacement therapy because: (1) each parathyroid cell contains the complete function of the organ; (2) the total number of cells needed for function is small; (3) no architectural arrangement of parathyroid cells is needed to support or enhance the function of the organ; and (4) transplantation of autologous parathyroid cells has been proven to reconstitute normal parathyroid function. Our hypothesis is that human stem cells in culture can be differentiated into parathyroid cells and used to reconstitute parathyroid function.

Methods: We have modified the differentiation procedure used by D'Amour (Nat. Biotechnol. (2005). 23 (12): 1534-41) to differentiate the BG01 human embryonic stem cells (hESC).

Results: Differentiated BG01 cells expressed the mRNA for certain biomarkers of normal parathyroid cells including calcium sensing receptor (CaSR; which is present on parathyroid cells), CXCR4 (an epithelial marker), GCM2 (a parathyroid specific marker), and parathyroid hormone (PTH). CaSR and CxCr4 were also present on approximately 90% of the cells by immuno-fluorescence. The differentiated cells also expressed parathyroid hormone (PTH). We have successfully replicated the differentiation seen in the BG01 cells in H1 hESC cells. We have been able to isolate CaSR+ cells from long term cultures of H1 cells that have undergone our differentiation protocol.

Conclusions: These data suggest that hESC cells were successfully differentiated into parathyroid cells. We are in the process of identifying pluripotent adult cells to be used with our differentiation scheme to create parathyroid for therapeutic purposes. These data give a solid rationale for the isolation of parathyroid stem cells from human tissue for parathyroid replacement therapy in clinical hypoparathyroidism.

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Paper 18 (10:30am - 10:45am)

IMPACT OF SECOND PRIMARY MALIGNANCY ON OUTCOMES OF DIFFERENTIATED THYROID CARCINOMA

Brian H Lang, Chung-Yau Lo, Irene Oi Wong, Benjamin Cowling
The University of Hong Kong

Background: Differentiated thyroid carcinoma (DTC) generally affects relatively young patients with a good life-expectancy and so the occurrence of second primary malignancy (SPM) poses a real concern to these patients. The study aimed at evaluating the risk of SPM in DTC patients' cohort and assessing whether its occurrence and timing have any impact on the clinical course of DTC.

Methods: A retrospective review of 1043 DTC patients managed at our institution from 1970 - 2008 was performed. All SPMs were captured by the territory-wide Clinical Management System. Among the 132 SPMs, 27 were synchronous (i.e. diagnosed within 6 months of DTC, group 1) and 69 were metachronous (diagnosed > 6months after DTC, group 2). The total person-years of observation were 10419. The standardized incidence ratio (SIR), based on the age- and sex-specific cancer incidence rates from the local cancer registry, was calculated. Kaplan-Meier analysis was used to estimate survivals and comparison of survival was performed by the log rank test.

Results: There was a 39% increase in SPM rate (SIR = 1.39, 95% CI: 1.09 - 1.73) in DTC patients compared with the general population. The 3 commonest SPM sites were breast (n=14), colon (n=10) and lung (n=8). Despite similar DTC-specific survival, those with SPM had a worse overall survival than those without SPM ($p < 0.001$). When DTC's features were compared, group 1 tumors were more advanced-TNM-stage than group 2 ($p < 0.001$), even though they were more often detected incidentally on imaging ($p < 0.001$) and smaller in size ($p = 0.005$). As a result, group 1 had worse 5-yr and 10-yr DTC-specific survivals than group 2 (77.65%, 77.65% vs 100%, 100%, $p = 0.002$, respectively). However, group 2 had worse 3-yr and 5-yr SPM-specific survivals than group 1 (77.52%, 77.52% vs 55.04%, 47.81%, $p = 0.042$). Fewer patients in group 2 were able to receive curative treatment for SPM after discovery (38/69 vs 21/27, $p = 0.040$).

Conclusion: Our patients' cohort was at increased risk of developing SPM. Despite similar DTC-specific survival, those with SPM had a worse overall survival than those without. Patients with synchronous SPM had more advanced DTC and were more likely to die from DTC than those with metachronous SPM. In contrast, those with metachronous SPM were more likely to die from SPM as fewer patients were able to receive curative treatment. Perhaps, closer postoperative SPM surveillance should be considered in the future.

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Paper 19 (10:45am - 11:00am)

MANAGEMENT OF CERVICAL NODE METASTASES DETECTED ON TOTAL-BODY I-131 IMAGING FOLLOWING INITIAL SURGERY FOR WELL-DIFFERENTIATED PAPILLARY THYROID CARCINOMA

Jeffrey F. Moley, Bruce H. Haughey, Perry W. Grigsby
Washington University School of Medicine

Background: Following surgery and post-operative I-131 treatment, patients undergo a post-therapy total-body I-131 scan. The purpose of this study was to evaluate the outcome of patients whose post-therapy scan demonstrated I-131 uptake in cervical lymph nodes.

Methods: This is a prospective cohort study of 95 patients with well-differentiated thyroid carcinoma. All patients underwent a total thyroidectomy and 66/95 (69%) had a lymph node dissection. Post-operatively, all patients were treated with I-131 (mean, 125 mCi) and 3 to 5 days later they underwent a post-therapy total-body I-131 scan. The post-therapy I-131 total-body scan demonstrated physiologic uptake in the thyroid bed and abnormal I-131 uptake in cervical lymph nodes in all 95 patients. Patients were subsequently evaluated by further total-body I-131 scans and treated with additional I-131 or surgical excision of cervical lymph nodes as clinically indicated. Patients were followed for a mean of 6.8 years and progression-free survival was evaluated.

Results: Patients received a total of one to three I-131 administrations (mean 235 mCi). Surveillance total-body imaging and serum thyroglobulin were performed to evaluate for persistent disease. I-131 uptake was eliminated from the thyroid bed in all patients. Persistent I-131 uptake was detected in cervical lymph nodes in 7/95 (7%) and these 7 patients underwent lymph node excision. All patients subsequently had a negative total-body I-131 scan and an undetectable serum thyroglobulin. Nine patients (9/95, 9%) developed recurrent disease in cervical lymph nodes requiring surgical excision. At last follow-up, all patients were free of disease.

Conclusions: Most patients (83%) with cervical lymph node metastasis detected on their initial post-therapy total-body I-131 scan are rendered free of disease with I-131. Surgical intervention was required in 17% (16/95). The use and timing of additional I-131 therapy versus surgical intervention in this group of patients needs to be further evaluated.

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Paper 20 (11:00am - 11:15am)

ROBOTIC THYROID SURGERY BY BILATERAL AXILLO-BREAST APPROACH USING DA VINCI SURGICAL SYSTEM

Kyu Eun Lee, Su-jin Kim, Jeonghun Lee, Do Hoon Koo, Seung Keun Oh, Yeo-Kyu Youn
Seoul National University College of Medicine

Background: Robotic surgery is useful in areas with difficult access like the pelvis. The ideal indications for robotic surgery are still to be established. The neck area, especially the thyroid gland poses a difficult challenge for many endoscopic surgeons. Robotic surgery is useful in this area due to its excellent magnification and endo-wrist function. We present our experience with robotic endoscopic thyroidectomy using the bilateral axillary breast approach.

Patients and Methods: From February, 2008 to August 2009, we applied da Vinci surgical system to BABA endoscopic neck surgery for 275 patients. The male to female ratio was 1:7.33. Mean age of the patients were 38.1 \pm 8.9 (13-66) years. After subcutaneous infiltration with diluted epinephrine solution, subplatysmal and subcutaneous space was dissected. Two circumareolar ports and 2 axillary ports were used and operative space was obtained with low pressure CO₂ gas insufflation. We could obtain sufficient robotic arm mobility. Total thyroidectomies and central node dissection were done in a manner similar to BABA endoscopic thyroid surgery.

Results: BABA robotic thyroid surgery included 9 thyroid lobectomies, 17 subtotal thyroidectomies, and 174 total thyroidectomies. The mean operation time was 210.0445.5 min. The mean console time was 126436.5 min. The mean operation time of total thyroidectomy was 208.6439.2 min. The intraoperative loss of blood was minimal. The mean hospital stay was 3.54 \pm 0.7 day. The pathologic diagnosis included 187 papillary carcinoma, 1 follicular adenoma, 1 Hashimoto's thyroiditis, 1 focal fibrosis, and 4 adenomatous goiter. There was 1 case of conversion to open surgery. There were 56 (28.0%) cases of transient hypoparathyroidism and 3 cases (1.5%) of permanent hypoparathyroidism. There were 15 cases (7.5%) of transient and 1 case (0.5%) of permanent recurrent laryngeal nerve palsy. One (0.5%) postoperative bleeding and one case (0.5%) of pneumothorax developed. Cosmetic results were excellent and patients were all satisfied.

Conclusion: The Robot BABA endoscopic thyroid surgery would be a feasible method for thyroidectomy with an excellent operative visualization, optimal robotic arm mobility, minimal adverse effect, and excellent cosmetic result.

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Paper 21 (11:15am - 11:30am)

INITIAL YUMC EXPERIENCE OF ROBOT-ASSISTED MODIFIED RADICAL NECK DISSECTION IN THE MANAGEMENT OF THYROID CARCINOMA WITH LATERAL LYMPH NODE METASTASIS

Sang-Wook Kang , So Hee Lee , Haeng Rang Ryu , Kang Young Rhee , Jong Ju Jeong , Kee-Hyun Nam and Woong Youn Chung
Department of Surgery, Yonsei University College of Medicine

Background: Since the introduction of endoscopic technique to thyroid operation, several trials of endoscopic lateral neck dissection have been reported for the purpose of avoiding a long cervical scar after surgery. However, it definitely took more effort and operation time than open surgery mainly due to 2-dimensional view and technical limitations caused by long and rigid instruments. With the incorporation of surgical robotic system into the thyroid surgery, still and meticulous dissection have been enabled and more precise and improved endoscopic techniques have been accomplished. In this study, our initial experience of robot-assisted modified radical neck dissection (MRND) in thyroid cancer with da Vinci robotic system is described.

Method: From Oct. 2007 to Oct. 2009, 995 patients have undergone robot-assisted thyroidectomy using a gasless, transaxillary approach (RAT-TAA) for thyroid cancer. Among them, 33 patients have been performed additional robotic MRND for lateral LN metastasis. We have performed this procedure using two skin incisions (a 7-8 cm ipsilateral axilla and a 0.8 cm anterior chest incision). The clinico-pathologic data of the patients were analyzed retrospectively.

Results : The mean age of patients was 37.249.2 years and gender ratio (male to female) was 7:26. Mean operation time was 280.8440.6 min. and mean post operative hospital stay was 5.441.6 days. The mean tumor size was 1.0940.52 cm and PTMC was in 20 cases (60.6%). Mean retrieved L/N numbers are 6.144.4 in central compartment and 27.7411.0 in lateral neck compartment. There was no serious post operative complication such as Horner syndrome and major nerve injury (vagus, spinal accessory, hypoglossal, marginal mandibular branch of facial nerve and recurrent laryngeal nerve). There were 3 cases of minor chyle leak and all of the cases were resolved through conservative management.

Conclusion : This noble procedure of robot-assisted MRND is technically feasible, safe and cosmetically excellent. Through this method, precise manipulation of robotic instruments makes it possible to perform complete compartment-oriented dissection without any injury of major vessels or nerves and any compromising of surgical oncologic principles. From our initial experience, the robot-assisted MRND can be the acceptable alternative as an operative method, currently in the low risk, well-differentiated thyroid cancer patients with lateral neck metastasis.

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Paper 22 (1:30pm - 1:45pm)

THE IMPACT OF THE 2009 ATA GUIDELINES ON THE CHOICE OF OPERATION FOR WELL-DIFFERENTIATED THYROID MICROCARCINOMAS

Keith S. Heller, Jennifer B. Ogilvie

New York University Langone Medical Center

Background: The choice of operation for differentiated thyroid cancer (DTC) is controversial. The 2009 ATA Guidelines state "lobectomy alone may be sufficient treatment for small (<1cm), low risk, unifocal, intrathyroidal papillary carcinomas in the absence of prior head and neck irradiation or... nodal metastases." This study was undertaken to determine how often these criteria are satisfied and whether size alone is sufficient to dictate surgical management.

Methods: The charts of all 346 pts undergoing initial surgery for DTC from 1/1/07 - 11/10/09 were reviewed. 130 pts with tumors \leq 10mm and negative lateral nodes were identified. These were divided into 2 groups: Group 1 - tumors \leq 5mm (57 pts) and Group 2 - tumors 6-10 mm (73 pts). Pathology reports were reviewed for adverse features including multifocality, extrathyroid extension, vascular invasion and central node metastases.

Results: DTC was found incidentally at the time of thyroidectomy performed for other indications in 52 (40%). Preoperative FNA was performed in 78 (60%): 44 papillary cancer (PTC), 22 suspicious for PTC and 12 follicular neoplasm. 4 pts had a history of radiation. 109/130 (84%) underwent total thyroidectomy and 21 (16%) had a central node dissection. Surgical pathology revealed PTC (103), follicular variant of PTC (19), other subtypes of PTC (6) and follicular cancer (2). 50% of patients had no adverse pathologic features. Adverse pathologic features included 45% with multifocal tumors, 8% with extrathyroid extension and 17% with vascular invasion. At least 1 central node was removed in 66 pts, and 14% had nodal metastases. Groups 1 and 2 were compared. 75% of DTC in Group 1 were incidental findings compared to only 12% in Group 2. In Group 1, 67% had no adverse features, compared with only 37% in Group 2 ($p=0.001$). Multifocality was the most common adverse finding: 32% in Group 1 vs. 55% in Group 2 ($p=0.004$). Pts with multifocal DTC who underwent total thyroidectomy had bilateral disease in 53% of Group 1, vs. 82% of Group 2 ($p=0.0005$). Positive central nodes were identified in 4% of Group 1 and 22% of Group 2 ($P=0.004$).

Conclusion: This study makes no claims that total thyroidectomy will decrease local recurrence or increase survival in patients with DTC. However, if the current ATA Guidelines are followed, the high incidence of adverse pathologic features suggests that total thyroidectomy should be strongly considered as the initial surgery for patients with DTC > 5mm.

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Paper 23 (1:45pm - 2:00pm)

A NOVEL RET INHIBITOR WITH POTENT EFFICACY AGAINST MEDULLARY THYROID CANCER IN VIVO.

Abbas K. Samadi, Anuj Shah, Ridhwi Mukerji, Barbara N. Timmermann, and Mark S. Cohen

University of Kansas Medical Center

Background: Medullary thyroid carcinoma (MTC) represents 5 to 7% of thyroid cancers, but remains a challenge to treat with over 50% of patients recurring or progressing despite optimal surgical resection. Although new targeted therapies are being tested clinically, there remains a paucity of chemotherapeutics with durable efficacy and tolerable toxicity profiles. The purpose of this study was to build upon previous in vitro work and evaluate a novel natural product RET inhibitor for its efficacy in a metastatic model of MTC in vivo.

Methods: A metastatic mouse model for MTC was established by injection of 8 million DRO-81-1 human MTC cells in the left neck posterior triangle nodal group of Nu/Nu female mice. In this model, animals demonstrate metastatic spread locally as well as to viscera especially the liver, spleen, and lungs. Primary tumors were measured daily by digital calipers and treatment with Withaferin A (WA at 8 mg/kg/day i.p. x 21 days) was started once tumor volume >100 mm³ (~2-3 wks. post-injection). Weights and body score were measured 3x/week for the duration of the study and animals were removed from the study once weight decreased by >10% or body score deteriorated.

Results: All control animals (saline; n=5) died from metastatic disease by 6 weeks post injection. All treated animals (WA; n=5) were alive after 12 weeks post injection (6 wks post-treatment); p<0.01. Four treated mice (80%) had complete regression of tumor without recurrence or metastatic disease after 12 weeks post-injection. The remaining animal was alive with tumor that continued to grow after therapy. This mouse had a larger tumor volume at the start of treatment (200 mm³). All treated animals demonstrated no clinical toxicity or weight changes for the duration of the study. Tumor cells treated with WA demonstrated inhibition of total and phospho-RET levels by Western-Blot analysis in a dose-dependent manner (almost complete inhibition with 3 uM WA treatment) as well as potent inhibition of phospho-ERK and phospho-AKT levels.

Conclusions: Withaferin A is a novel natural product RET inhibitor with potent antitumor effects in a metastatic model of MTC with 80% of treated animals demonstrating a complete response to therapy without recurrence. Animals demonstrated no weight changes or clinical toxicities at the treatment dose given. Further studies on long-term efficacy, toxicity and dose-escalation are warranted to evaluate this compound for clinical translation.

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Paper 24 (3:30pm - 3:45pm)

OUTCOMES AND QUALITY OF LIFE AFTER PARTIAL PANCREATECTOMY FOR NON-INSULINOMA PANCREATOGENOUS HYPOGLYCEMIA SYNDROME

Kimberly A. Vanderveen, Clive S. Grant, Geoffrey B. Thompson
Mayo Clinic

Background: Noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS) is an increasingly important cause of endogenous hyperinsulinemic hypoglycemia. Particularly in patients who have undergone prior Roux-Y gastric bypass for obesity or other gastric or vagal operations, the pathophysiology is strongly suspected to be a secondary phenomenon related to the prior procedure. Whereas partial pancreatectomy has been documented to be successful in controlling hypoglycemia early postoperatively, later follow-up indicated relapse of identical symptoms. The goal of this study was to assess the frequency and severity of recurrent symptoms in operated NIPHS patients.

Methods: All patients who had undergone pancreatic resection for NIPHS at our institution from January 1996 through December 2008 were reviewed for demographics, preoperative biochemical and radiologic evaluation, operative procedure and postoperative complications. Additionally, a mail survey including questions on pre- and post-surgical symptoms, European Quality of Life Survey (EQ-5D), and Fear of Hypoglycemia Scale (FOHS-98) was sent to all surviving patients. The EQ-5D is a validated, 5-category quality of life (QOL) instrument. The FOHS-98 has been validated in medically-treated diabetics, addressing psychological impact and behavioral modifications in these patients who experience hypoglycemia. This tool seemed applicable to our patients.

Results: 75 patients underwent pancreatic resection for NIPHS (57; 2004-8); 69 were eligible for survey participation (5 deceased, 1 incarcerated). 48 patients (70%) completed the survey, mean follow-up of 53 months. Forty-one patients (87%) reported recurrent symptoms; one patient underwent total pancreatectomy for severe persistent symptoms. Median time to recurrent symptoms was 16 months (range, <1 - 157 mo.). Despite symptom recurrence, almost all patients reported overall improvement in pre- versus postoperative QOL; median EQ-5D overall health scores increased from 40 to 75 out of 100 ($p < 0.001$). Moreover, they noted marked reduction in psychological stress and hypoglycemic symptoms with greater than 50% decrease in median scores on the overall, worry, and behavioral scores on the FOHS-98 ($p < 0.001$).

Conclusions: Although nearly 90% of patients developed recurrence of their preoperative hypoglycemic symptoms, almost all reported significant overall improvements in QOL and marked reduction in symptom severity after pancreatic resection.

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Paper 25 (3:45pm - 4:00pm)

BETTER PRESERVATION OF ENDOCRINE AND EXOCRINE FUNCTION FOLLOWING CENTRAL VERSUS DISTAL PANCREATECTOMY FOR MID-GLAND LESIONS

Leaque Ahmed, Joseph DiNorcia, Minna K. Lee, BA, Patrick L. Reavey, Elizabeth A. Yakaitis, BA, James A. Lee, Beth A. Schroppe, John A. Chabot, and John D. Allendorf
Columbia University College of Physicians and Surgeons

Background: Benign and low-grade malignant neoplasms of the neck or body of the pancreas traditionally are treated by pancreaticoduodenectomy or distal pancreatectomy (DP) when enucleation is not appropriate. These extended resections result in a loss of normal pancreatic tissue that may lead to endocrine and exocrine insufficiency. Central pancreatectomy (CP) is a tissue-sparing option for lesions of the mid-pancreas. This study compares rates of glycemic control and pancreatic insufficiency in patients undergoing central versus distal pancreatectomy.

Methods: We identified patients who underwent central or distal pancreatectomy between March 1991 and June 2009 and retrospectively collected demographic and perioperative data. We compared pathology characteristics, operative morbidity, and postoperative pancreatic function in 50 patients undergoing CP who were matched for age, gender, race, and pathology to 50 DP patients using Wilcoxon signed-rank test for continuous and McNemar's test for categorical variables.

Results: Sixty-seven patients with a mean age of 57.5 years underwent CP for varying pathology. The proximal pancreas was sutured (45, 67.2%) or stapled with reinforcement (22, 32.8%). The distal pancreas was reconstructed via pancreaticogastrostomy (65, 97%) or pancreaticojejunostomy (2, 3%). The median operative time was 310.5 minutes with a median EBL of 400ml. The overall morbidity was 38.8% with no perioperative deaths. One patient required reoperation for hemorrhage. The median length of stay was 6 days. The median follow-up was 34 months. When compared to a matched group of DP patients, there were no significant differences in length of stay, pancreatic fistula, morbidity, and mortality. The CP group had less pancreas resected (length 4.35 vs. 9.00cm, $p < 0.0001$) for smaller lesions (diameter 2.0 vs. 2.5cm, $p = 0.004$). The CP group also had a lower rate of new-onset or worsening diabetes than the DP group (14% vs. 40%, $p = 0.012$). Of the new-onset or worsening diabetics, only 1 (2%) required insulin in the CP group whereas 14 (28%) were insulin-dependent in the DP group ($p = 0.001$). There were no differences in pancreatic exocrine function as assessed by the need for enzyme supplementation.

Conclusion: CP is a safe, effective treatment for benign and low-grade malignant neoplasms of the mid-pancreas. Patients undergoing CP have a markedly decreased insulin requirement compared to DP patients.

ABSTRACTS CONT.

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Paper 26 (4:00pm - 4:15pm)

COST-EFFECTIVE ANALYSIS FOR ADRENAL LESIONS: IMMEDIATE LAPAROSCOPIC ADRENALECTOMY VERSUS OBSERVATION

Michael T. Stang, Linwah Yip, Matthew R. Rosengart, Michaele J. Armstrong, , Sally E. Carty, Adrienne L. Melck

University of Pittsburgh Medical Center

Introduction: The management of adrenal masses that are <6 cm, non-functional and have complex and/or lipid-poor imaging characteristics is controversial. The options include resection or observation with serial imaging and biochemical studies; however, the optimal duration of nonoperative follow-up is unknown. We evaluated the cost-effectiveness of immediate laparoscopic adrenalectomy versus observation for these lesions.

Methods: We reviewed 122 patients evaluated for an adrenal mass between 1/04 and 12/05. The number and type of imaging (CT or MRI), biochemical studies, operative procedure, and length of follow-up was determined. Patients were classified as either having immediate surgery (IS) or undergoing observation (OBS) with serial imaging and biochemical studies. Intention-to-treat analysis comparing total hospital charges and adjusted costs was done using the Wilcoxon rank-sum test; $p < .05$ was considered significant.

Results: A total of 16/122 (13%) patients had nonfunctional adrenal masses <6cm with lipid-poor and/or complex imaging characteristics; 9 and 7 patients were grouped into the IS and OBS cohorts, respectively. The IS cohort had no postoperative complications and a mean length of stay of 1.9 days (range, 1-4). The OBS cohort was followed for a median of 31 months (range, 2-67), receiving an average of 1.9 CTs, 2.4 MRIs, and 1.7 24-hour urinary analyses. Two OBS patients underwent adrenalectomy after 7 and 9 months. With this short-term follow-up, the mean cost of IS was significantly higher than OBS (\$10,541 v. \$6,889, $p=.03$). After projecting for annual surveillance with CT, urine metanephrines and a low-dose dexamethasone suppression test, OBS would exceed the cost of IS after 5 years (\$10,725).

Conclusion: Patients with a <6cm, nonfunctional adrenal lesion that have lipid-poor and/or complex imaging characteristics can be followed initially with annual imaging and functional studies. In the absence of adequate natural history data for these unique lesions, our institutional preference is to follow these indefinitely. However, beyond 4 years of surveillance, it becomes more cost-effective to proceed with laparoscopic adrenalectomy. The decision for immediate surgery must also consider patient compliance, psychologic impact, and the cumulative radiation effects of yearly follow-up.

NOTES

Paper 27 (4:15pm - 4:30pm)

IMPACT OF RESECTIONAL STANDARDS IN THYROID CANCER INVADING THE AERODIGESTIVE TRACT ON INDICATION AND SURVIVAL

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Background: Radical surgery in patients with thyroid cancer invading trachea and/or esophagus is controversial and not standardized.

Patients and Methods: Since 1995, 106 consecutive patients (male/female n=61/45, mean age 41.54±7.8 yr) with thyroid cancer (differentiated thyroid cancer (DTC) n=58, medullary thyroid cancer (MTC) n=23, poorly and undifferentiated thyroid cancer (PDTC/UTC) n=25) invading trachea and/or esophagus underwent resection (n=74) or shaving (n=32) procedures. Resection procedures on trachea were classified as window resection (type 1 (laryngocricoid) n=18 and type 2 (trachea) n=12), sleeve resection (type 3 (laryngocricoid) n=12 and type 4 (trachea) n=14), and cervical evisceration (type 5 (laryngectomy) n=9 and type 6 (laryngoesophagectomy) n=9). Disease specific survival (DSS), local recurrence rate, and prognostic factors were analyzed.

Results: Surgical morbidity was highest in cervical evisceration (55%) when compared to type 1+2 (30%), type 3+4 (35%), or shaving (12.5%, P<.01). Incomplete (R1) resection was found in 25/32 (78%) after shaving and 7/74 (9.5%) after resection (P<.001). During mean follow up 59.44±19.9 months, 14/32 (43.8%) shaving and 9/74 (12.1%) resection patients developed locoregional recurrence (P<.001). After resection procedures, 5 and 10 year DSS in patients with DTC, MTC, PDTC/UTC were 92, 74, 7% and 83, 40, 0% (P<.001), respectively. Type of resection had no impact on DSS. Prognostic factors for reduced DSS were tumor invaded resection margin (Odds ratio (OR) 3.1), PDTC/UTC (OR 5.9), and distant metastases at the time of resection (OR 2.6). As prognostic factor for local recurrence, only R1 resection (OR 3.2) was detected.

Conclusion: Shaving is associated with low morbidity but high risk for R1 resection and local recurrence. Resection procedures offer good long term prognosis, particularly in DTC and MTC. There is, however, increasing morbidity with increasing extent of surgery. Histological tumor type and required extent of resection mainly predict decision making in surgery of advanced thyroid cancer. In selected cases with PDTC or DTC/MTC with distant metastases but stable disease, limited aerodigestive tract resection in terms of palliation and locoregional tumor control can be considered.

NOTES

Paper 28 (7:45am - 8:00am)

EFFECT OF THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY ON THYROIDECTOMY RATES AND MALIGNANCY RISK IN CYTOLOGICALLY INDETERMINATE THYROID NODULES

Jennifer L. Rabaglia, Wareef Kabbani, Shelby Holt, Lori Watumull, Jeffrey Pruitt, William H. Snyder, Fiemu E. Nwariaku
University of Texas Southwestern Medical Center

Background: Cytologically indeterminate thyroid nodules are a diagnostic and therapeutic challenge. To improve diagnostic accuracy, the National Cancer Institute recently recommended the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) for interpretation of fine-needle aspiration (FNA) cytology. Our objective was to determine the effect of TBSRTC on thyroidectomy rates and malignancy risk in cytologically indeterminate lesions.

Methods: Thyroid FNA records for patients at a single academic institution between January 2000 and November 2009 were examined. We compared two time periods; one prior to adoption of TBSRTC (pre-TBSRTC, 1/00-9/03) and one post TBSRTC (1/09-11/09). The former group included cytology classified as indeterminate or atypical, whereas cases with atypical cells of undetermined significance (ACUS) were included in the latter data set. We compared thyroidectomy rate (histopathology) and malignancy rate between both groups. Statistical comparisons were performed using the Fisher's exact test and Chi-square analysis (p-value of 0.05 = significant).

Results: Demographics were similar in both groups. 938 FNAs were performed in the first period compared to 501 in the second period. We identified 70 (7%) cytologically indeterminate cases (cellular atypia or indeterminate architecture) in the pre-TBSRTC group, of which 17 were clearly classified as cellular atypia. This compares to 69 (13.8%) patients with the finding of ACUS in the post-TBSRTC group. We found no statistically significant difference in thyroidectomy rates between the two groups (31/70, 44% pre vs. 20/69, 29% post; $p=0.07$). However, the rate of malignancy within lesions with clear atypia was significantly higher on final surgical histology in the pre-TBSRTC group (8/17, 47% vs. 6/69, 8.7%; $p=0.0007$).

Conclusion: TBSRTC streamlined classification of cytologically indeterminate lesions without changing thyroidectomy rates. However, application of TBSRTC is associated with a lower rate of malignancy in thyroid nodules with ACUS versus the pre-TBSRTC label of "atypical". These findings imply that standardization of cytologic classification can alter diagnostic accuracy. Additional, multi-institutional evaluation and subsequent refinement of this recommendation is warranted in order to increase diagnostic accuracy and avoid either insufficient or excess utilization of surgical management.

NOTES

Paper 29 (8:00am - 8:15am)

SINGLE NUCLEOTIDE POLYMORPHISMS ACT AS MODIFIERS AND STRONGLY CORRELATE WITH DEVELOPMENT OF SIMULTANEOUS MEDULLARY AND PAPILLARY THYROID CARCINOMAS IN TWO LARGE, NON-RELATED FAMILIES WITH RET V804M PROTO-ONCOGENE MUTATION.

Alexander L. Shifrin, Jennifer B. Ogilvie, Michael T Stang, Angela Musial Fay, Cristina Xenachis, Yen-Hong Kuo, Jerome J. Vernick
Jersey Shore University Medical Center

Background: Single nucleotide polymorphisms (SNPs) have been reported to function as modifiers of RET proto-oncogene, resulting in the expression of medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC). The RET V804M mutation is rare and reports showing SNPs associated with it are limited. We recently reported a high rate (40%) of simultaneous MTC and PTC, associated with primary hyperparathyroidism and absence of pheochromocytoma (so called "MEN 2C"), in a large family with the RET V804M mutation. We now present a second, non-related RET V804M family, with simultaneous MTC and PTC. We correlated the presence of specific SNPs to the development of simultaneous MTC and PTC in both families.

Methods: Two non-related Italian-American families of 107 (Family 1) and 31 members (Family 2) with RET V804M mutation were evaluated for presence of MTC, C cell hyperplasia (CCH) and PTC. Sequencing was performed on exons 10, 11, 13, 14, 15 and 16 of the RET proto-oncogene through amplification of genomic DNA using polymerase chain reaction (PCR) followed by nucleotide sequence analysis on an automated capillary DNA sequencer. Development of MTC and PTC was correlated to the presence of specific SNPs.

Results: In Family 1, 40/107 members were found to carry the RET V804M mutation. Of these 40 members, 15 underwent total thyroidectomy and were found to have MTC (10/15) or CCH (5/15). 6 of 15 (40%) had simultaneous MTC/CCH and PTC. 11 members were tested for SNPs. In Family 2, 3/31 members were RET V804M positive: 1 had MTC and PTC, 1 had micro MTC and PTC, and 1 had CCH. All 3 were tested for SNPs. Three SNPs were detected in both families: Exon 11 (G691S), Exon 13 (769L), and Exon 15 (904S). All three SNPs were present in 100% of patients with overt MTC. SNPs in Exon 13 (769L) were present in all RET positive patients. SNPs in Exon 11 (G691S) and Exon 15 (904S) were present only in patients with overt MTC, and were absent in patients with micro MTC or CCH.

Conclusions: We present two non-related families with RET V804M mutation and high incidence of simultaneous MTC and PTC. SNP analysis revealed a similar pattern between the two families that correlated with phenotypic expression. SNPs in Exon 11 (G691S) and Exon 15 (904S) were found in 100% of patients with overt MTC. SNPs in Exon 13 (769L) were present in all RET positive patients, and may serve as modifiers in the development of simultaneous MTC and PTC in patients with RET V804M mutation.

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Paper 30 (8:15am - 8:30am)

SPRY2 EXPRESSION CORRELATES WITH BRAF MUTATION IN THYROID CANCER

Lizhong Xu, Dafna Bar-Sagi, Kopal N. Patel

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Background: Activating mutations of the MAPK pathway (BRAF, RAS, RET/PTC) are the most common genetic alterations in thyroid cancer (TC). BRAF mutations often confer an aggressive TC phenotype. Sprouty 2 (Spry2) is an inducible inhibitor of MAPK signaling and has been implicated in negative feedback regulation of the MAPK pathway. The aim of this study was to investigate the role of Spry2 in TC.

Methods: BRAF (+) TC cell lines were analyzed for Spry2 expression and expression of downstream MAPK proteins, pMEK and pERK. BRAF (+) cells were treated with increasing concentrations (5-20 microM) of MEK inhibitor, U0126, for 24 hours. MTT cell viability assays were performed. TC cell lines were also transfected with Spry2 shRNA and control shRNA. Cells were analyzed for Spry2, pMEK and pERK expression. BRAF (-) TC cell lines were used as control. In addition, 30 human papillary thyroid cancers (PTCs) from our tumor bank were analyzed for BRAF and RAS mutations, RET/PTC rearrangements and Spry2 expression.

Results: Increased baseline expression of pMEK and Spry2 was found in BRAF (+) cells. MEK inhibition in BRAF (+) cells resulted in decreased pMEK and Spry2 expression and a significant decrease in cell viability when compared to BRAF (-) cells ($p < 0.02$). BRAF (+) cells treated with Spry2 shRNA showed decreased Spry2 expression and increased pMEK expression. From our tissue samples, 10 PTCs had BRAF mutation, 2 had RET/PTC rearrangement and 2 had RAS mutation. Increased Spry2 expression was seen only in BRAF (+) tumors (8/10).

Conclusions: These data confirm that only BRAF (+) TC cells are sensitive to MEK inhibition. Moreover, Spry2 expression correlates with BRAF status, implicating Spry2 as a negative feedback regulator of the MAPK pathway in TC. Increased Spry2 expression serves as a surrogate marker of MAPK pathway activation and may help maintain tumor cell homeostasis and equilibrium. Evasion of MAPK pathway feedback inhibition may be a fundamental requirement for oncogenic transformation and helps explain why MEK inhibition alone has not been sufficient to induce major clinical responses.

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Paper 31 (8:30am - 8:45am)

LAPAROSCOPIC RADIOFREQUENCY THERMAL ABLATION OF NEUROENDOCRINE HEPATIC METASTASES: LONG-TERM FOLLOW UP

Eren Berber, Hizir Akyildiz, Jamie Mitchell, Mira Milas, Allan Siperstein
Cleveland Clinic

Background: Since our first report 13 years ago, laparoscopic radiofrequency thermal ablation (RFA) has been incorporated into the treatment algorithm of patients with neuroendocrine liver metastases. The aim of this study is to report long-term oncologic results.

Methods: Eighty-nine patients with neuroendocrine hepatic metastases underwent 119 laparoscopic RFA sessions within a 13-year time period. All patients had unresectable disease and indication for RFA was progression of liver involvement and/or hormonal symptoms. Octreotide and chemoembolization were used adjunctive to RFA in follow up in appropriate cases. Chest-Abdomen-Pelvis CT scans were obtained quarterly for the first 2 years and then biannually. Clinical and survival data were obtained from a prospective, IRB-approved database. Univariate Kaplan Meier survival and multivariate Cox Proportional Hazards Model were used for statistical analyses. Data are expressed as mean \pm standard error of the mean (SEM).

Results: There were 35 women and 54 men with a mean age of 56 \pm 1.4 years. There were 55 patients with carcinoid tumors, 23 with pancreatic islet cell tumors, and 11 with medullary thyroid cancer. Mean tumor size was 3.6 \pm 0.2 (range 1-10 cm) and number of lesions 6 \pm 1 (range 1 to 16). Peri-operative morbidity was 6%, with 0.1% 30-day mortality. Hormonal symptoms were present in 33% of patients preoperatively and symptom relief was achieved in 97% of these patients after RFA. The median follow-up was 30 \pm 3 months. Twenty-two percent of patients developed local liver recurrence, 63% new liver lesions, and 59% extrahepatic disease in follow up. Repeat RFA (28% of patients), and chemoembolization (13%) were used to achieve further local hepatic tumor control in these patients. The Kaplan-Meier median disease-free survival was 1.3 years and overall survival 6 years after the first RFA procedure. On univariate analysis, gender, liver tumor volume, symptomatology, and presence of extrahepatic disease effected survival. On multivariate analysis, liver tumor volume, symptomatology and extrahepatic disease were independent predictors of survival.

Conclusions: To our knowledge, this is the largest prospective experience with RFA of neuroendocrine liver metastases. Effective symptom palliation and long-term local tumor control are possible in these patients, who are not surgical candidates due to aggressive liver involvement, with minimal morbidity and mortality.

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Paper 32 (8:45am - 9:00am)

SECOND OPINION CYTOPATHOLOGY REVIEW OF THYROID FINE NEEDLE ASPIRATION BIOPSIES REDUCES THE NEED FOR DIAGNOSTIC THYROIDECTOMY

Tomer Davidov, Stanley Z. Trooskin, Beth-Ann Shanker, Dana Yip, Oliver Eng, , Jessica Crystal, , Malik F. Deen, Michael May, Renee L. Artymyshyn

University of Medicine & Dentistry of New Jersey - Robert Wood Johnson Medical School

Background: Follicular thyroid carcinoma (FTC) cannot be distinguished reliably from benign follicular neoplasia by fine needle aspiration (FNA) biopsy. Given an estimated 20% risk of malignancy, many patients with suspicious FNAs require thyroid surgery for diagnosis. Some centers have shown significant discordance when a second pathologists evaluates the same FNA. We sought to determine whether routine cytopathology second opinion reduces the need for diagnostic thyroidectomy, especially in patients with suspicious FNAs.

Methods: 331 thyroid FNA specimens obtained from outside centers from 2004 to 2009 were reviewed at our institution. FNA results were categorized into benign (nodular goiter, thyroiditis, colloid nodule, hyperplastic focus), suspicious (follicular or hurthle cell neoplasm, follicular or hurthle cell lesion, "malignancy cannot be excluded"), malignant (papillary, medullary, and anaplastic thyroid carcinoma), and nondiagnostic (inadequate cellularity or preservation artifact). Final pathology of 250 patients who underwent thyroidectomy was compared to FNA results.

Results: Average patient age was 51 with a female predominance (79%). The overall pathology concordance for all 331 FNAs was 66% (218/331). Concordance was highest at 86% (74/86) with malignant FNAs. Concordance in the 129 patients with FNAs deemed suspicious by initial pathology review was only 37% (48/129) on second opinion. Suspicious FNAs were thought to be nondiagnostic in 21% (27/129) and benign in 42% (54/129) of patients. Suspicious FNAs on second opinion were found to be malignant in 23% (11/48) on final pathology compared to 13% (17/129) of the suspicious FNAs from initial pathology opinion. Benign FNAs on second opinion were found to be benign in 95% (21/22) on final pathology. Twelve patients with nondiagnostic FNAs underwent repeat FNAs. Of these, 67% (8/12) were interpreted as benign and 33% (4/12) as suspicious or frankly malignant. Of the 4 who underwent surgery, 2 were found to have malignancy, 1 papillary microcarcinoma, and 1 was benign. Overall, routine cytopathology second opinion of suspicious thyroid FNAs avoided surgery in 35% and potentially obviated the need for diagnostic thyroidectomy in as many as 56% (72/129) of patients.

Conclusions: Routine second opinion review of suspicious thyroid FNA biopsies reduces the need for unnecessary diagnostic thyroidectomy by as much as 56%.

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Paper 33 (9:00am - 9:15am)

DO THE RECENT AMERICAN THYROID ASSOCIATION (ATA) GUIDELINES ACCURATELY GUIDE THE TIMING OF PROPHYLACTIC THYROIDECTOMY?

Elizabeth G. Grubbs, Thereasa A. Rich, Yan Xing, Stephen G. Waguespack, Anita K. Ying, Douglas B. Evans, Jeff E. Lee, Nancy D. Perrier
MD Anderson Cancer Center

Introduction: In 2009, the ATA published consensus guidelines directing the timing of surgical intervention for the treatment of hereditary medullary thyroid cancer (MTC). The recommendations for prophylactic thyroidectomy (PThy) were based on a combination of new RET mutation-based risk levels and clinical criteria including patient age, family history (FH), calcitonin (Ct) level and ultrasonographic (US) findings. The aim of this study was to assess whether the clinical criteria outlined in the ATA guidelines could accurately predict the presence of MTC on final pathology.

Methods: A retrospective study of an endocrine surgery database at a tertiary care center was performed. Patients undergoing PThy were included. We evaluated mutation-based risk levels in combination with ATA criteria for resection: aggressive FH, elevated Ct and abnormal US at the time of PThy for "lower risk" (level A & B) mutations and age <5 years (y) for "high risk" (level C) mutations. Logistic regression analysis was performed to identify predictive factors of MTC on final pathology.

Results: 55 pts underwent PThy between 1972 and 2009. 20 (36%) patients had a level A or B mutation and 35 (64%) had a level C mutation. The median age at PThy was 11.5 y (range 2-68). Only 4 patients (8%) underwent PThy prior to age 5. On final pathology, 44% (24/55) of patients had MTC; median size of tumor was 3mm (range 1-12) and no patient had nodal metastasis. The majority of patients with MTC (16/24, 67%) had a level C mutation and the youngest age of MTC in a level C mutation carrier was 5y. The youngest age of MTC in level A or B carriers was 15y. The single factor that predicted an overall increased risk of MTC at time of PThy was meeting at least one criteria in the ATA mutation-based guidelines for surgical intervention ($p=0.02$). Meeting individual clinical criteria (FH, Ct, US, age <5) was not predictive of MTC nor was risk level of mutation alone. In a subset analysis of level C patients, age was the only significant predictor of MTC ($p=0.04$). Utilization of ATA criteria had a negative predictive value (NPV) of MTC at the time of PThy of 92%.

Conclusion: ATA criteria that includes risk assessment of RET mutation are important in predicting the presence of MTC in patients who are candidates for PThy. A NPV of 92% makes delay of PThy reasonable if all criteria are met. In the context of an experienced surgeon, the recent guideline suggestions are useful in determining the appropriate timing of PThy.

ABSTRACTS CONT.

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Paper 34 (9:15am - 9:30am)

TRANSORAL THYROID AND PARATHYROID SURGERY

E. Karakas, T. Steinfeldt, T. Schlosshauer, A. Gockel, J. Jäger, R. Westermann, D.K. Bartsch
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Background: Transluminal endoscopic interventions via so-called natural orifices are gaining increasing interest as they allow surgical treatment without any incision of the skin. Moreover minimally invasive procedures have found their way into thyroid and parathyroid surgery. After development of an entirely transoral access for thyroid and parathyroid resection our aim was to evaluate the safety of the new technique, especially potential and clinically relevant contamination of the access route.

Method: We performed thyroid resections in 10 orally intubated pigs via an entirely transoral access to the thyroid region. Preparation and resection was done using a modified rigid rectoscope and conventional laparoscopic instruments. Prior to and after thyroid resection recurrent laryngeal nerve function was documented by intraoperative neuromonitoring (IONM). The mucosa of the bottom of the mouth was sealed with a continuous absorbable suture. After a 14 days observation period an autopsy, including macorscopol evaluation of the bottom of the mouth, the access route and the thyroid region as well as laboratory and microbiological investigations were performed. Additionally we performed the new transoral technique in 10 human corpses.

Results: In all animals the transoral hemithyroidectomy was done without complications. IONM showed a regular signal every time. Vital signs, laboratory values, behavior, body temperature as well as nutrition and increase in weight (Mean 5,1kg) were normal. The access route and the operating field showed no signs of inflammation or infection. Further investigations showed, that in contrast to pigs, an access way behind the hyoid bone was not feasible in human corpses and led to a modification of the access way mentioned before. However, 9 out of ten normal sized human parathyroid glands could be detected and resected via the modified transoral way.

Conclusion: Entirely transoral thyroid and parathyroid surgery via a sublingual access is feasible and safe. Firstly focussing on parathyroid surgery the first transoral parathyroid resection in a patient suffering from primary hyperparathyroidism is forthcoming.

ABSTRACTS CONT.

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