

## • ABSTRACTS FROM SCIENTIFIC FORUM •

### Internal Medicine Residency Program of the University of Puerto Rico School of Medicine

#### Annual Research Symposium

On May 3, 2014, the Internal Medicine Residency Program of the University of Puerto Rico School of Medicine hosted its annual research symposium at the facilities of the UPR Cancer Center. The aims of this annual event, which began in 2008, are to showcase the mentored research work done by the residents as a requirement of the residency training and promote research and inter-disciplinary collaboration. A panel of four (4) judges with experience in research and not related with the projects evaluated the residents' oral presentations in the categories of organization and clarity; significance and quality; and presentation skills. The event also included a keynote lecture by one of the departmental faculty members. The three best presentations received an award certificate and the opportunity to present again at the annual meeting of the UPR School of Medicine Alumni Society. By this means, the Internal Medicine Residency Program provides an opportunity to share the results of the residents' research efforts with their peers and the university community while advancing their knowledge of the basic principles of research, including how research is conducted, evaluated, and applied to patient care.

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#### **Prevalence of Synchronous Oligopolyposis in Hispanics with Incident Colorectal Cancer: A Population-Based Analysis**

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Objective: In Puerto Rico (PR), colorectal carcinoma (CRC) is the first cause of cancer death and the second most common cancer among men and women. Familial CRC accounts for 10-15% of all CRCs and several studies suggest that inheritance has a significant impact in the pathogenesis of up to a third of all CRC cases. However, little is known about the prevalence of polyposis syndromes among Hispanics. Therefore, the objective of this study was to determine the prevalence of oligopolyposis ( $\geq 20$  synchronous colorectal adenomas) among Hispanics with incident CRC. Methods: Pathological reports from patients with CRC from 2007-2011 were retrieved from the PR Central Cancer Registry. Reports were analyzed by age, gender, stage at diagnosis, and location. Colorectal polyp burden was calculated using pathology reports and data was normalized

based on colon segment size. UPR-MSD IRB approved the study. Results: A total of 1685 colectomy specimens with CRC were analyzed: 53.5% were men, with a mean age of 68 years ( $SD \pm 11$ ), and mainly Stage III (40.3%). The mean number of polyps was 11 ( $SD \pm 9.6$ ). Only 10.2% of CRC patients had oligopolyposis, with most patients being  $>50$  years (96.5%), having tumors in the proximal colon (62.3%), and with an earlier stage at diagnosis (35.9%) vs. patients without oligopolyposis ( $p < 0.001$ ). Conclusion: In our cohort of Hispanics with incident CRC, oligopolyposis was seen in 10% of cases. Our observations suggest that genetic syndromes associated with colorectal polyposis may account for a higher than expected number of CRC cases.

#### **Exercise in Puerto Rican Breast Cancer Survivors**

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Objective: Physical activity is known to reduce the risk of recurrence in breast cancer patients. However, the specific type of interventions that motivates breast cancer patients to exercise has not been established. The objective of this study was to test a culturally tailored exercise intervention for Puerto Rican breast cancer survivors. Methods: An

intervention was designed where patients were randomly assigned into the control group (no exercise), the intervention group that will get a culturally adapted written exercise intervention materials, and an exercise control group that will not get the culturally tailored intervention materials. Anthropometric, cardiorespiratory capacity (6-minute walk), strength and flexibility, WOMAC index and serum biomarkers (adiponectin, C-reactive protein, and Leptin) were assessed at baseline and after 16-weeks. One-way repeated measures ANOVA or Kruskal-Wallis test was utilized to compare differences among baseline and 16-weeks values. UPR-MSIRB approved the study. Results: A total of 45 participants were recruited. Mean age was 58 years (range 27-80). At the end of the 16 week period, no differences ( $p > 0.05$ ) were found in BMI, strength and flexibility measures as cardiorespiratory capacity (6-minute walk) or WOMAC index. Likewise, no differences ( $p > 0.05$ ) were found in levels of biological markers evaluated, leptin, adiponectin and C-reactive protein. Conclusion: Possible explanations for the no significant effect of this intervention were: the intervention was not closely supervised, it was not group-based, and there was no nutritional education provided during the intervention, all of which may be a cause for poor adherence to the intervention regimens.

**Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: A 6-year Retrospective Review at the University District Hospital**

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Objective: The Philadelphia chromosome (Ph) is found in 15-30% of adults with acute lymphoblastic leukemia (ALL), with additional abnormalities reported in 41-86%. This retrospective study evaluated Ph+ ALL patients, with the intent to describe their clinical and cytogenetic features. Methods: 16 records from the University District Hospital diagnosed with Ph+ ALL (year 2008 to 2013) were reviewed, retrieving information on: gender, age, co-morbidities, blood and bone marrow (BM) counts, karyotype, and clinical outcome. UPR-MSIRB approved the study. Results: Of a total of 67 ALL patients, 17 (25%) were Ph+. Of 16 available records, gender was equally represented, and age ranged from 38 to 80 years. Frequent co-morbidities included: hypertension, diabetes mellitus, and prior history of cancer. Mean (SD) values for WBC, hemoglobin, platelets and % BM blasts were, respectively:

51.7 (62.4), 10.3 (1.5), 59.2 (62.6), and 85.3 (13.8). Nine of 14 patients (64%) had additional aberrations, including: deletions [-20/20q-, -7/7p-, 9p-, 12p-], additions [+9, +10, +17, 21q+], and translocations [t(4;5), t(5;15), t(9;14), 2nd t(9;22)]. Therapy in 10 patients included a tyrosine kinase inhibitor. All 16 patients died: 7 early, 7 within a year, and 2 after 24 months. Median survival time was 6.17 months (95% CI: 1.00 – 11.17 months). 4 patients had recurrence, of which 2 had additional cytogenetic abnormalities. Conclusions: Within our ALL population, the prevalence of Ph+ with or without additional abnormalities correlates well with the medical literature. However, there are differences in the nature of them. Therefore, future study is merited for further definition. **THIRD AWARD**

**Quality of Life in Patients with Differentiated Thyroid Cancer at the General Endocrinology Clinics of the University Hospital of Puerto Rico**

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Objective: The diagnosis and treatment of differentiated thyroid cancer (DTC) is associated with good prognosis. However, quality of life can be affected by treatment and long term side effects. Our study evaluates the quality of life in a cohort of patients in Puerto Rico diagnosed with DTC. Methods: Patients with DTC were identified at the Endocrinology Clinics at the University Hospital of Puerto Rico, with medical chart review and a Spanish University Of Washington Quality Of Life Questionnaire was administered to each patient. Descriptive analysis and bivariate analysis between domain scores and variables of interest were evaluated using the Mann-Whitney test or Kruskal-Wallis tests. UPR-MSIRB approved the study. Results: Seventy-five patients with DTC were identified. The most common histopathology was papillary thyroid cancer. From those treated with radioiodine, 60.6% received  $\leq 150$  mCi. A total of 82.7% of the patients reported that their health was the same or better than it was before treatment. The mean composite score reflected a little effect on quality of life. Patients with diagnosis at an age  $\geq 45$  years reported a significantly better score on the pain domain

( $p < 0.05$ ) than those diagnosed earlier. Patients who received  $>150$  mCi had a tendency towards a worse score on the same domain ( $p = 0.05$ ). Conclusion: There is overall little effect on the quality of life in patients with DTC. Patients who received  $>150$  mCi and those diagnosed younger showed lower scores on the pain domain than their counterparts.

#### **Prevalence of Vitamin D Insufficiency and Deficiency among Medical Residents of the University Hospital in San Juan, Puerto Rico**

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Objective: Vitamin D has been attracting increasing attention due to higher prevalence of vitamin D insufficiency and deficiency than expected in areas with sufficient sun exposure. Even though sunlight exposure and diet are the main determinants of Vitamin D status, other factors, such as age, race, use of sunscreen, medications, and malabsorptive conditions, affect vitamin D levels. However, there is limited data of the prevalence of vitamin D deficiency and insufficiency in Puerto Rico. Methods: To answer that question we evaluated a sample of 51 Internal Medicine residents of 25 to 39-years old of the University Hospital in San Juan, Puerto Rico by means of a questionnaire about basic socio-demographic characteristics, anthropometric data, and lifestyle characteristics and obtained blood sampling for 25-hydroxyvitamin D, calcium, phosphorus, blood urea nitrogen, creatinine, aspartate aminotransferase, and alanine aminotransferase levels. UPR-MSC IRB approved the study. Results: The median 25-hydroxyvitamin D level was 21 ng/mL (range, 7-38 ng/mL). Forty-five participants (88.2%) had 25 hydroxyvitamin D concentrations  $<30$  ng/mL. We found vitamin D deficiency in 43.1% of the population and insufficiency in 45.1%. Contributory factors to our findings include limited exposure to sunlight during the periods of higher sun intensity, increased body mass index and a limited area of body exposed to sunlight. A relationship between lower physical activity levels and hypovitaminosis D was also found. Both calcium intake and vitamin D intake, which were markedly below recommended daily allowance, were positively correlated with 25-hydroxy vitamin D levels, but with a weak association.

#### **Electrocardiographic Findings in Patients with Spontaneous Intracerebral Hemorrhage**

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Objective: Central nervous system vascular insults are responsible for the development of multiple electrocardiographic (ECG) abnormalities. In this study, the most common ECG abnormalities in patients with spontaneous, non-traumatic intracranial hemorrhages (ICH) were analyzed. Methods: A retrospective review of records from the University Hospital was performed. Clinical and radiographic data along with the admission ECG were obtained. The baseline ECG of each patient was reviewed. All data was analyzed using Pearson's chi-square test to identify the differences between groups. Logistic regression analysis was conducted to identify factors that correlated mortality and radiological findings with ECG findings. All data analysis was conducted using STATA. UPR-MSC IRB approved the study. Results: A total of 168 records were reviewed, from which 77 were included. T wave abnormalities were the most common ECG finding encountered (55% of patients), followed by QT prolongation and left ventricular hypertrophy. Presence of ST depressions was associated to increased ICH volume ( $p = 0.002$ ) and increased mortality ( $p = 0.004$ ). Corrected QT interval  $>460$ ms was associated to right sided hemorrhages ( $p = .015$ ) and, although not statistically significant, a trend was observed between long QT and increased mortality ( $p = 0.13$ ). Presence of T wave abnormalities was also seen in hemorrhages with volumes  $>30$ mL, although this finding was not statistically significant ( $p = 0.10$ ). Conclusion: ECG abnormalities in spontaneous, non-traumatic intracranial hemorrhages are common and consist mainly on T wave abnormalities and QT prolongation. QT prolongation is associated with bleeding of the right hemisphere and the presence of ST depressions may represent a risk factor for in-hospital mortality.

#### **Intestinal and Extraintestinal Cancer in Patients with Inflammatory Bowel Disease in the Puerto Rican Population**

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Objective: The association between colorectal cancer (CRC) and inflammatory bowel disease (IBD) has been studied. However, there is a lack of population-based studies that estimate the incidence of extraintestinal cancer in IBD patients. The objective of our study was to determine the

incidence rates of intestinal and extraintestinal cancer in Puerto Rican patients with IBD. Methods: As a retrospective cohort study, data from 527 IBD patients from our UPR Center for IBD were merged with the database of the Puerto Rico Central Cancer Registry in order to determine the incidence of intestinal and extraintestinal cancer between 1987-2010. UPR-MSD IRB approved the study. Results: Fifteen cancer cases were identified in fourteen of our 527 patients with IBD. The cancer incidence among our IBD population was 284/10,000. Seven (2%) patients developed neoplasia among 337 with CD, while seven (4%) patients developed neoplasia among 182 with UC. Five of 527 IBD patients developed CRC, with an incidence of 95/10,000. Ten of 527 IBD patients developed extraintestinal cancer with an incidence of 190/10,000. Sixty-six % of the tumors were extraintestinal. Conclusion: The incidence of CRC was similar and low in both CD (0.6%) and UC (1.6%), but seems to be higher than in the general population. The same trend was observed for extraintestinal cancer. Cancer in our patients developed at a younger age (48) than expected for the general population (66). A difference between the incidence of cancer developed by our CD versus UC patients was not seen ( $p=0.264$ ). **HONORARY AWARD**

#### **Clinical Characterization and Mutation Spectrum in Caribbean Hispanic Families with Lynch Syndrome**

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Objective: To describe the mismatch repair (MMR) genes mutation spectrum in Puerto Rican Hispanics (PRH) families with Lynch syndrome (LS) and to characterize MMR mutation-positive and mutation-negative colorectal cancer (CRC) patients with regards to clinicopathologic criteria. Methods: Proband for the study were Caribbean Hispanics with suspected familial CRC who were identified through PURIFICAR database. For each proband, a family pedigree was completed. To confirm the cancer diagnosis of the proband, medical documentation was reviewed. Patients that were suspected for LS (proband) had tumor microsatellite instability and MMR protein expression testing. Genetic testing for the MMR genes was performed in patients who showed MMR-negative protein expression. UPR-MSD IRB approved the study. Results: Twenty CRC Caribbean Hispanic patients were identified. In 9 patients, there was a germline mutation in a MMR gene; with mutations in the MSH2 gene in 4 unrelated probands of them. Most individuals with MMR mutations had family history of both CRC and LS-associated cancer. The most common tumor location sites for the probands

were transverse and descending colon. Three MLH1 gene mutations were identified. One patient carried a mutation on the MSH6 gene. Conclusion: MMR mutation spectrum of LS has not been sufficiently studied in a Caribbean population, which includes PRH. Studying and describing the results found in the PR high-risk population enables for the comparison of LS characteristics and mutations across ethnicities and countries. Genetic ancestry differences in PRH, when compared to other Hispanics, gives the potential for identifying novel MMR mutations associated with LS. **SECOND AWARD**

#### **Prevalence of Sleep Disordered Breathing in a Population of Patients with Coronary Artery Disease Undergoing Coronary Artery Bypass Grafting in Puerto Rico**

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Objective: This is an ongoing study aiming to describe the prevalence of high risk for Sleep Disordered Breathing (SDB) in patients with coronary artery disease (CAD), who undergo Coronary Artery Bypass Graft (CABG). Methods: 40 Puerto Rican patients scheduled for CABG at Cardiovascular Center of Puerto Rico and the Caribbean participated in this cross sectional study. Risk for SDB was determined using the Stop Bangs questionnaire. Comparisons of categorical variables by Obstructive Sleep Apnea (OSA) risk (low vs. high) were performed using Fisher's Exact Test. Exact logistic regression models were fitted to estimate prevalence odds ratios (POR) with 95% confidence intervals (CI) for the association of risk factors for OSA. UPR-MSD IRB approved the study. Results: 80% of the patients enrolled (23 men and 17 women) were overweight or obese. The mean (SD) age among participants was 64.5 (8.8). We observed significant differences for OSA risk by gender, BMI and neck circumference ( $p<0.05$ ). For every unit change in the measure of the neck circumference, the possibility for high risk OSA is 59% higher (POR=1.59, 95% CI: 1.18-2.48). The possibility to be high risk for OSA in overweight/obese patients was 13.40 (POR=13.40, 95% CI: 1.43-194.73) than the possibility of high risk for OSA in underweight/normal patients. Conclusion: To our knowledge no previous study describes the prevalence for high risk for SDB in a population with CAD scheduled to undergo CABG. Our results were higher than two previous studies, one for CAD non-Hispanic patients, and the other for middle-age population in PR.

### **Incidence of Instent Restenosis among Puerto Ricans**

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**Objective:** Hispanics have 20% less incidence of coronary artery disease than the United States. Previous studies have shown that blacks and Hispanics have a significantly greater risk of adverse cardiac events after PCI relative to white patients. Little is known about the incidence of restenosis among Puerto Ricans. It is the purpose of this study to find the incidence of restenosis among the Puerto Rican population and compare it with the USA. **Methods:** A retrospective analysis was done from 2009-2011 for patient who had angioplasty and another intervention at the same target lesion. 5443 stents were inserted, 500 records were reviewed and 93 patients developed stent restenosis. UPR-MSB IRB approved the study. **Results:** The mean age for stent restenosis was  $63 \pm 12$  years. Fifty-one were males and forty-two females. The mean BMI was  $26 \pm 9.7$ . Fifty-seven percent had Diabetes Mellitus type 2, 66% dyslipidemia and 85% hypertension. Seventy-seven percent of the patients received a drug eluting stent and twenty percent a bare metal stent. The mean period for restenosis was 20 months. The incidence of stent restenosis was 1.8% of the total population. **Conclusions:** The incidence of instent restenosis was 1.8% in the Puerto Rican population in comparison to 3-20% of the American population. This corroborates that the incidence of stent restenosis is significantly less than the United States population. Probably this reflects the proven less aggressive coronary atherosclerotic process in the Hispanic population when compared with the USA, even a high incidence diabetic population.

### **A Clinical Paradox: Gender Disparities in Cardiac Device Implant Rates and Efficacy among Hispanic Patients**

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**Objective:** Cardiac device implantation has become a mainstay of therapy for multiple cardiovascular disorders, with the number of implants per year increasing worldwide. However, data about cardiac device implantation in Puerto Rico is still insufficient, particularly with regards to gender differences. The objective of this study is to analyze the cardiac device implant data in Puerto Rico from 2007 to 2012 with the goal of determining any trends in total implant rates; and differences in implant rates and mortality between males and females. **Methods:** Clinical and demographic data were obtained from all cardiac devices implanted in Puerto Rico between 2007 and 2012. Data was procured from the three main manufacturers of cardiac devices in Puerto Rico. Patient outcomes were recorded until June, 2013. Statistical tests were used to determine the association between variables and significance of results. UPR-MSB IRB approved the study. **Results:** A total of 19361 cardiac devices were implanted in Puerto Rico between 2007 and 2012, which represents an increase when compared to a previously published study. Pacemakers were the most common cardiac device implanted in Puerto Rico during the study period. There are significant differences in the number of implanted cardiac devices between males and females. Females with cardiac devices experienced a significantly lower mortality when compared to males. **Conclusion:** Cardiac device implants in Puerto Rico have been continuously increasing during the past years, with a preferential use in males when compared to females. Nevertheless, females with cardiac devices show a decreased mortality when compared to males. *FIRST AWARD*