

*Department of Medicine
Temple University School of Medicine*



Announce

2012 Annual Fellows and Residents Research Forum

*Sol Sherry Awards for
Excellence in
Research*

Wednesday, June 6, 2012

Medical Education and Research Building

The Fellows and Residents Research Forum was initiated over 25 years ago to provide the Fellows and the Residents in the Department of Medicine with an opportunity to present their research effort to the Members of the Department. The Forum is a reflection of the ongoing research activities in the Department, and a year-end summation of the projects carried out by the Fellows and Residents.

Dedication

Dr. Sol Sherry
1916-1993



Sol Sherry, M.D., joined Temple University School of Medicine as professor and chairman of the Department of Medicine in 1968. In 1970, Dr. Sherry founded and served as director of the University's specialized Center for Thrombosis Research, the largest of its kind in the United States, which was later named in his honor. He served as dean of the School of Medicine from 1984-86. He was a recipient of an honorary doctor of science degree, the University's first Distinguished Professor and was honored with the establishment of the Sol Sherry Chair in Medicine.

For his contributions to medical research, teaching and patient care, Dr. Sherry was the recipient of other numerous awards and honors. He was Master of the American College of Physicians and The John Phillips Memorial Medalist of the American College of Physicians; a Fellow of the Royal College of Physicians (London), and recipient of the Robert P. Grant Medal of the International Society on Thrombosis and Hemostasis--a society which he founded in 1977. Dr. Sherry also received awards from the American Heart Association, the Philadelphia County Medical Society, the Texas Heart Institute and the Swedish Society of Cardiology.

**Fellows and Residents Research Forum
Wednesday, June 6, 2012
Medical Education and Research Building
Rooms 217/219**

12:00 – 1:00 PM Poster Viewing and Lunch (Rooms 219 A & B)

1:00 – 2:00 PM Poster Discussions (Rooms 219 A & B)

2:00 – 2:15 PM Break

2:15 – 5:30 PM Oral Presentations (Rooms 219 A & B)

5:30 PM Keynote Address (Room 217)

“Why does obesity lead to insulin resistance, inflammation and cardiovascular disease?”

Guenther Boden, M.D.

Laura H. Carnell Professor of Medicine

Section of Endocrinology, Diabetes and Metabolism

Temple University School of Medicine

**6:00 PM Kal & Lucille Rudman Foundation Acknowledgment,
Presentation of Awards & Reception (Room 217)**

Poster Discussions – Room 219A

Cardiology

Faculty Facilitators: René Alvarez, Daniel Edmundowicz, José Missri⁺, Brian O’Murchu

Valdimir Lakhter, D.O. (Cardiology) Resident **Abstract #19**

The Effect of Left Ventricular Dysfunction and Chronic Kidney Disease on Fractional Flow Reserve Values

Chad J. Zack, M.D. (Cardiology) Resident **Abstract #41**

Smoking is a Strong Independent Predictor for Functional Significance of Intermediate Coronary Lesions

Chad J. Zack, M.D. (Cardiology) Resident **Abstract #42**

Left Ventricular Noncompaction Under the Guise of Peripartum Cardiomyopathy

Robert Hamburger, D.O. (Cardiology) Resident ***Abstract #13**

Evaluation of Right Coronary Artery Originating from Left Sinus of Valsalva by Dipyridamole Nuclear Stress Testing

Abdulrahman Morad, M.D. (Cardiology) Resident ***Abstract #26**

Central Venous Saturation is a Surrogate for Mixed Venous Saturation in Calculating Cardiac Output

Val Rakita, M.D. (Cardiology) Resident ***Abstract #45**

Factors Affecting Physicians’ Behaviors & Management of Cardiovascular Risk

Val Rakita, M.D. (Cardiology) Resident ***Abstract #46**

Effects of Blood Pressure Self Measurement & Telemedicine Communication on Physician Prescribing Habits

Cancer

Faculty Facilitators: Michael Bromberg, David Essex, Koneti Rao, Ron Rubin⁺

Ali Mahta, M.D. (Internal Medicine) Resident **Abstract #22**

Paraneoplastic Encephalopathy and Ataxia in a Patient with Small Cell Lung Cancer

Saad A. Khan, MBBS (Hematology/Oncology) Fellow ***Abstract #15**

Survivin Expression in Pancreas Adenocarcinoma

*Denotes the abstract will be both an oral & poster presentation

⁺Lead Facilitator

Poster Discussions – Room 219A

Chronic Obstructive Pulmonary Disease

Faculty Facilitators: Gerard Criner⁺, Nathaniel Marchetti, James Mamary, Kartik Shenoy

Nishant Goel, M.D. (Pulmonary) Fellow

Abstract #11

Clinical Predictors of Thromboembolic Events in Chronic Obstructive Pulmonary Disease Subjects in the COPDGene Study

Manuel Jimenez, M.D. (Pulmonary) Fellow

Abstract #14

High Intensity Non-Invasive Positive Pressure Ventilation (NPPV) for Stable Hypercapnic COPD Patients

Jeffrey Stewart, M.D. (Pulmonary) Fellow

Abstract #38

Clinical Characteristics of COPD Patients According to the Pattern of Emphysema on High Resolution CT

Maria Elena Vega, M.D. (Pulmonary) Fellow

Abstract #40

COPD Exacerbation is Associated with Substantial Activation of Circulating Inflammatory Monocytes

Matthew Lammi, M.D. (Pulmonary) Fellow

Abstract #20

Dynamic Hyperinflation is Reduced After LVRS and is Associated With Improved Functional Outcomes

Idiopathic Pulmonary Fibrosis

Faculty Facilitators: David Ciccolella, Gilbert D'Alonzo⁺, Steven Kelsen, Victor Kim

Brian Civic (Pulmonary) Fellow

Abstract #2

Quantitative CT Scan Analysis Predicts Outcome in Patients with IPF

Sean Duffy, M.D. (Pulmonary) Resident

***Abstract #5**

Upper Lobe Emphysema is Associated with Lower Survival in Patients with Idiopathic Pulmonary Fibrosis

Nicholas Panetta, M.D. (Pulmonary) Fellow

Abstract #28

Correlation Between Pulmonary Artery Diameter and Mean Pulmonary Artery Pressure in Patient with Pulmonary Fibrosis

*Denotes the abstract will be both an oral & poster presentation

⁺Lead Facilitator

Poster Discussions – Room 219B

Endocrinology

Faculty Facilitators: Sharon Herring, Matthew O'Brien, Elias Siraj, Kevin Williams⁺

Gauri Dhir, M.D. (Endocrinology) Fellow

Abstract #3

A Case of Familial Dysalbuminemic Hyperthyroxinemia (Fdh) - A Syndrome that Can be Confused with Hyperthyroidism

Alyson Dobracki, D.O. (Geriatrics) Fellow

Abstract #44

Under-recognition of Weight Loss in Community-Dwelling Elders

Gastroesophageal Reflux Disease

Faculty Facilitators: Frank Friedenber⁺

Kian Makipour, M.D. (Gastroenterology) Fellow

***Abstract #23**

A Population-Based Assessment of Heartburn in Urban Black Americans

Ronald Andari Sawaya, M.D. (Gastroenterology) Resident

Abstract #35

Use of the Montreal Global Definition as an Assessment of Quality of Life in Reflux Disease

Gastroparesis

Faculty Facilitators: Henry Parkman⁺

Nina George, D.O. (Gastroenterology) Resident

***Abstract #9**

Small Intestinal Bacterial Overgrowth in Gastroparesis

Nina George, D.O. (Gastroenterology) Resident

***Abstract #10**

Small Intestinal Bacterial Overgrowth: What's the Best Test to Correlate Symptoms?

Alexandra Modiri, M.D. (Gastroenterology) Resident

***Abstract #25**

Gastroparesis Symptoms Correlate with Headache Severity

Colorectal Cancer

Faculty Facilitators: Oleh Haluszka⁺

Alexandra Modiri, M.D. (Gastroenterology) Resident

***Abstract #24**

Predictors of Colorectal Cancer Testing Using the 2009 California Health Inventory Survey

*Denotes the abstract will be both an oral & poster presentation

⁺Lead Facilitator

Poster Discussions – Room 219B

Infectious Diseases

Faculty Facilitators: Thomas Fekete, Susan Gersh, Rafik Samuel⁺

Banafsheh Soltani, M.D. (Infectious Diseases) Fellow **Abstract #37**
*Clinical Experience with Telavancin for Treatment of
Methicillin-Resistant Staphylococcus aureus (MRSA) Bloodstream Infection*

Carolyn Fernandes, M.D. (Infectious Diseases) Fellow **Abstract #6**
*Development of Daptomycin Resistance While on Therapy
Leading to Therapeutic Failure*

Nephrology Transplant

Faculty Facilitators: Crystal Gadegbeku⁺, Anuradha Paranjape

Sridhar K. Reddy, M.D. (Nephrology) Fellow ***Abstract #30**
*Post-Kidney Transplantation Self-Reported Health is
Independent of Allograft Function*

Abdulrahman Morad, M.D. (Cardiology) Resident ***Abstract #27**
*Effects of Renal Transplantation on Left Ventricular
Remodeling are Dissociated from Hypertension Control*

Rheumatology

Faculty Facilitators: Philip Cohen⁺

Rebecca Sharim, M.D. (Rheumatology) Resident **Abstract #36**
*Factors Associated with a Prolonged Hospital Length of
Stay for Patients with Acute Gout*

Roberto Caricchio, M.D. (Rheumatology) Resident ***Abstract #1**
*Caspase-activated DNase is Required for Maintenance of
Tolerance to Lupus Nuclear Autoantigens*

Michelle Doll, M.D. (Rheumatology) Resident **Abstract #4**
*Leptin and Leptin Receptor Antagonism in Mouse Models
of Rheumatoid Arthritis*

*Denotes the abstract will be both an oral & poster presentation

⁺Lead Facilitator

Oral Presentations – Fellows Room 219A

Chair: Koneti Rao

Judges: Philip Cohen, Crystal Gadegbeku, Oleh Haluszka, Sharon Herring, Steven Kelsen, Kevin Williams

2:15 PM	Abhinav Sankineni, M.D., MPH (Gastroenterology) <i>Slow Esophageal Propagation Velocity: Association with Dysphagia for Solids</i>	Abstract #34
2:30 PM	Saad A. Khan, MBBS (Hematology/Oncology) <i>Survivin Expression in Pancreas Adenocarcinoma</i>	*Abstract #15
2:45 PM	Brett R. Laurence, M.D. (Infectious Diseases) <i>Assessment of Internal Medicine Residency Competency in Infectious Diseases Using an Educational Intervention Tool</i>	Abstract #21
3:00 PM	Jason Krahnke, D.O. (Pulmonary) <i>Noninvasive Positive Pressure Ventilation Use in Acute Exacerbation of COPD after Hospitalization for Hypercapnic Respiratory Failure May Decrease 30 Day Readmission</i>	Abstract #17
3:15 PM	Kian Makipour, M.D. (Gastroenterology) <i>A Population-Based Assessment of Heartburn in Urban Black Americans</i>	*Abstract #23
3:30 PM	Sajad Salehi, M.D. (Endocrinology) <i>Comparison of In Vivo Effects of Insulin on SREBP-1c and INSIG-1/2 in Rat Liver and Human and Rat Adipose Tissue</i>	Abstract #32
3:45 PM	Sridhar K. Reddy, M.D. (Nephrology) <i>Post-Kidney Transplantation Self-Reported Health is Independent of Allograft Function</i>	*Abstract #30
4:00 PM	Carolyn Fernandes, M.D. (Infectious Diseases) <i>Physician Responses to Positive Blood Cultures</i>	Abstract #7
4:15 PM	Abhinav Sankineni, M.D., MPH (Gastroenterology) <i>Gastric Histopathology on Full Thickness Gastric Biopsy Provides Prognostic Information for Treatment Responses to Gastric Electric Stimulation</i>	Abstract #33
4:30 PM	Christian J. Fidler, M.D. (Hematology/Oncology) <i>Expression of Aurora A and Phospho-Aurora-A is Predictive of Survival in Patients with Head and Neck Cancer</i>	Abstract #8
4:45 PM	Jason Krahnke, D.O. (Pulmonary) <i>Patients with Severe COPD and Diffuse Emphysema on CT Scan have More Sputum Symptoms</i>	Abstract #18
5:00 PM	Priyanka Sachdeva, M.D. (Gastroenterology) <i>Symptom Recurrence After Stopping Proton Pump Inhibitors (PPIs) in Patients Undergoing Esophageal pH Monitoring: “The Reverse Therapeutic PPI Trial”</i>	Abstract #31
5:15 PM	Neel Gandhi, M.D. (Hematology/Oncology) <i>Assessing Impact of Age on Transplant Outcome in Multiple Myeloma. A Single Institution Review</i>	Abstract #43

*Denotes the abstract will be both an oral & poster presentation

Oral Presentations – Residents Room 219B

Chair: *Henry Parkman*

Judges: *René Alvarez, Michael Bromberg, Gilbert D'Alonzo, Thomas Fekete, Frank Friedenber, Nathaniel Marchetti, Anuradha Paranjape*

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|---------|--|---------------|
| 2:15 PM | Abdulrahman Morad, M.D. (Cardiology)
<i>Effects of Renal Transplantation on Left Ventricular Remodeling are Dissociated from Hypertension Control</i> | *Abstract #27 |
| 2:30 PM | Alexandra Modiri, M.D. (Gastroenterology)
<i>Predictors of Colorectal Cancer Testing Using the 2009 California Health Inventory Survey</i> | *Abstract #24 |
| 2:45 PM | Jeanette Guziel (Pulmonary)
<i>Prevalence and Predictors of Pulmonary Nodules and Other CT Abnormalities Concerning for Malignancy in Smokers at Risk for Lung Cancer in COPD Gene</i> | Abstract #12 |
| 3:00 PM | Robert Hamburger, D.O. (Cardiology)
<i>Evaluation of Right Coronary Artery Originating from Left Sinus of Valsalva by Dipyridamole Nuclear Stress Testing</i> | *Abstract #13 |
| 3:15 PM | Nina George, D.O. (Gastroenterology)
<i>Small Intestinal Bacterial Overgrowth in Gastroparesis</i> | *Abstract #9 |
| 3:30 PM | Rajeeve Subbiah, M.D. (Cardiology)
<i>Prevalence and Mechanism of Pulmonary Hypertension in Chronic Hemodialysis by Invasive Measurements</i> | Abstract #39 |
| 3:45 PM | Alexandra Modiri, M.D. (Gastroenterology)
<i>Gastroparesis Symptoms Correlate with Headache Severity</i> | *Abstract #25 |
| 4:00 PM | Abdulrahman Morad, M.D. (Cardiology)
<i>Central Venous Saturation is a Surrogate for Mixed Venous Saturation in Calculating Cardiac Output</i> | *Abstract #26 |
| 4:15 PM | Sean Duffy, M.D. (Pulmonary)
<i>Upper Lobe Emphysema is Associated with Lower Survival in Patients with Idiopathic Pulmonary Fibrosis</i> | *Abstract #5 |
| 4:30 PM | Nina George, D.O. (Gastroenterology)
<i>Small Intestinal Bacterial Overgrowth: What's the Best Test to Correlate Symptoms?</i> | *Abstract #10 |
| 4:45 PM | Roberto Caricchio, M.D. (Rheumatology)
<i>Caspase-activated DNase is Required for Maintenance of Tolerance to Lupus Nuclear Autoantigens</i> | *Abstract #1 |
| 5:00 PM | Valdimir Lakhter, M.D. (Cardiology)
<i>Smoking is a Strong Independent Predictor for Functional Significance of Intermediate Coronary Lesions</i> | *Abstract #41 |
| 5:15 PM | Chad Zack, M.D. (Cardiology)
<i>Left Ventricular Noncompaction Under the Guise of Peripartum Cardiomyopathy</i> | *Abstract #42 |

Caspase-activated DNase is Required for Maintenance of Tolerance to Lupus Nuclear Autoantigens

NR Jog, L Frisoni, Q Shi, M Monestier, S Hernandez, J Craft, ET Prak, R Caricchio

OBJECTIVE: Caspase-activated DNase (CAD) is an endonuclease that is activated by active caspase 3 during apoptosis and is responsible for degradation of chromatin into nucleosomal units. These nucleosomal units are then included in apoptotic bodies. The presence of apoptotic bodies is considered important for the generation of autoantigen in autoimmune diseases, such as systemic lupus erythematosus (SLE), that are characterized by the presence of antinuclear antibodies. The present study was carried out to determine the role of CAD in SLE and to investigate the ability of lupus autoantibodies to bind to CAD-deficient or CAD-sufficient apoptotic cells.

METHODS: The Sle1, Sle123, and 3H9 mouse models of SLE, in which autoimmunity is genetically predetermined, were used. To determine the role of chromatin fragmentation in SLE, CAD deficiency was introduced in these mouse models.

RESULTS: Deficiency of CAD resulted in increased anti-double-stranded DNA antibody titers in lupus-prone mice. Surprisingly, the absence of CAD exacerbated only genetically predetermined autoimmune responses. To further determine whether nuclear modifications are needed in order to maintain tolerance to nuclear autoantigens, we used the 3H9 mouse, an anti-DNA heavy chain knockin; in this model, the autoreactive B cells are tolerized by anergy. In accordance with findings in the CAD-mutant Sle1 and Sle123 mice, CAD-deficient 3H9 mice spontaneously generated anti-DNA antibodies. Finally, we showed that autoantibodies with specificities toward histone-DNA complexes bind more to CAD-deficient apoptotic cells than to CAD-sufficient apoptotic cells.

CONCLUSION: We propose that in mice that are genetically predisposed to lupus development, nuclear apoptotic modifications are needed to maintain tolerance. In the absence of these modifications, apoptotic chromatin is abnormally exposed, facilitating the autoimmune response.

Quantitative CT Scan Analysis Predicts Outcome in Patients with IPF

Brian Civic MD, Irene Swift MD, Nick Panetta MD, Sean Duffy MD, Rubina Khair MD, Nina George MD, John Gaughan, PhD, Gerard J Criner MD

Background: Idiopathic pulmonary fibrosis (IPF) is a fibrotic lung disease that results in death. The rate of disease progression is variable and difficult to predict. Quantitative computed tomography (CT) analysis offers an objective evaluation of lung parenchyma that could provide additional prognostic information.

Purpose: To evaluate quantitative CT indices as predictors for mortality.

Methods: 89 patients were selected from the Temple Lung Center Outpatient Clinic. Patients had to have pulmonary function tests (PFT), a 6-minute walk distance (6-MWD), and a non-contrast CT thorax within a 3-month period. PFT and 6-MWD were performed according to ATS criteria. CT scans were analyzed using Slicer v2.8 and evaluated for fibrosis and emphysema. Skewness and kurtosis of each patient's Hounsfield units histogram was used as a measure of fibrosis. Primary outcome was time to death or transplant from each patient's CT scan date. Student's T-test was used to determine differences between patients that were alive at follow-up and those that died or were transplanted. Univariate analysis and multivariate Cox proportional hazards model were performed to determine which variables were associated with shorter time to death or transplant.

Results: Two-thirds of patients died or were transplanted during follow-up. Patients that died or were transplanted had significantly worse pulmonary function and fibrosis on CT scan compared to patients that were alive at follow-up.

Conclusions: Fibrosis on CT scan, assessed quantitatively, may predicted worse outcome in patients with IPF.

Partially funded by the Kal and Lucille Rudman Foundation

A Case of Familial Dysalbuminemic Hyperthyroxinemia (FDH) - A Syndrome That Can Be Confused with Hyperthyroidism

Gauri Dhir, MD; Elias S. Siraj, MD.

**Section of Endocrinology, Diabetes & Metabolism
Temple University School of Medicine**

Objective: Many conditions result in increases in serum total T4 (TT4) and/or T3 (TT3) but little change in serum free T4 (FT4) and/or free T3 (FT3). Familial Dysalbuminemic Hyperthyroxinemia (FDH) is one such condition which is often confused with hyperthyroidism.

Case Presentation: A 50 year old female presented to her internist with complaints of worsening anxiety, sweating, and palpitations. Laboratory tests showed a TSH of 0.22 mIU/L (NL: 0.4-4.5), TT4 of 14.4 mcg/dL (NL: 4.5-12.5), FT4 of 1.1 ng/dL (NL: 0.8-1.8), T3 Uptake of 22% (NL: 22-34), and TT3 of 163 ng/dL (NL: 76-181). Her 24 hour RAI uptake was 23 % and scan showed diffusely enlarged gland. With the impression of hyperthyroidism, she was treated with methimazole followed by RAI treatment. On the 4th day following RAI treatment she presented to the emergency room with severe neck pain/swelling, palpitations and sweating. Subsequently, she was referred to us for further management. We made a diagnosis of radiation thyroiditis and moderate hyperthyroidism.

Discussion: We believe that the patient has FDH, which led to a misleading diagnosis of hyperthyroidism and subsequent treatment with RAI. This is an autosomal dominant condition, whereby mutant albumin molecules have low affinity but high capacity for T4 while maintaining normal behavior to T3. This leads to a high TT4 (but normal TT3) levels, but FT4 as well as TSH levels are generally normal, indicating an essentially euthyroid state

Conclusion: Elevated TT4 level not accompanied by elevated FT4 (and FT3) levels does not always indicate hyperthyroidism and should prompt some one to look for causes of euthyroid hyperthyroxinemia which include FDH.

Leptin and Leptin Receptor Antagonism in Mouse Models of Rheumatoid Arthritis

Michelle Doll, Laszlo Otvos Jr., Wen-Hai Shao, Philip Cohen

**Department of Medicine, Temple Hospital, and Temple University
Philadelphia, PA**

Introduction: Leptin is a peptide hormone that has been implicated in a variety of functions, including the regulation of appetite and metabolism, and more recently inflammation and autoimmunity. Abnormal leptin levels have been associated with osteoarthritis and even rheumatoid arthritis in some studies, possibly due to activation of inflammatory signaling via NF- κ B through binding to its receptor ObR. Antagonism of ObR is being investigated as a strategy to decrease inflammation associated with these conditions. Peptide fragments of leptin have been developed to bind to ObR, and include the peptide Allo-aca used in this study. The K/BxN serum transfer model is one of the many mouse models for rheumatoid arthritis. Transfer to normal mice of K/BxN sera results in a severe inflammatory arthritis. Using this model, we tested the effects of leptin and the ObR binding peptide Allo-aca on the progression of arthritis.

Methods: Arthritis was induced in C57BL/6 mice by injecting them with 150ul of serum from K/BxN mice. The C57BL/6 mice were then treated with either 0.05mg/kg leptin, 0.1 mg/kg peptide Allo-aca, or saline control, on days 0, 1, and 2. Disease progression was measured by taking ankle thickness measurements daily. On day 14, the mice were sacrificed and joint specimens taken for pathology analysis. Serum taken on day 14 was analyzed by ELISA for the presence of TNF-alpha. In a follow up experiment, K/BxN serum treated mice were given either leptin alone, leptin and Allo-aca simultaneously or leptin with Allo-aca given after a 3 day delay. Each joint was then scored from 0-3 depending on the amount of inflammation of visual exam; the maximum score was 12.

Results: All experimental mice developed the expected serum transfer arthritis, with increases in ankle thickness apparent by day 4 for leptin-treated and control mice and day 6 for Allo-aca treated mice. The severity of arthritis as measured by ankle thickness, was most pronounced in mice treated with leptin, peaking at an average increase of 228 um on day 6. In contrast, mice injected with peptide Allo-aca peaked at an increase of 200um on day 7. Control mice peaked on day 6 at 180um. Measureable arthritis began to decline after day 7. Joint specimens did not reveal inflammatory infiltrates or erosions, and ELISA testing for TNF-alpha was negative. However, in the second experiment, allo-aca given simultaneously with leptin did ameliorate the effects of leptin alone, by decreasing the arthritic score. When given with the three day delay, the effects of Allo-aca were negligible, and arthritic scores approached those of mice treated with leptin alone.

Conclusion: The peptide Allo-aca may improve the degree of swelling early in experimental arthritis and delay the onset of severe joint swelling, yet ultimately causing increased peak thickness compared to control. The lack of inflammatory markers in day 14 specimens may be related to waning observable arthritis and undetectable residual inflammation. When given simultaneously with leptin, Allo-aca may ameliorate the exacerbation of serum transfer arthritis that leptin seems to cause. Allo-aca may be useful in mitigating inflammation in states of leptin excess, when given early in the disease process.

Upper Lobe Emphysema is Associated with Lower Survival in Patients with Idiopathic Pulmonary Fibrosis

B Civic, MD, I Swift, MD, S Duffy, MD, R Khair, MD, N George, MD, G J Criner

Temple University School Medicine, Philadelphia, PA, United States

Background: Idiopathic pulmonary fibrosis (IPF) is a progressive, fibrotic lung disease that ultimately results in death. The rate of disease progression is variable and difficult to predict. Quantitative computed tomography (CT) analysis offers an objective evaluation of lung parenchyma that could provide additional prognostic information.

Purpose: To evaluate quantitative CT indices as predictors for mortality and hospitalization.

Methods: 43 patients were selected from the Pennsylvania IPF registry. Patients had to have pulmonary function tests (PFT), a 6-minute walk (6MWT), and a non-contrast CT thorax within a 3-month period. Scans were analyzed using Slicer v2.8, available at www.airwayinspector.org. Skewness and kurtosis of each patient's hounsfield units' histogram were used as a measure of fibrosis. Mortality was determined using the Social Security Death Index. Patients were grouped by time to death from baseline CT date. ANOVA was used to compare the amount of emphysema and fibrosis between the groups. The amount of emphysema, skewness, and kurtosis was also compared between patients who died or were hospitalized and those that did not.

Results: Patients that died or were hospitalized had significantly more emphysema in the upper lobes, 4% vs. 0.8%, compared to those who did not, p-value 0.048. There were no significant differences in fibrosis.

Conclusions: Patients that died in less than one year from their CT scan date had significantly more emphysema in the upper lobes compared to patients that survived more than 2 years. The degree of emphysema in the upper lobes should be considered in the evaluation of patients with IPF and may portend a worse survival.

Partially funded by the Kal and Lucille Rudman Foundation

Development of Daptomycin Resistance While on Therapy
Leading to Therapeutic Failure

C. Fernandes¹, H. Nace¹, P. Ender², T. Le², K. Mascitti², J. Jahre², T. Fekete¹,
and B. Suh¹

¹Temple Univ. Sch. of Medicine, Philadelphia, PA
and ²St. Luke's Hosp., Bethlehem, PA

Background: Daptomycin (D) is bactericidal for *Staphylococcus aureus* (SA). It is approved for skin/skin structure infections and bacteremia. We observed an MIC increase in 8 patients, on D therapy, resulting in therapeutic failures.

Methods: Cases were collected from a retrospective chart review of inpatients with SA bacteremia ≥ 7 days initially susceptible to D, received D for >48 hrs and demonstrated D resistance on therapy.

Results: There were 8 cases: ages 34-66 yrs; 6 males; renal failure (5/8); IVDU (4/8); DM (2/8); HIV (1/8). 7/8 had MRSA bacteremia, and 1 had MSSA. Five had proven IE. Most patients had or developed additional foci of infection: epidural or skin abscesses, osteomyelitis, septic arthritis, and septic PE. Bacteremia ranged 7-35 days (mean 21). All received vancomycin (V) for 3-42 days (V MIC 0.5-2.0 μ g/ml). The initial MIC for D was $< 1.0\mu$ g/ml for all strains. All patients received IV D 6 mg/kg body weight, adjusted for renal function. Treatment duration with D ranged 7-21 days. All strains had repeat V and D MICs done: V MICs $\geq 2.0\mu$ g/ml in 7/8, and 1 MIC $< 0.5\mu$ g/ml. D MICs post-treatment rose to $\geq 1.5\mu$ g/ml (range 1.5-6.0) in all cases. All cleared their bacteremia with alternative regimens. Survival was good in 6/8.

Conclusions: We observed 8 patients with SA bacteremia who developed D non-susceptible MIC (>1.0) on therapy, with treatment failures. Prior V use may be an important predisposing factor; other factors may include renal insufficiency and IVDU. Close MIC monitoring of D in SA persistent bacteremia may be warranted.

Physician Responses to Positive Blood Cultures

Carolyn Fernandes MD, Peter Axelrod MD, Thomas Fekete MD

Background: Antibiotics are often started before blood cultures results are final. We investigated antibiotic use in the 24 h following notification of a positive blood culture.

Methods: A 6-week prospective observational study of inpatients with a positive blood culture. Antibiotics at the time and within 24h of notification of Gram stain results were evaluated for appropriateness. We adjudicated whether the positive culture was a pathogen (TP) or contaminant (FP). Primary outcome was appropriate antibiotic use within 24h of notification. Secondary outcomes included repeat cultures, patient disposition and hospital stay.

Results: 171 patients were included: 100 TP and 71 FP. Most were on Medicine (33% ICU) and had cultures sent on admission. At notification, 84% TP and 58% FP were on antibiotics (74% and 63% appropriate based on Gram stain). A new antibiotic was ordered in 66% of TP and 20% FP with a median time to initiation of 3 hours. Within 24 h, 88% of TP and 36% of FP patients were on appropriate treatment based on Gram stain. Only admission to inpatient Medicine was associated with appropriate treatment (RR 1.47, P = 0.005). Being on the right antibiotic within 24 h showed a trend towards shorter hospital stay; 19 vs. 25 d (RR 0.41, P = 0.17)

Conclusions: Most patients with true bacteremia are on appropriate treatment within 24 h of notification, but 12% were not. Physician antibiotic prescribing indicates that they often can differentiate TP from FP before cultures are finalized.

Expression of Aurora A and Phospho-Aurora-A is Predictive of Survival in Patients with Head and Neck Cancer**Christian J. Fidler, Donghua Yang, Fang Zhu, Raneeh Mehra, Igor Astsaturov, John Ridge, Erica Golemis, Barbara Burtness.****Fox Chase Cancer Center, Philadelphia, PA**

Introduction: The Aurora kinases represent a family of serine/threonine kinases important in regulating cell cycle progression. Aurora-A is required for centrosome function and mitotic spindle assembly. Aurora-A phosphorylation supports the activity of many proteins involved in cell proliferation and survival, including important EGFR effectors such as AKT and RAS. High expression of Aurora A has been shown in patients with breast, lung, gastrointestinal, genitourinary, and gynecological cancers. The Aurora kinases are known to promote tumor formation and progression, which has led investigators to develop multiple inhibitors of Aurora kinases for clinical use. The expression of Aurora-A kinase in head and neck cancers is not well understood. We assessed the overall survival (OS) for a cohort of patients with squamous cell carcinoma of the head and neck (SCCHN) based upon Aurora-A and phospho-Aurora-A kinase expression (reflecting active Aurora-A). We also related this to SCCHN subtype, using p16 expression as a surrogate for human papillomavirus association, because of the recognition that p16 + cancers have far superior prognosis.

Methods: Tumor tissue from 89 patients with SCCHN operated on at the Fox Chase Cancer Center was analyzed for Aurora-A and phospho-Aurora-A expression. Aurora kinase expression was determined using AQUATM, with the median values used to distinguish over-expressers. Aurora-A and phospho-Aurora-A expression was correlated with T and N stage and OS, in p16+ versus p16- tumors. The p16 status was determined by immunohistochemistry.

Results: T stage was inversely related to Aurora-A expression when adjusted for p16 status (Spearman's rho -0.24, $p = 0.04$). Aurora-A expression was not related to N stage (Spearman's rho -0.03, $p = 0.79$). OS was 36 months for over-expressers of Aurora-A and 92 months for patients with low levels of Aurora-A expression (HR 1.9, 95% CI 1.05-3.46). 20 patients were positive for p16 by IHC. There was no difference in survival amongst p16 positive patients based on Aurora-A expression (53.3 months vs 57.2 months, $p = 0.679$). Amongst the 69 p16 negative patients, OS was 93.6 months for patients with low levels of Aurora-A expression and 35.9 months for those with elevated levels of Aurora-A (HR 1.84, 95% CI 0.89-3.79). There was a trend towards improved survival in patients with lower levels of phospho-Aurora-A expression (63.9 vs 57.6 months, $p = 0.129$).

Conclusions: Increased expression of Aurora-A in this cohort of SCCHN patients is associated with a significant decrease in OS. Increased expression of Aurora-A in patients with p16 positive tumors does not seem to impact survival, though the number of patients was small. Aurora-A represents a possible therapeutic target in patients with SCCHN.

Small Intestinal Bacterial Overgrowth in Gastroparesis**Nina George DO, Abhinav Sankineni MD MPH, Henry Parkman MD**

Introduction: Lactulose breath testing (LBT) is a method for detection of small intestinal bacterial overgrowth (SIBO), a condition that can lead to variety of gastrointestinal symptoms some of which are similar to those in gastroparesis. There are few studies that evaluate gastrointestinal symptoms and most optimal breath test in gastroparesis patients with SIBO.

Aim: To determine the incidence, symptoms and risk factors of bacterial overgrowth in patients with gastroparesis undergoing LBT.

Methods: Patients undergoing LBT (lactulose breath test) evaluation for SIBO from December 2009 to August 2011 were included. LBT was considered positive using two conventional criteria: 1) hydrogen level increase > 20 ppm above baseline by 90 minutes (H2@90min); 2) dual hydrogen peaks (>10 ppm increase over baseline prior to second peak >20ppm (DPHBT). Results of gastric emptying scintigraphy (GES) were recorded; delayed gastric emptying was present if there was a delay of solid meal present either at 2 hours (>60% retention), 4 hours (>10% retention) or 1 hour with liquid meal (>50% retention). Patients filled out a questionnaire regarding current medications, medical and surgical history and the Patient Assessment of Upper Gastrointestinal Disorders-Symptom Severity Index (PAGI-SYM).

Results: Of the 740 patients who underwent LBT, 471 patients underwent GES with 201 having delayed GES. Mean age of patients with delayed GES who underwent LBT was 44.3±1.0 years, and BMI of 24.9±0.5; 87% were female, 23% diabetic, 49% used gastric acid suppressants, 29% used opiate analgesics, 35% used pro-motility medications, and 27% had history of gastrointestinal surgery. Overall, 79 (39%) patients had evidence of SIBO by LBT: 30 (15%) had positive H2@90min, 53 (26%) positive DPHBT. In gastroparesis patients with positive H2@90min, there was increased severity bloating (3.80±0.20 vs 3.29±0.12; p=0.02), early satiety (3.57±0.27 vs 3.05±0.13; p=0.045) and postprandial fullness (4.20±0.18 vs 3.52±0.12; p<0.01) compared to negative H2@90min patients. In comparison, gastroparetics with positive DPHBT tended to have increased symptom severity of vomiting (1.90±0.25 vs 1.50±0.15; p=0.08), stomach appearing visibly larger (3.10±0.24 vs 2.82±0.14; p=0.17), diarrhea (2.06±0.27 vs 1.88±0.15; p=0.28) and flatulence (2.83±0.21 vs 2.57±0.13;p=0.15).

Conclusion: In this cohort of gastroparesis patients, a positive lactulose breath test assessed using H2@90min, but not DPHBT, was associated with increased symptoms of bloating, early satiety and postprandial fullness compared to negative tests; such symptoms therefore may represent bacterial overgrowth in gastroparesis patients.

Small Intestinal Bacterial Overgrowth: What's the Best Test to Correlate Symptoms

Nina George DO, Abhinav Sankineni MD MPH, Henry Parkman MD

Objective: Lactulose Breath Testing (LBT) is used for evaluation of symptoms suggestive of small intestinal bacterial overgrowth (SIBO). There are several different definitions for positive breath test with no clear standard.

Aim: To determine the incidence, symptoms and risk factors for small intestinal bacterial overgrowth (SIBO) using various definitions for positive LBT in evaluation of SIBO.

Methods: All patients who underwent LBT evaluation for SIBO at Temple University Hospital from December 2009 to August 2011 were included. LBT was considered to be positive using three different definitions: 1) breath hydrogen level increase > 20 ppm above baseline by 90 minutes (H₂@90min); 2) dual hydrogen peaks (>10 ppm increase over baseline prior to second peak >20ppm (DPHBT); and 3) positivity for either of the LBT definitions (combined breath test, CBT). Patients filled out a questionnaire regarding current medications, medical and surgical history as well as the Patient Assessment of Upper Gastrointestinal Disorders-Symptom Severity Index (PAGI-SYM). Data was analyzed using independent T-Tests, expressed as mean±SEM, and chi-square analysis.

Results: Total sample consisted of 740 patients, with mean age of 46.8±0.8 years and BMI of 26.0±0.29; 89% were females and 21% males with chief complaints of bloating (25%), abdominal pain (21%) and diarrhea (13%). 19% of patients were diabetic, 23% had prior gastrointestinal surgery, 44% used gastric acid suppressants, 25% used opiate analgesics for pain, and 26% used pro-motility agents. A total of 286/740 (39%) had positive LBT; 108/740 (15%) had positive H₂@90min, 141/740 (19%) had positive DPHBT. There was an increased prevalence of prior gastrointestinal surgery with positive H₂@90min ($\chi(1)=8.97$; $p<0.01$), and CBT ($\chi(1)=8.94$; $p<0.01$) compared to negative LBT. Patients with positive DPHBT had increased symptoms of vomiting (1.46±0.14 vs 1.08±0.07; $p=0.01$), constipation (2.67±0.14 vs 2.27±0.80; $p=0.01$), flatulence (3.01±0.12 vs 2.75±0.07; $p=0.03$), reflux laying supine/prone (1.72±0.12 vs 1.48±0.07; $p=0.04$) and bitter taste (1.83±0.12 vs 1.51±0.07; $p=0.01$) compared to negative DPHBT test. Similar associations of increased symptoms of reflux (1.66±1.0 vs 1.45±0.08; $p=0.045$) and bitter taste (1.81±0.10 vs 1.44±0.07; $p<0.01$) were seen with positive CBT compared to negative CBT patients. In addition, patients with positive H₂@90min had increased symptoms of bitter taste (1.87±0.14 vs 1.51±0.06; $p=0.01$) compared to negative H₂@90min.

Conclusion: Positive lactulose breath testing for SIBO is associated with reflux, vomiting, constipation and flatus type symptoms. Interestingly, different definitions for positive LBT lead to different symptom associations with SIBO.

Clinical Predictors of Thromboembolic Events in Chronic Obstructive Pulmonary Disease Subjects in the COPDGene Study

N. Goel MD, V. Kim MD, D. Ciccolella MD, P.A. Bercz MD, JP Gaughan Phd Edwin Silverman MD, James Crapo MD, G.J. Criner MD and the COPDGene Investigators

Introduction: Patients with Chronic Obstructive Pulmonary Disease (COPD) are at increased risk for venous thromboembolism (VTE) because of immobilization, heightened systemic inflammation, cigarette smoking, and venous stasis. Prevalence of VTE in patients hospitalized with an acute COPD exacerbation has been reported to be as high as 20%. However, VTE remains under diagnosed in this patient population. There are sparse data on the risk factors and characteristics of COPD patients who develop VTE.

Methods: Subjects in the COPDGene study completed standardized questionnaires to assess information about respiratory symptoms, smoking behavior, and past medical history. Spirometry, six minute walk test and CT scan of the thorax were performed. Subjects were divided into those who reported VTE (VTE+) and those without VTE (VTE-).

Results: A total of 10,220 subjects were analyzed. The number and prevalence of VTE+ subjects are listed in Table 1. The prevalence of VTE in GOLD 2-4 subjects was higher compared to nonsmoking controls and GOLD U, 0, and 1 subjects (5.7% vs. 3.7% and 3.4%, respectively). In an analysis of GOLD 2-4 subjects, VTE+ subjects had a shorter 6-minute walk distance compared to VTE- subjects (969.50 ± 427.23 feet vs. 1153.29 ± 427.23 feet, p<0.0001). Compared to the VTE- group, the VTE+ group had higher SGRQ scores (45.74 ± 20.86 vs. 40.69 ± 21.85, p<0.05), higher frequency of COPD exacerbations (1.03 ± 1.48/patient/year vs. 0.73 ± 1.23/patient/year, p<.005) and were more likely to report using oxygen (41.0% vs. 26.9%, p < 0.0001). With every decrement of 50 feet walked during 6-minute walk test and each additional exacerbation in the year prior to enrollment, the odds ratios of having a VTE were 1.16 (CI 1.10, 1.22; p< 0.001) and 1.17 (CI 1.07, 1.29; p<0.001) respectively. Smoking history was higher in VTE+ subjects (58.29 ± 36.62 pack-years vs. 52.74 ± 26.93 pack-years, p<0.05). There were no significant differences in percent emphysema, functional residual capacity, total lung capacity, or lung function between the two groups.

	VTE+	VTE-	Total	Prevalence (%)
All Subjects	436	9843	10279	4.2
Nonsmoking controls	4	104	108	3.7
Gold Stage U ⁺ , 0 ⁺⁺ , 1	220	6235	6455	3.4
Gold Stage 2-4	210	3446	3656	5.7*

+ Undefined: post-bronchodilator FEV1/FVC ≥ 0.70, FEV1 < 80% predicted; ++ Smoking Control;
 * p < 0.001 compared to those in non-smoking control, Undefined and GOLD grade 0 & 1 groups

Conclusion: GOLD 2-4 subjects with a history of VTE had an increased frequency of exacerbations, diminished exercise capacity, worse health related quality of life, an increased use of oxygen, and higher smoking history. Presence of these factors may indicate a higher likelihood of VTE in patients presenting with acute COPD exacerbation.

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Prevalence and Predictors of Pulmonary Nodules and Other CT Abnormalities Concerning for Malignancy in Smokers at Risk for Lung Cancer in COPDGene

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Rationale: The U.S. National Lung Screening Trial (NLST) suggests that screening with Low-Dose CT scans (LDCT) can reduce lung cancer deaths by 20%. The literature also suggests that 90% of positive results during screening with CT are false positives resulting in costly and invasive subsequent testing. For this reason, it is essential to preemptively characterize patients at risk for a positive result. Numerous studies have shown COPD and emphysema to be independent risk factors for lung cancer, but little is known about clinical characteristics that may increase risk for a CT abnormality concerning for malignancy.

Methods: From the full COPDGene cohort of 10,276 individuals, 3761 who would have met NLST inclusion criteria (between 55 and 74 years of age, history of cigarette smoking of at least 30 pack years, and if former smokers quit \leq 15 years ago) were analyzed. Any non-calcified nodule >4 mm or other CT abnormality of high concern for malignancy was classified as an "abnormal finding". Employing univariate and multivariate logistic regression, those with an abnormality were compared to those without, and predictors of an abnormality were observed.

Results: From the COPDGene cohort of 10,276 individuals, there were 1018 (9.9%) abnormalities. From the 3761 (36.6%) who met NLST inclusion criteria, there were 455 (12.1%) abnormal findings. Age (Chi-Square 18.28, $p < 0.0001$), GOLD stage (Chi-Square 16.73, $p = 0.0050$), and pack-years smoking (Chi-Square 6.10, $p = 0.0136$) were independent predictors of an abnormal CT concerning for malignancy. When controlling for age and pack-years; 6MWT O₂ ($p = 0.0005$, OR 5.83, CI 2.19-14.82), BODE ($p = 0.0049$, OR 1.99, CI 1.24-3.19), emphysema diagnosis (Chi-Square 7.52, $p = 0.0233$), steroid use (Chi-Square 5.07, $p = 0.0244$), B-agonist use ($p = 0.0272$, OR 1.26, CI 1.03-1.54), and SGRQ ($p = 0.0304$, OR 1.60, CI 1.05-2.44) remained predictive of an abnormal finding. Gender and race were not significantly associated with an abnormal CT concerning for malignancy.

Conclusions: COPD patients have a high incidence of lung cancer. As more patients are screened for lung cancer with a sensitive screening tool such as CT, it is important to recognize the predictors of abnormal findings. Patients with more severe structural, functional, and clinical COPD have a higher probability of CT abnormalities suspicious for malignancy, and early detection of lung cancer should be directed to these patients.

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**Evaluation of Right Coronary Artery Originating from Left Sinus of Valsalva by
Dipyridamole Nuclear Stress Testing**

Francis Burt, Jason Litsky, Robert Hamburger, Amit Pursnani

Background: The current ACC/AHA guidelines give a Class 1 recommendation for revascularization of patients with an anomalous origin of the right coronary artery (RCA) from the left sinus of valsalva who have an inter-arterial course (IAC) and evidence of ischemia. We evaluated dipyridamole myocardial perfusion imaging (MPI) in this population.

Methods: We identified twenty-three patients with anomalous RCA originating from the left sinus of valsalva during invasive angiography who also underwent MPI, excluding patients with previous CABG and non-dominant RCA.

Results: The mean age was 61 years. Four patients had CAD (stenosis >50%) of the RCA. Nineteen patients had an IAC (undetermined in four patients). Among patients with no CAD, 7/13 patients had ischemia in the RCA territory. Follow-up (mean 3.7 years) on 20/23 patients revealed 100% survival.

Conclusions: A subset of these patients demonstrate reversible perfusion defects on dipyridamole MPI, in the absence of obstructive CAD. Most of our patients had an IAC, including many with normal perfusion. Our data suggest a mechanism other than systolic compression of the IAC may cause ischemia. Furthermore, there were no known deaths and perfusion abnormalities were mild in our patient population, suggesting that this anomaly may be less “malignant” than previously suspected.

High Intensity Non-Invasive Positive Pressure Ventilation (NPPV) for Stable Hypercapnic COPD Patients

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Rationale: The efficacy of chronic intermittent NPPV in severe stable COPD is unclear. Some investigators have proposed the technique of high intensity NPPV as a more effective means to provide NPPV in severe COPD. However, the higher inflation pressures and back-up respiratory rates used in high intensity NPPV may impair tolerance in severely obstructed COPD patients. The purpose of this study is to examine the tolerance of high intensity NPPV in severe, stable, hypercapnic COPD.

Methods: This is a single arm, pilot study of four stable hypercapnic COPD patients with FEV1<50%, FEV1/FVC <70%, TLC >90%, BMI<35, PaCO₂ ≥50mmHg. Exclusion criteria included: patients with FEV1<15%, obstructive sleep apnea (AHI>15/hr), history of pneumothorax, current NPPV users, inability to maintain O₂ saturation >90% on

5 L/min of O₂ at rest, chronic systemic steroid use, history of any major non COPD comorbidity or diffuse parenchymal disease. Physiological parameters, exercise capacity and health related quality of life (HRQL) measurements were recorded at baseline and three months after receiving home nocturnal high intensity NPPV for at least 6hr daily.

Results: Mean age was 64.6 ± 7.8 years, three were female, the mean body mass index was 25 ±1.7 kg/m² with an average BODE index of 6.2 ± 1.7. NPPV with breathing frequencies 16 ± 1.8 breaths/min and mean inspiratory/expiratory pressures of 27 ± 2/4 cmH₂O led to improvement on blood gases, exercise capacity and health related quality of life. (**see tables**) No serious adverse events occurred during the study period.

Conclusions: High intensity NPPV was well tolerated on a chronic intermittent outpatient basis by these severely obstructed and hyperinflated COPD patients. NPPV use in severe but stable hypercapnic COPD was associated with a reduction in daytime hypercapnia, sleepiness scores and perception of dyspnea.

Variable	Prior NPPV	3m after NPPV
pH	7.4 ±0.02	7.41 ±0.03
PaCO ₂ *	54.2 ±0.8	51.5 ±3.1
HCO ₃ **	33.2 ±0.5	31.7 ±0.5
PO ₂ *	54.2 ±3.8	51.5 ±3.1
TLC%	106.8±12.4	105.5 ±8.3
RV%	165.5±40.8	161 ± 40.7
FEV1%	23.3 ±3.6	23.0 ±4.0
FEV1/FVC	29 ±8.4	32.2 ±3.8
MIP%	71.51 ±4.8	66.5 ±26.2
6MWT +	218.4±24.5	245.7±49.6

HRQL Scale	Prior to NPPV	3 month after NPPV
Chronic Respiratory Questionnaire		
Dyspnea	17.3 ±4.8	18.5 ±7.1
Fatigue	14.0 ±1.4	16.8 ±2.9
Emotional Functioning	32.0±3.6	34.8 ±2.1
Mastery	34.8 ±2.1	19.5 ±2.1
Calgary Sleep Apnea Quality of Life Index		
A (Daily Functioning)	5.0 ±0.7	6.2 ±2.0
B (Social Interaction)	6.82±0.3	6.4 ±0.4
C (Emotional Functioning)	5.9 ±0.8	6.1 ±0.5
D (Symptoms)	3.95 ±1.4	2.9 ±1.4
Epworth Sleepiness Scale	7.0 ±1.8	4.8 ±0.95
Medical Research Council Score	4.3 ±0.8	2.8 ±1.3
Borg dyspnea scale after 6MWT		
Dyspnea	6.5 ±1.3	3.0 ±2.9
Fatigue	2.0 ±3.5	3.0 ±2.4

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Survivin Expression in Pancreas Adenocarcinoma

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Many pancreas cancer patients are treatment refractory and die from their disease. We want to personalize patient treatment, rationally selecting effective agents. We examined Survivin as a biomarker predictive of treatment response.

From 88 pancreas cancer surgery patients: 150 tumor samples collected into tissue microarrays, analyzed by AQUA automated immunohistochemistry system. We examined nucleus/cytoplasm levels separately; Survivin's function differs depending on cellular location.

Median expression score for each cellular compartment was the cutoff to divide patients into high/low Survivin groups: nucleus 5838 (2126-13728), cytoplasm 4177 (2173-9914) total 4543 (2120-10344).

Samples linked to database of patient demographics, tumor characteristics, treatments and outcomes. Correlations were found with survivin expression:

Statistically significant higher survivin levels seen in: lymph nodes vs primary tumors. Higher cytoplasmic levels significantly correlated with undifferentiated tumor grade; and head of the pancreas tumors vs elsewhere.

Disease Free Survival (DFS) was significantly longer in patients with higher than median nuclear survivin expression ($p=0.048$). Patients treated with Gemcitabine had a statistically significant longer DFS ($p=0.0481$), but did not achieve statistical significance for patients treated with radiation ($p=0.094$) or Fluorouracil ($p=0.0698$).

There was a trend to longer Overall Survival in patients with higher than median nuclear survivin expression when treated with Gemcitabine ($p=0.0868$), Fluorouracil ($p=0.0856$) and radiation ($p=0.0862$).

This analysis confirms the importance of subcellular localization in survivin determination. Nuclear survivin significantly correlated with DFS. It highlighted drugs that might work better in those with higher survivin levels. Survivin is a promising biomarker with potential clinical significance in pancreas cancer.

Noninvasive Positive Pressure Ventilation Use in Acute Exacerbation of COPD after Hospitalization for Hypercapnic Respiratory Failure May Decrease 30 Day Readmission

Jason S. Krahnke DO, Jonathan Galli MD, Kartik V. Shenoy MD, John P. Gaughan PhD, A. James Mamary MD, Gerard J. Criner MD

Rationale: COPD patients with hypercapnic respiratory failure have a worse prognosis, are more likely to be admitted to the hospital, and experience faster deterioration of their symptoms. The benefits of using home NIPPV for chronic hypercapnic respiratory failure is unknown and may be important to prevent re-hospitalization and relapse of patient symptoms. Additionally, clinical factors that influence physician ordering of home NIPPV in COPD patients is not well defined.

Methods: We conducted a retrospective, single center, chart review on COPD patients admitted for hypercapnic respiratory failure who received NIPPV during hospitalization. The admissions were over a 3 month period and all patients had a discharge COPD diagnosis ICD code of 496.21. All patients had an admission PaCO₂ >45mmHg. Patients were divided into two groups: those that were discharged with NIPPV versus those not prescribed NIPPV. Data was collected regarding 30-day re-hospitalization rates, length of hospital stay, intubation, ICU admission, mortality, pulmonary function tests, echocardiogram, patient comorbidities, and demographics. All pulmonary function test results were historical data obtained from an electronic database. Data analysis was performed using Student's t-test, Fisher's exact test.

Results: 28 patients (12 female), age 61.4±10 years, BMI 31.5±10.1 kg/m², FEV₁ 34±11.9 %, admission PaCO₂ 58.4±14.7 mmHg.

Conclusion: Patients prescribed home NIPPV had a similar hospital readmission rate compared to patients not prescribed home NIPPV despite differences in COPD disease severity. Physicians were more likely to prescribe home NIPPV to patients with higher PaCO₂ levels.

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Patients with Severe COPD and Diffuse Emphysema on CT Scan have More Sputum Symptoms

Jason S. Krahnke DO, Chandra Dass MD, Sudheer R. Bolla MD, Gerard J. Criner MD, Victor Kim MD

Rationale: In patients with COPD, chronic sputum production has been associated with an increased risk of respiratory infection and an accelerated decline in lung function. The relationship between emphysema phenotype and sputum symptoms has not been well defined.

Methods: We analyzed subjects enrolled in a single-center telemedical COPD management plan where daily symptom reporting using an electronic diary is utilized for the early detection and treatment of acute exacerbations. Patients were followed for up to two years. We selected patients with an FEV₁ <50% and ≥90 days of daily recorded data. Their sputum characteristics were recorded daily using semiquantitative scales and combined to form a Sputum Index. Patients were divided into tertiles based on their average Sputum Index during the observation period. CT scans were obtained within 6 months of enrollment. Percent emphysema (defined as the total percentage of both lungs with attenuation values <-950HU) was quantitated using SLICER (<http://www.slicer.org/>), and a thoracic radiologist performed qualitative assessment to characterize the type, location and severity of emphysema. Differences in patterns of emphysema between tertiles were assessed using Fisher's exact test.

Results: 25 subjects (14 male), age 65±8 years, FEV₁ 24± 6%, 6MWT 221±97 meters.

Conclusion: There was no difference in percent emphysema based on presence and severity of sputum quantity, color, and consistency. However, patients with increased sputum symptoms were more likely to have a diffuse distribution of emphysema and were less likely to have paraseptal emphysema. These findings need further validation in a larger cohort.

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The Effect of Left Ventricular Dysfunction and Chronic Kidney Disease on Fractional Flow Reserve Values

Vladimir Lakhter, Chad Joseph Zack, Ricardo Escarcega Alarcon, Riyaz Bashir, Brian O'Murchu, Michael Brown, Alfred Bove

Background: Fractional flow reserve (FFR) has been successfully used to identify functional significance of intermediate coronary artery lesions. Previous studies have shown that microvascular dysfunction after myocardial infarction causes decreased coronary response to adenosine without affecting the overall validity of FFR. This study sought to test the utility of FFR in the setting of microvascular dysfunction associated with moderate to severe left ventricular (LV) dysfunction with ejection fraction (EF) <35% and stage III-V chronic kidney disease (CKD).

Methods: We retrospectively studied 379 vessels in 316 consecutive patients who underwent coronary angiography and FFR determinations. Lesions chosen for the study were all determined to be intermediate (40-69% stenosis of their diameter) by the individual operator. Two groups of patients were selected based on the presence of LV dysfunction <35% and CKD III-V (eGFR <60). The incidence of finding an abnormal FFR value (defined as FFR <0.8) was then compared to those with a left ventricular ejection fraction > 35% and eGFR > 60, respectively.

Results: Abnormal FFR values were found in 37.3% of patients with EF <35% and in 34.2% for the group with EF >35% (P = 0.645). Mean FFR values were 0.811 ± 0.09 EF <35% vs. 0.825 ± 0.10 EF >35% (P = 0.271) respectively. Analysis of the CKD group showed that 26.9% of patients with eGFR <60 (not on hemodialysis) and 36.2% of patients with GFR >60 had abnormal FFR values (P = 0.132). Patients on hemodialysis had a 39.4% rate of abnormal FFR values that was not statistically significant from the control (P = 0.719). Mean FFR values were 0.82 ± 0.09 eGFR>60 vs. 0.83 ± 0.07 eGFR<60 no HD vs. 0.81 ± 0.09 HD.

Conclusions: These data suggest that the presence of moderate to severe LV dysfunction or CKD III-V does not affect the rate of abnormal FFR values. Therefore, assessment of intermediate lesions with FFR in patients with an EF <35% or eGFR <60 ± hemodialysis should be performed if clinically indicated.

Dynamic Hyperinflation is Reduced After LVRS and is Associated with Improved Functional Outcomes

M.R. Lammi, N. Marchetti, G.J. Criner

Rationale: Although dynamic hyperinflation (DH) is reported to be a major reason for improvement after lung volume reduction surgery (LVRS), it has not been well studied. Also, it is not known if reductions in DH correlate with improvements in exercise performance post-LVRS.

Methods: Fifty-nine consecutive patients who underwent LVRS at Temple University Hospital from 2/2004-2/2011 were analyzed. All patients underwent pre-operative pulmonary rehabilitation. Cardiopulmonary exercise tests (CPETs) were symptom-limited maximal tests using the NETT protocol. Inspiratory capacity was measured every 2 minutes during exercise, and end-expiratory lung volumes (EELV) were calculated. The main measure of DH was EELV/TLC ratio matched at metabolic isotimes, which were determined based on the post-rehabilitation VCO_2 max. Comparisons were also made at isowork, which was the lowest peak workload achieved by the patient on any of their pre- or post-operative CPETs. Differences in DH before and after surgery were compared using ANOVA with repeated measures. Correlations between changes in DH and changes in exercise capacity were performed using Pearson and Spearman rank correlations. Data are reported as mean \pm SD.

Results: Patients (59% female, age 66.5 years) had very severe airflow obstruction (29.5 \pm 8.3% predicted), were hyperinflated (TLC 125 \pm 17% predicted) and gas trapped (199 \pm 41% predicted). There was no change in dynamic hyperinflation after pulmonary rehabilitation. Dynamic hyperinflation, as measured by EELV/TLC @50, 75, and 100% VCO_2 max, was significantly reduced after LVRS at 6, 12, 24, and 36 months ($p < 0.001$ at all time points, Figure 1). Similar significant reductions in DH were also present when EELV/TLC was measured at rest and isowork ($p < 0.001$). There was no significant correlation between post-rehabilitation levels of dynamic hyperinflation and functional outcomes. There were significant correlations between reductions in DH (EELV/TLC @ 50% VCO_2 max) and improvements in 6-minute walk distance (Pearson $r = -0.411$, $p = 0.02$, $n = 33$) and exercise capacity (Watts) on CPET (Spearman $r = -0.536$, $p = 0.001$, $n = 33$) when comparing post-rehabilitation and 6 month post-LVRS values. Similar correlations existed when EELV/TLC was measured at 75% and 100% VCO_2 max.

Conclusions: Dynamic hyperinflation is significantly reduced after LVRS, and this improvement persists for up to 36 months after surgery. Reductions in DH correlate with improved exercise performance following LVRS.

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**Assessment of Internal Medicine Residency Competency in Infectious Diseases
Using an Educational Intervention Tool**

**Brett Laurence MD, Rafik Samuel MD, Robert Bettiker MD,
Thomas Fekete MD**

The focus of resident education is to enhance patient care. The ACGME lists medical knowledge and effective patient care as core competencies. We report the use of an easily accessible on-line didactic curriculum provided to residents of all training levels to improve the practice of infectious diseases. The project initially gauged resident knowledge in core infectious diseases principles via a custom-made multiple choice test. Two unique, National Boards style multiple-choice tests were created using patient vignettes and questions of direct tests of knowledge. All questions were reviewed by Infectious Diseases faculty including seasoned question writers. Internal Medicine residents were randomized to a web-based educational intervention group with bi-weekly modules for 32 weeks or to no additional intervention. Each module required an average of five to ten minutes to read and included a timestamp at completion. At the end of the intervention, all residents were re-challenged with the alternative exam and the results were compared to the American College of Physicians (ACP) In-Training Exam (ITE) scores for further validation. The incoming intern class for the following year was also tested to ensure reproducibility of the exam. Phi coefficients were significant for the majority of questions indicating question reliability. Preliminary results demonstrate that the two tests were comparable with total mean scores among all residents of 62% and 65%. Average performance increased by training level with mean scores of 59%, 65%, and 69% among first, second, and third-year residents, respectively. Final results of the intervention will be available this summer.

**Paraneoplastic Encephalopathy and Ataxia in a Patient with
Small Cell Lung Cancer**

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A 63 year-old male presented with progressive gait imbalance and slurred speech over a period of 2-3 weeks. The neurologic exam was significant for gait imbalance, truncal ataxia, dysmetria and dysarthria. A Brain MRI demonstrated a nonspecific enhancing lesion in the right basal ganglial area in addition to a prominent enhancement along the inferior surface of the cerebellum. A CT scan of the chest showed a large mass lesion involving the right upper lobe with mediastinal extension. A trans-thoracic biopsy was performed and the pathology was compatible with small cell lung cancer with endocrine features. Cerebrospinal fluid (CSF) analysis showed slightly elevated protein but it was not remarkable for any viral encephalitides and cytology was negative for any atypical or malignant cells. Pathology from a brain and dural biopsy afterwards failed to demonstrate any metastatic lesion or any leptomeningeal involvement. Given the history, our impression was a paraneoplastic neurologic syndrome due to the lung cancer. Systemic chemotherapy and plasmapheresis were initiated immediately. However; the patient deteriorated clinically and became encephalopathic.

Paraneoplastic neurological syndromes, by definition, include any neurological dysfunction in a cancer patient in the absence of direct mass effect of the primary tumor or metastatic involvement of the central nervous system. These syndromes are mainly caused by onconeural antibodies produced by tumor cells with some cross reactivity with components of the nervous system. Immunosuppressive therapy and plasmapheresis, in addition to chemotherapy remains the mainstay of treatment, however; the success rate is variable and the overall prognosis is usually grim.

A Population-Based Assessment of Heartburn in Urban Black Americans

**Kian Makipour MD, Amiya Palit MD, Sweetang Shah MD, Vishwas Vanar MD,
Frank K. Friedenberg, MD, MSEpi**

Background: Prevalence data for heartburn in the urban Black American community is lacking. In order to estimate prevalence for this community we analyzed data from an ongoing cohort study in progress at our hospital. Comprehensive interviews allowed for exploration of factors associated with heartburn.

Methods: Complex, stratified sampling design. Survey invitations are hand delivered to random blocks in a single zip code tabulation area. One member per eligible household is invited to complete a computer-based survey. Heartburn was defined as ≥ 3 days/week of symptoms as defined by the Montreal Definition and Classification of GERD. Scaling and weighting factors were utilized to estimate population-level prevalence. Multivariate logistic regression was used to identify independent predictor variables for heartburn.

Results: Enrolled 379 participants corresponding to a weighted sample size of 22,409 (20,888-23,303) citizens. Demographic characteristics of the sample closely matched those of the entire targeted population. Overall, the weighted prevalence of heartburn ≥ 3 times per week was 17.6% (16.4% - 18.8%). Variables independently associated with heartburn were BMI, daily caloric and fat intake, diabetes mellitus (OR=2.95;2.59-3.36), cigarette smoking, and alcohol consumption (OR=2.55;2.25-2.89). Factors inversely associated included illicit drug use and increased physical activity. Waist:hip ratio showed no relationship.

Conclusions: The prevalence of heartburn ≥ 3 times per week is high in the Black American community. Adverse lifestyle behaviors showed particularly important associations. Our study needs to be replicated in other communities with similar demographics.

Predictors of Colorectal Cancer Testing Using the 2009 California Health Inventory Survey

**Alexandra Modiri MD, Kian Makipour MD, Javier Gomez MD, Frank Friedenber
MD, MS (Epi)**

Background and Aims: Many Americans never undergo a colon cancer test. Our aim was to identify key variables associated with undergoing colon cancer testing (CCT) at a population level using the 2009 California Health Inventory Survey.

Methods: Participants in CHIS are recruited by random-digital-dialing every other year. Under/oversampling is performed for pre-specified subject groups to reflect the entire state population. For inferential analysis boot-strapping with replacement was performed on the weighted sample to attain variance estimates at the 95% CI. We restricted our analysis to White, Black, and Hispanic/Latinos aged 50-80 years.

Results: There were 30,857 unique respondents corresponding to a weighted sample of 10.59 million. In the past 5 years, 63.0% had received a CCT; of these, 70.5% underwent colonoscopy. Regression modeling demonstrated that those who underwent testing were more likely to be male (OR=1.06), Black (1.30), have a family member with colon cancer (1.71), and have health insurance (2.71). Progressive levels above the poverty line were associated with receiving a test. The strongest variable was physician recommendation (3.90). For the Hispanic/Latino group, additional variables associated with testing were understanding the physician (2.44) and naturalized citizenship status. Trend analysis, 2001-2009 showed increases in CCT for all racial/ethnic subgroups.

Conclusion: Blacks, males, insured, family history of colon cancer, and those living above the poverty line were most likely to undergo a CCT. For Hispanics/Latino, US-born individuals and those with difficulty understanding their physician are associated with no testing. The strongest variable associated with testing for all groups was physician recommendation.

Gastroparesis Symptoms Correlate with Headache Severity

Alexandra Modiri, MD, Monika Kowalczyk, MD, Henry Parkman, MD

BACKGROUND: Headaches are prevalent in many patients who suffer from gastroparesis. It is known that there is an association between migraine headaches and cyclic vomiting syndrome. Limited information exists about the relationship between headaches and symptoms of gastroparesis.

AIMS: Our aims were to 1) Assess prevalence of headaches in patients who suffer from gastroparesis. 2) Compare headache severity in those with mild and severe gastroparesis. 3) Determine if symptoms of gastroparesis correlate with severity of headache.

METHODS: Newly referred patients with gastroparesis between April 2010 and November 2011 were asked to participate in the study. Patients completed Patient Assessment of Upper Gastrointestinal Disorders Symptoms (PAGI-SYM) and headache questionnaire (HQ) regarding frequency, intensity, and the types of headaches.

RESULTS: 84 patients (42.7±1.6 years old, 82.1% females, 27.3% diabetic) completed the study. Overall, 56 (67%) patients experienced headaches (HA). Among these, 28 (50%) had migraine HA, 7 (12.5%) had tension HA, 3 (5.2%) had cluster HA, and 3 (5.2%) cervicogenic HA. There were no differences between patients with severe gastroparesis (PAGI-SYM≥3) compared to mild gastroparesis (PAGI-SYM<3) with respect to demographic characteristics, etiology of gastroparesis and gastric emptying of solids at 2 hours (53.6%±3.66 vs.47.7%±5.7, p=0.37), and 4 hours (25.5%±2.8 vs. 23.3%±3.5, p=0.63). Patients with severe gastroparesis had more severe headaches compared to those with mild gastroparesis (HQ 2.3±0.09 vs. 1.9±0.13, p=0.02). Gastroparesis symptoms demonstrated a strong correlation with headache severity (PAGI-SYM r=0.45, p=0.0005). PAGI-SYM subscales heartburn/regurgitation, nausea/vomiting, upper abdominal pain, and lower abdominal pain had significant correlation with headache severity (r=0.32, r=0.47, r=0.27, r=0.34, respectively; all p < 0.05). There was no correlation between frequency of nausea or vomiting and frequency of headaches.

CONCLUSION: Headache is present in over two-thirds of patients with gastroparesis. There is a strong correlation between severity of gastroparesis symptoms and severity of headache. Headache and gastroparesis may share a common pathogenesis and treatment of headache may be important in managing gastroparesis patients.

Central Venous Saturation is a Surrogate for Mixed Venous Saturation in Calculating Cardiac Output**Alkhouli M, Morad A, Solaiman A, Bove AA, O'Murchu B****Background:**

Using Pulmonary Artery (PA) catheterization, blood oxygen saturation is a gold standard in calculating cardiac output (CO). However; PA catheter insertion carries a non-negligible risk of major complications and may not be readily available. We propose that calculating CO by using central venous saturation (CVS) instead of PA mixed venous saturation (MVS) is both feasible and accurate. Previous studies exploring this hypothesis were performed with small number of patients and showed inconsistent results.

Methods: The study was conducted at Temple University Hospital in three stages:

Stage I: we reviewed charts of 100 patients who had central venous catheter or PICC (peripherally inserted central line) placement for any indication to determine the most common location for the distal port of a central venous catheter. The location was confirmed by chest X ray in all cases.

Stage II: we retrospectively analyzed data for every patient who had right heart catheterization with simultaneous measurements of pulmonary artery and superior vena cava (SVC) saturations or pulmonary artery and right atrium (RA) saturations between January-June 2011. This analysis established the relationship between MVS and CVS.

Stage III: The correlation found in stage II was applied prospectively to all patients undergoing right heart catheterization with simultaneous PA and SVC saturation measurements between July-Dec 2011. Patients with known cardiac or none-cardiac shunts were excluded.

Results:

Stage I: The majority of central lines tips were found to be either in the distal SVC or at the SVC/RA junction (59% in the SVC, 29% at the SVC/RA junction, 6% in the distal left innominate vein, and 6% in the right atrium)

Stage II: 407 patients who had simultaneous PA/SVC saturation and 162 patients who had simultaneous PA/RA saturation measurements were enrolled. Regression analysis showed a very strong correlation between MVS and CVS if the MVS was measured from the SVC or the RA (R value=0.93, 0.95 respectively) (Figure- left).

The relationship between PA and SVC saturation was found to be $(PA=1.64+ .962*SVC)^*$ with 95% confidence interval. The correlation between PA and SVC saturations was strong irrespective of Hgb, age, gender, weight, or the cardiac output (low, normal or high). Also, the location of the procedure (inpatient or outpatient) had no impact on the correlation.

Stage III: 343 patients undergoing right heart catheterizations were then enrolled prospectively in stage III. The CO was measured by the assumed Fick method using PA saturation, SVC saturation and the estimated PA saturation (calculated using the formula above*)

Mean CO was 5.33 ± 1.23 , 5.31 ± 1.32 , and 5.54 ± 1.46 using measured PA, estimated PA and measured SVC saturations respectively. The regression curve demonstrated a strong correlation between calculated CO using SVC or estimated PA saturations and the calculated CO using the measured PA saturation (the conventional method). (R-value= 0.89, 0.89 respectively) (Figure - right)

Conclusion:

We conclude that in patients who have central venous access, an estimated cardiac output can be easily obtained with good accuracy by using SVC, RA or estimated PA saturations to replace the measured PA saturation in the assumed Fick formula.

Effects of Renal Transplantation on Left Ventricular Remodeling are Dissociated from Hypertension Control

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Background: Patients with chronic kidney disease (CKD) on hemodialysis (HD) frequently have left ventricular hypertrophy (LVH) related to long-standing hypertension (HTN). Diabetes mellitus (DM), obesity and metabolic abnormalities also contribute to LVH. In these patients, renal transplantation is expected to ameliorate HTN control and promote favorable left ventricular (LV) remodeling and LVH regression. However, these salutary mechanisms can be partially offset by adverse hypertensive and metabolic effects of immunosuppressant therapies including calcineurin inhibitors (CNI) and corticosteroids.

Methods: We investigated the effects of renal transplantation on HTN, DM and “paired” (pre vs. post transplant) echocardiographic data relevant to LV remodeling in HD patients with preserved LV systolic function (LVEF > 40%) prior to transplant.

Results: Following renal transplantation, there was no significant change in LA (42±1 to 43±1 mm) or LV dimensions (LVEDD: 50.4±1 to 51.7±1 mm, LVESD: 31.5±1.1 to 32±1 mm), LVEF (50.4±1% to 51.7±1%), LV free wall (12.7±0.1 to 12.4±0.1 mm) or septal thickness (12.8±0.1 to 12.8±0.1 mm) or LV mass (364±19 to 332±19 g). These findings were in contrast with the observed attenuation in HTN (SBP: 143±3 to 132±2.3, DBP: 82±2 to 74±1.8 mmHg, MAP: 102±2 to 93±1.4 mmHg, p<0.001), although patients required an average of 2 HTN medications both before and after transplant. Unlike improvements in HTN, there was significant increase in DM (40% to 65%, p<0.02) and weight gain (82±3 to 87±3 kg, p< 0.004) after transplantation.

Conclusions: In spite of attenuating systemic hypertension, we observed an overall neutral effect of renal transplantation on the LV, rather than a net effect of favorable LV remodeling or LVH regression. It is plausible that metabolic mechanisms independent of hypertension, yet associated with increased prevalence of DM and obesity (perhaps modulated by immunosuppressive drugs) offset the favorable anti-hypertensive effect on LV remodeling following kidney transplantation.

Correlation Between Pulmonary Artery Diameter and Mean Pulmonary Artery Pressure in Patient with Pulmonary Fibrosis

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Rationale: Prior studies have shown that pulmonary artery (PA) diameter as measured on computed tomography (CT) may correlate with the presence of PHTN. We undertook this analysis to evaluate the correlation between PA size and the presence of PHTN in patients with pulmonary fibrosis.

Methods: Patients with pulmonary fibrosis were retrospectively reviewed for demographic data, past medical history, tobacco history, medications, pulmonary function testing, high resolution CT (HRCT), transthoracic echocardiographic data, and right heart catheterization (RHC) data. PHTN was defined as a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg with a pulmonary capillary wedge pressure ≤ 15 mmHg measured on RHC. PA diameter was measured on HRCT for all subjects. We analyzed the relationship between the PA diameter and mPAP using regression analysis and Pearson correlations. In addition, PA diameter measurements were corrected for body surface area and lung volume.

Results: Fifty-nine patients were studied. Fourteen had PHTN. Patients with PHTN had significantly larger PA diameters on HRCT than did those patients without PHTN (3.57 ± 0.37 cm versus 3.17 ± 0.37 cm, $p = 0.001$). There was a significant correlation between PA diameter, as measured on HRCT, and mPAP obtained by RHC ($r^2 = 0.15$, $p = 0.003$). The correlation between PA diameter, corrected for body surface area and corrected for lung volume, and mPAP was not statistically significant.

Conclusion: An increased PA diameter on HRCT should increase one's suspicion for the presence of PHTN in patients with pulmonary fibrosis.

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**Post-Kidney Transplantation Self-Reported Health is Independent of
Allograft Function**

**Sridhar K Reddy, Swati Rao, Tapan Patel, Heather Hammer, Megan Urbanski,
Nicole Sifontis, Serban Constantinescu, Patricio Silva, Iris Lee, Andreas
Karachristos, Manoj Maloo, Ashokkumar Jain, Avrum Gillespie**

Allograft dysfunction, common in an inner city population, may erode both patient satisfaction with transplantation and self-reported health. The purpose of this study is to examine the association between self-reported health, disease burden, treatment satisfaction and clinical markers in an inner city population of kidney transplant recipients.

Fifty-four patients completed a survey specifically designed for this study. The survey data was merged with common laboratory test data and analyzed in SPSS, version 18. The mean age of participants was 56.7 years, males and females were equally represented and mean serum creatinine was 1.65 mg/dl. Respondents were 64.1% African American, 18.9% Hispanic and 17% Caucasian.

Most patients (77.4%) were satisfied with their transplantation experience. Yet, only 49.1% reported that they were not at all burdened by their current kidney disease. Serum creatinine was not correlated with disease burden, self-reported health or satisfaction with treatment. Patients indicating some level of disease burden were more likely to report poorer health (Pearson .395, $p=.003$), less likely to be satisfied with their current treatment (Pearson .475, $p<.001$), and they also had lower serum albumin (Pearson $-.304$, $p=.027$) compared to those who reported no burden. Patients who reported more disease burden had shorter allograft vintage (Pearson $-.468$, $p=.001$). Interestingly, burden-free patients were more likely to be African American or Hispanic (Chi-Square 7.711, $p=0.021$).

In conclusion, post-kidney transplantation self-reported health, disease burden, and satisfaction with treatment are not correlated with allograft function. Patients who reported any kidney disease burden have poorer self-reported general health, less satisfaction with current treatment, shorter allograft vintage, and lower serum albumin. Lastly, African Americans and Hispanics are more likely to be burden-free from their kidney disease.

Symptom Recurrence after Stopping Proton Pump Inhibitors (PPIs) in Patients Undergoing Esophageal pH Monitoring: "The Reverse Therapeutic PPI Trial"

Priyanka Sachdeva, Murali Pathikonda, Abhinav Sankineni, Daniel Cassilly, Martha J. Harrison, Henry P. Parkman

Background: An empiric therapeutic trial with a PPI is recommended for patients with suspected GERD-related symptoms. If symptoms improve, they are often attributable to GERD. If they don't, patients may need further evaluation. Although PPIs are often stopped for esophageal pH monitoring, there is little data on the recurrence of reflux symptoms.

Aim: 1) To determine if recurrence of symptoms after stopping anti-reflux medication suggests GERD is responsible for symptoms.

Methods: 116 patients undergoing 48 hr wireless Bravo® capsule esophageal pH monitoring were prospectively included. All patients were given questionnaires on the day of probe placement inquired about GERD-related symptoms. Patients stopping PPI for ≥ 7 days or H2 blocker for ≥ 2 days were included. Endoscopy reports were reviewed to determine if patients had esophagitis at the time of Bravo® placement.

Results: 100 patients were tested off anti-reflux therapy. Pre-mature detachment of pH capsule occurred in 3 patients. The remaining 97 patients included 30 males, mean age 51 yrs. 10 patients did not complete the questionnaire while 19 were never on medication. Of the remaining 68 patients, most (25 patients) experienced worsening of their symptoms on stopping medication during the test and had an abnormal pH test ($\chi^2(1) = 2.68, p = 0.05$). Of the 15 patients with endoscopic esophagitis, 11 patients had increased acid exposure and 4 had normal acid exposure (25% vs 7.5%, $\chi^2(1) = 5.60, p = 0.018$). Patients who had increased acid exposure had more severe heartburn than those who did not (2.88 ± 0.24 vs $1.68 \pm 0.22, p < 0.001$). Symptom score for heartburn during the day correlated with percent time pH < 4% for both days ($r = 0.41, p < 0.001$).

Conclusions: Worsening of symptoms after stopping PPIs, heartburn severity off medications, and presence of esophagitis is associated with a positive Bravo® study for acid reflux. Thus, factors that suggest GERD after stopping PPI treatment include worsening of heartburn symptoms and evidence of endoscopic esophagitis. Further testing might then include "on therapy" evaluation for persistent symptoms.

Comparison of In Vivo Effects of Insulin on SREBP-1c and INSIG-1/2 in Rat Liver and Human and Rat Adipose Tissue

Sajad Salehi, Peter Cheung, Carol Homko, Weiwei Song, Catherine Loveland-Jones, Senthil Jayarajar, Guenther Boden

We have performed euglycemic-hyperinsulinemic clamps in rats and human subjects to study mechanisms by which insulin regulates de novo lipogenesis (DNL), an important contributor to non-alcoholic fatty liver disease, as well as hepatic and systemic insulin resistance. In rat liver, raising plasma insulin levels (to ~ 1.5 nmo1/1) increased sterol regulated element binding protein-1 (SREBP-1) mRNA ~ 4 fold and the transcriptionally active form of SREBP-1c protein ~ 3 -fold while decreasing insulin stimulated gene 1 and -2 (INSIG-1/2) mRNAs and proteins. In human and rat adipose tissue, hyperinsulinemia increased SREBP-1c mRNA 3-4 fold but decreased the active SREBP-1c protein. In rat adipose tissue INSIG-1/2 mRNA and protein increased, whereas in human adipose tissue only INSIG-2 mRNA increased.

Hyperinsulinemia had no effect on carbohydrate regulated element binding protein (C/EBP β), fatty acid synthase (FAS) and acetyl-CoA carboxylase (ACC) mRNAs.

We conclude, 1) that hyperinsulinemia increased the transcriptionally active form of SREBP-1c protein in the liver but not in adipose tissue, possibly because INSIG-1/2 proteins, which can prevent SREBP-1c activation, decreased in the liver and increased in adipose tissue and 2) that hyperinsulinemia and activation of SREBP-1c may be necessary, but are not sufficient to stimulate DNL.

Gastric Histopathology on Full Thickness Gastric Biopsy Provides Prognostic Information for Treatment Responses to Gastric Electric Stimulation

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Patients with gastroparesis may have dysfunction or paucity of enteric nerves and/or interstitial cells of Cajal (ICC) that may contribute to pathophysiology, symptoms, or treatment outcomes. **AIM:** To evaluate ICCs and neural structures in the enteric nervous system in patients with gastroparesis and to determine if these influence treatment outcomes with gastric electric stimulation (GES). **METHODS:** Full thickness gastric biopsies were obtained from patients with gastroparesis undergoing surgical placement of a gastric electric stimulator. Biopsies were obtained from the anterior gastric body using 35 mm gastrointestinal stapler (Ethicon TA35). Biopsies were placed in formalin, followed by paraffin embedding, sectioning, and immunohistochemical staining for the presence of ganglion cells and ganglions with neuron specific enolase (NSE Monoclonal Antibody; DAKO, Carpinteria, CA) and for ICCs (c-Kit Antibody; Ventana, Tucson, AZ). The number of ganglia and ICCs were counted on 5 consecutive high power fields (400x hpfs). Patients were followed over time and classified as responders or non-responders to GES using the modified Clinical Patient Grading Assessment Scale (CPGAS): 0=no change, +7=completely better. **RESULTS:** 74 patients (average age 38.1±11.7 years; 61 females) with refractory gastroparesis (35 diabetic, 35 idiopathic, 4 post Nissen) underwent implantation of a gastric electric stimulator from July 2010 to November 2011. Of the 66 patients who had full thickness biopsy specimens, 45 improved with GES whereas 19 patients stayed the same or worsened. The number of ICC cell bodies per hpf were decreased in patients who did not improve with GES compared to those who improved: ICCs in outer longitudinal muscle layer [0.82±0.11 vs 1.42±0.15; p=0.002]; inner circular muscle layer [2.20±0.19 vs 2.86±1.49; p=0.028]; and myenteric plexus [0.91±0.16 vs 1.02±0.09; p=0.54]. The CPGAS improvement score at follow-up (average 6.5 months) was correlated with the number of ICC cell bodies in the outer longitudinal muscle layer (r=0.272; p=0.003), the inner circular muscle layer (r=0.210; p=0.021), and myenteric plexus (r=0.181; p=0.057). The number of ganglion cell bodies (4.20±0.69 vs 3.95±0.34) and number of ganglia (1.07±0.14 vs 1.06±0.06) were similar in patients not improving and those that did. Although patients that improved were older (39.7±11.3 vs 33.6±11.3 yrs; p=0.05) and tended to have diabetes (78.8 vs 62.5%; p=0.149), these were not associated with changes in ICCs or neurons. **CONCLUSIONS:** This histologic study of gastroparesis patients with refractory symptoms shows that nonresponders to GES had lower number of ICCs than patients that did respond. In contrast, the neural structures quantitatively appeared similar. Thus, information from gastric full thickness specimens may provide prognostic information on the outcome of GES treatment for gastroparesis.

Slow Esophageal Propagation Velocity: Association with Dysphagia for Solids.

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Background: Spastic disorders of the esophagus, associated with rapid esophageal propagation velocity, are classically associated with dysphagia and/or chest pain. The aim of this study was to characterize patients with slow esophageal propagation velocity (SPV) on high resolution esophageal manometry (HRM).

Methods: A review of patients undergoing HRM was conducted during 1 year study period. Patients with achalasia, aperistalsis and diffuse esophageal spasm were excluded. Patients with CFV ≤ 2.3 cm s⁻¹ were defined as having SPV, while normal propagation velocity (NPV) was defined as ≥ 2.6 cm s⁻¹. A composite isobaric contour of all swallows for each patient was generated to determine composite distal contraction latency (cDL).

Key Results: A total of 650 HRMs were reviewed and 552 met inclusion criteria. 173 patients had SPV and 339 had NPV. There was a greater female predominance in the SPV group compared to NPV (75.7% vs 66.4%, p=0.03). Patients in the SPV group reported more dysphagia for solids (66.3% vs 53.3%; p=0.004) and nausea (68.6% vs 59.0%; p=0.04) than NPV group. Dysphagia for solids was the only symptom significantly associated with SPV group (OR = 2.21, CI = 1.21 – 4.02; p = .01). There was a negative correlation between CFV and cDL, r=-0.494, p<0.001.

Conclusions & Inferences: Patients with SPV have a higher prevalence of dysphagia for solids and nausea when compared to NPV. Dysphagia for solids was the only symptom significantly associated with SPV group. Thus, abnormal esophageal propagation velocity (both slow and rapid) is associated with dysphagia.

Use of the Montreal Global Definition as an Assessment of Quality of Life in Reflux Disease

R. A. Sawaya, A. Macgill, H. P. Parkman, F. K. Friedenberg

According to the Montreal Consensus Group's classification, gastroesophageal reflux disease develops when the reflux of stomach contents causes *troublesome* symptoms and/or complications such as esophagitis. The characteristic gastroesophageal reflux disease symptoms included in this statement are retrosternal burning and regurgitation. *Troublesome* is meant to imply that these symptoms impact on the well-being of affected individuals; in essence, quality of life (QOL). Whether heartburn and regurgitation symptoms would be characterized as more *troublesome* in those with confirmed pathologic acid reflux was determined. A second purpose was to assess how well *troublesome* scores correlated with the results of a validated, disease-specific QOL instrument. Subjects who underwent esophagogastroduodenoscopy (EGD) with 48-hour wireless esophageal pH testing off proton pump inhibitor therapy were interviewed. Esophagitis on EGD or pH < 4.0 for $\geq 4.5\%$ of time over the 2-day period was considered positive for acid reflux. Assessment of how *troublesome* their symptoms of heartburn and regurgitation were made using separate 0–100 visual analog scales (VAS). Subjects were then asked to complete the Quality of Life in Reflux and Dyspepsia (QOLRAD) 25-item questionnaire. Sixty-seven patients (21 males, 46 females) with mean age 47.8 ± 15.6 years were identified. Forty (59.7%) had an EGD or pH study positive for acid reflux. Overall 35/40 (87.5%) complained of either heartburn or regurgitation. There was no difference ($P = 0.80$) in heartburn VAS *troublesome* ratings for those with (54.0 ± 43.9) and without (56.7 ± 37.6) confirmed acid reflux. The same was true for regurgitation VAS *troublesome* ratings ($P = 0.62$). Likewise, mean QOLRAD scores did not differ between those with and without confirmed acid reflux by pH or EGD (4.5 ± 1.7 vs. 4.3 ± 1.7 ; $P = 0.61$). There was a moderately strong inverse correlation between patient self-rated VAS *troublesome* scores for both heartburn and regurgitation with each dimension (emotional distress, sleep disturbance, eating problems, physical/social functioning, and vitality) of the QOLRAD ($P < 0.05$ for all comparisons). In regression analysis, both heartburn and regurgitation *troublesome* ratings were associated with the overall QOLRAD score independent of pH data, frequency of reflux episodes, age, and gender. Use of the term *troublesome* in the Montreal Consensus Group classification is supported by our findings. It correlates well with the results of a validated disease-specific QOL instrument. Use of heartburn and regurgitation VAS may serve as accurate measures of the burden of reflux disease on patients. It is likely that these scales will not have sufficient discriminate value to identify individuals with pathologic acid reflux from those with negative studies.

Factors Associated with a Prolonged Hospital Length of Stay for Patients with Acute Gout

Rebecca Sharim, MD, Marissa Blum, MD MS

OBJECTIVE: Management of gout in the inpatient setting has been poor. This study aimed to describe characteristics of patients hospitalized with acute gout and to determine factors associated with length of stay.

METHODS: Medical records of patients hospitalized with a primary or secondary diagnosis of gout (ICD-9-CM: 274.9) were retrospectively reviewed from 2005-2011. Charts were abstracted for demographic data (age, sex, race), medical conditions, length of stay, and time to rheumatology consultation and diagnosis of gout. Bivariate analyses were performed using Fisher's exact tests, t-tests, and analysis of variance. Multivariable regression testing was performed to evaluate factors associated with length of stay after adjustment.

RESULTS: A total of 205 patients were evaluated, including 50 (24.4%) females and 155 (75.6%) males. 7.8% of patients were white, while 82.9% were black and 7.8% were Latino. 83.9% of patients had carried a prior diagnosis of gout. Co-morbid conditions included cardiac disease (58.5%), neurological disease (21.5%), pulmonary disease (33.2%), diabetes (45.8%), and chronic kidney disease (44.8%). Rheumatology was consulted in 99.5% of admissions (n=204). Multivariable regression of log length of stay revealed a diagnosis of gout made after 24 hours of symptom onset and female sex were significantly associated with an increased length of stay (β -coefficient, p-value [0.46, p=0.000, and -0.313, p=0.016, respectively]).

CONCLUSION: In this retrospective cohort study, a later diagnosis of gouty arthritis and female sex were associated with an increased length of stay after controlling for potential confounders. These data should guide future management of gout to reduce length of hospitalization.

**Clinical Experience with Telavancin for Treatment of Methicillin-Resistant
Staphylococcus aureus (MRSA) Bloodstream Infection**

**Banafsheh Soltani MD, Suyin Chi MD, Brett Laurence MD, Carolyn Fernandes MD,
Byungse Suh MD PhD**

Background: Telavancin is a lipoglycopeptide approved for complicated skin infections. It has potent anti-gram positive activity, including *Staphylococcus aureus*. Its utility in treating staphylococcal bloodstream infections has not been widely reported. We report six cases of MRSA bloodstream infections treated with telavancin.

Methods: Cases were collected from a retrospective chart review from November 2009-July 2011. All patients who received telavancin for >48 hours for MRSA bloodstream infection were included.

Results: In the six cases, age ranged 25-69 years; four were male, all patients were IVDU. Co-morbidities included HCV (3/6) and HBV exposure (2/6). Duration of bacteremia was 8-23 days. Three patients had endocarditis; the others had embolic disease. Telavancin duration was 5-51 days (mean 23). All patients failed vancomycin therapy: three changed to daptomycin then to telavancin and three were changed from vancomycin to telavancin. Of those three, one was changed to daptomycin for thrombocytopenia and AKI on telavancin. All survived to discharge: two were discharged to complete IV therapy; the others completed IV therapy as inpatients. All patients had negative blood cultures at discharge. One patient was lost to follow-up after completing therapy. There were two treatment failures; both readmitted with osteomyelitis: one at 4 weeks; the other at 10 months after completion of therapy. Both grew MRSA from bone and wound cultures but had negative blood cultures. Both were active IVDU.

Conclusions: In an era of increasingly limited therapies for resistant organisms, telavancin may be an option for MRSA blood stream infections not responsive to vancomycin or daptomycin.

Clinical Characteristics of COPD Patients According to the Pattern of Emphysema on High Resolution CT

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Background: High resolution computed tomography (HRCT) has been used to phenotype patients with emphysema. The clinical features of these phenotypes are poorly defined.

Methods: We analyzed data from subjects enrolled in the Genetic Epidemiology of COPD (COPDGene) Study. Subjects with HRCT were characterized according to the pattern of emphysema: bullous (BLE), centrilobular (CLE), paraseptal (PSE), and panlobular (PLE). From the full cohort of 10,279 subjects, 3,094 had a predominant pattern of emphysema on HRCT, as determined by visual assessment by radiologists at each study site, and were selected for analysis.

Results: There were 177, 2217, 618, and 82 subjects in the BLE, CLE, PSE and PLE groups, respectively. PSE and BLE patterns were associated with younger age (PSE 55.4 ± 7.7 , BLE 56.8 ± 8.2 , CLE 61.1 ± 8.9 , PLE 63.9 ± 8.5 years, $p < 0.0001$), male gender (PSE 64.9%, BLE 66.1%, CLE 46.2%, PLE 51.2%, $p < 0.0001$), and African American race (PSE 52.3%, BLE 52.0%, CLE 29.6%, PLE 19.5%, $p < 0.0001$). Subjects with PSE pattern had the lowest pack years (PSE 40.8 ± 21.2 , BLE 44.8 ± 25.9 , CLE 48.3 ± 25.9 , PLE 51.7 ± 27.4 years, $p < 0.0001$) and were more likely to be current smokers (PSE 73.9%, BLE 65.0%, CLE 51.1%, PLE 25.6%, $p < 0.0001$). PLE pattern was associated with the lowest FEV1, followed by CLE, BLE and PSE (Figure 1) and highest percentages of emphysema (PLE 26.1 ± 16.5 , CLE 8.7 ± 10.4 , BLE 6.7 ± 9.7 , PSE 2.2 ± 2.8 percent, $p < 0.0001$) and gas trapping (PLE 53.4 ± 23.7 , CLE 28.2 ± 20.4 , BLE 20.8 ± 20.2 , PSE 14.1 ± 10.3 percent, $p < 0.0001$). PLE pattern was associated with a higher rate of exacerbations (figure 2). Subjects with PLE pattern had the highest BODE index, followed by CLE, BLE and PSE (PLE 3.41 ± 2.59 , CLE 1.75 ± 1.94 , BLE 1.34 ± 1.75 , PSE 0.93 ± 1.32 , $p < 0.0001$). The quality of life scores (St. George Respiratory Questionnaire) and level of dyspnea (modified Medical Research Council scale) were greatest (representing worse quality of life) for PLE, followed by CLE, BLE and PSE.

Conclusions: PSE pattern of emphysema appears to be a milder or earlier form of emphysema, affecting predominately younger African Americans. Panlobular emphysema appears to be a more severe, or a later form of emphysema, associated with a higher degree of airflow obstruction and worse quality of life.

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**Prevalence and Mechanism of Pulmonary Hypertension In Chronic Hemodialysis
by Invasive Measurements**

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Introduction: Among patients undergoing chronic hemodialysis, pulmonary hypertension (PH) (defined as pulmonary artery systolic pressure [PASP] ≥ 35 mmHg) has been observed in up to 48% of patients using echo Doppler technique. Recently, PH has been defined by consensus as a mean PA pressure (MPA) ≥ 25 mmHg. Using this definition of PH, we analyzed data from cardiac catheterization to determine the prevalence and mechanisms of PH among patients undergoing chronic hemodialysis.

Methods: Hemodynamic data from 104 stable patients undergoing cardiac catheterization were retrospectively analyzed. All patients included did not have significant valvular disease, a history of known causes of PH, and were undergoing non-emergent catheterization.

Results: Mean age was 60 ± 12 and 39.1% were women. Eighty nine (86%) were dialyzed through an arteriovenous fistula or graft. Of those patients forty two (47%) had PH (MPA > 25 mmHg). Among patients with PH, MPA was 34 ± 6 compared to 17 ± 5 in patients without PH ($p < 0.001$). Compared to patients without PH, patients with PH had higher wedge pressure (18 ± 6 vs 7 ± 4 mmHg; $p < 0.001$) and higher transpulmonary gradient (15.9 ± 5 vs 10.1 ± 4 ; $p < 0.001$). Cardiac output was not different in patients with compared to without PH (6.6 ± 2 vs 7.1 ± 2 L/min; $p = 0.41$). Pulmonary vascular resistance (PVR) was significantly higher in PH patients (2.6 ± 1.2 vs 1.4 ± 0.8 Wood Units; $p < 0.001$). Systemic vascular resistance was also significantly higher in PH patients (17 ± 5 vs 14 ± 5 Wood Units; $p = 0.047$)

Conclusions: PH is frequently encountered in patients undergoing hemodialysis. PH in this population appears to be due a combination of both pre and post capillary mechanisms and is not associated with increased cardiac output.

COPD Exacerbation is Associated with Substantial Activation of Circulating Inflammatory Monocytes

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Rationale: Little is known regarding the phenotypic characteristics of peripheral blood mononuclear cells (PBMCs) in stable COPD let alone those in acute exacerbation (AECOPD).

Methods: Patients hospitalized for AECOPD were enrolled. Blood samples were collected at hospitalization before systemic steroid administration, and then 2-3 days and 10 weeks later following recovery. PBMCs were isolated and multi-parameter flow cytometric analyses were performed at each time point.

Results: Six patients hospitalized with GOLD stage III - IV who presented in AECOPD were enrolled. Our results show a substantial increase in circulating pro-inflammatory CD14^{Hi}/CD16⁻ monocytes ($p=0.0154$) at the time of exacerbation as compared to stable disease. In addition, these pro-inflammatory CD14^{Hi}/CD16⁻ monocytes are more frequently CCR2 ($p=0.0154$) and CCR5 ($p=0.0465$) positive during exacerbation. Interestingly, these cells also express elevated levels of the scavenger receptor CD163 ($p=0.0154$), a receptor which is known to be critical for the mobilization of activated monocytes to sites of chronic inflammation. In contrast, circulating non-inflammatory "patrolling" CD14^{dim}/CD16⁺ monocytes are present at diminished levels ($p=0.0102$) during exacerbation, and the expression of the "sensing" receptor CX3CR1 is slightly decreased ($p=0.1151$) in this population of cells.

Conclusion: During AECOPD, the phenotypic expression of circulating monocytes shows a substantial increase in the numbers of pro-inflammatory cells, with a significant increase in the numbers of cells which are typically mobilized to sites of tissue damage and inflammation. These results suggest that episodes of exacerbation are accompanied by activation of systemic inflammation that may provide an inflammatory cell reservoir for traffic to the lungs.

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Smoking is a Strong Independent Predictor for Functional Significance of Intermediate Coronary Lesions

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Background: Fractional flow reserve (FFR) is a validated method used for physiologic assessment of functional significance of intermediate coronary artery lesions (40 - 69% stenosis). We sought to determine if the traditional Framingham risk factors known to increase atherosclerotic burden influenced physiologic assessment of intermediate coronary lesions.

Methods: We retrospectively studied all patients in our FFR database from initiation in April 2004 until November 2010. This included 379 vessels in 316 consecutive patients who underwent coronary angiography and FFR determinations. FFR measurements were performed on lesions that were determined to be intermediate by the individual operator. Statistical significance of finding an abnormal FFR value was determined between the groups with and without traditional risk factors for coronary artery disease. Abnormal FFR were defined as having a value of <0.8 .

Results: Of the traditional risk factors only active smoking and women < 55 years of age were found to have an increased likelihood of having an abnormal FFR. In 49.5% of the patients that were current smokers had an abnormal FFR value compared to only 29.6% of non-smokers ($P < 0.001$) (OR 2.2, 1.4 - 3.6, 95% CI). Women < 55 years of age were also more likely to have an abnormal FFR (48.5% vs. 30.3%, $P = 0.05$; OR 2.2, 0.99 - 4.7, 95% CI). However, multivariate regression analysis found that only current smoking was an independent predictor of abnormal FFR in these angiographically intermediate lesions. The gender effect was lost after adjusting for smoking as there was a significantly higher prevalence of current smokers in women < 55 years of age. (60.5% vs. 18.8 % $P = .000002$).

Conclusions: Our results suggest that active smoking was strongly associated with an abnormal FFR in patients undergoing functional evaluation of intermediate coronary lesions. Women younger than 55 years of age also had higher incidence of abnormal FFR, but this was most likely due to higher prevalence of current smokers in this group.

Left Ventricular Noncompaction Under the Guise of Peripartum Cardiomyopathy

Chad J. Zack, Amit Pursnani, Emily Tsai

Left ventricular noncompaction is a rare genetic cardiomyopathy which is anatomically characterized by deep trabeculations in the ventricular wall and multiple deep communicating intertrabecular recesses. This disorder can present with left ventricular systolic dysfunction and heart failure, thromboemboli, arrhythmias, or sudden death.

An 18-year-old woman G1P0 at 36 3/7 weeks pregnant presents to the hospital with a three day history of lower extremity swelling and headache. The patient was found to have significant proteinuria and hypertension and was admitted for severe preeclampsia. After a cesarean section, the patient became progressively short of breath. A chest x-ray taken at that time showed marked pulmonary edema. An echocardiogram was obtained which showed an ejection fraction of 10 to 15% with a dilated left ventricle and atrium. The patient was initially diagnosed with peripartum cardiomyopathy and treated with loop diuretics. On the subsequent day, the patient continued to clinically deteriorate and was intubated and placed on ventilatory support for five days. After extubation, a more thorough history was taken from the patient and her mother. It became apparent that the patient's symptoms had preceded her pregnancy and had been ongoing for the past several months. The images of the transthoracic echocardiogram were re-examined and prominent trabeculations and intertrabecular recesses were found in the left ventricular apex. These trabeculations and recesses composed a greater than two to one ratio when compared with the noncompacted region of the left ventricular myocardium, meeting diagnostic criteria for left ventricular noncompaction. The patient also underwent a cardiac MRI which confirmed the diagnosis of left ventricular noncompaction. The patient was placed on appropriate medical therapy for systolic heart failure and on oral anticoagulation to prevent the development of left ventricular thrombus.

This case illustrates the value of a complete history and the importance of having radiographic imaging interpretations integrated with clinical data. This may lead to an accurate diagnosis of this disease which is important as it carries different risks than peripartum cardiomyopathy and may necessitate additional intervention and medication.

Assessing Impact of Age on Transplant Outcome in Multiple Myeloma. A single institution review

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High dose melphalan followed by an autologous stem cell transplant has been shown to improve progression-free and overall survival in the treatment of multiple myeloma. It is unknown whether the age of a patient receiving an autologous stem cell transplant for multiple myeloma has an impact on overall outcome. A review was performed of patients transplanted at Temple from 2000-2011. Patients who received tandem transplants, allogeneic transplants, or who were transplanted on protocol were excluded. Disease status prior to transplant and disease status 100 days after transplant was recorded for both patients younger and older patients. Data from transplants of 113 patients were analyzed. 32 patients (28%) were age 65 and older, and 81 patients (72%) were younger than age 65. Prior to transplant, 20/32 patients (63%) age 65 and above were in CR or VGPR compared to 23/81 (28%) of patients younger than age 65. At 100-day restaging after transplant, 25/32 patients (78%) age 65 and above achieved a CR or VGPR compared to 43/81 patients (53%) younger than 65. There was one transplant-related death in each age group corresponding to a transplant-related mortality of 3% and 1% in the older and younger age groups, respectively. Based on our analysis, multiple myeloma patients age 65 and above have experienced a consolidative benefit to high-dose therapy followed by autologous SCT compared to younger patients, particularly with respect to transplant-related mortality and disease status 100-days after transplant. Prospective studies evaluating the impact of age should be performed for further investigation.

Under-recognition of Weight Loss in Community-Dwelling Elders

Alyson Dobracki, D.O.

Objectives: Intentional and unintentional weight loss has been shown to produce negative outcomes in morbidity and mortality in older populations. This study sought to identify the scope of under-recognition of weight loss in the elderly.

Design: Retrospective chart review.

Setting: The EMR of 143 PCPs in a community-based health care system.

Participants: The study included 1948 community-dwelling patients age 70 and older who were seen by their PCP during the month of September 2011.

Measurements: Data included age, gender, height and weights, documentation by the PCP of weight loss and the number of missed opportunities to document weight loss. A missed opportunity was defined as an office visit in which weight loss went unrecognized.

Results: Weight loss occurred in 643 patients (33% of total), 237 (37%) were recognized, but 406 (63%) were not. Of those who lost weight, 133 (21%) were recognized at the first visit by 46 different PCPs, and 95 (71%) of these were recognized by the same 18 PCPs. If weight loss was initially unnoticed, there was an average of 2.3 missed opportunities and 4.7 months elapsing before its recognition. There were no universal predictors of weight loss recognition.

Conclusion: In this sample, weight loss in elderly outpatients was unrecognized in the majority of cases. Only a small number of providers identified the majority of weight loss cases. Even with the use of an EMR, most providers did not document the acknowledgement of weight loss. Given the problems associated with weight loss, its under-recognition could potentially have serious consequences in the elderly.

Factors Affecting Physicians' Behaviors and Management of Cardiovascular Risk

Val Rakita, MD

Intro: A significant reduction in cardiovascular disease (CVD) mortality is related to aggressive management of modifiable CVD risk factors. Patients at increased risk for CVD not only benefit from standard pharmacotherapy, but also from physician counseling regarding life-style behavioral changes such as weight loss and exercise.

Methods: This was a secondary analysis of a telemedicine trial among an underserved inner-city and rural population (n=388) with a 10% or greater CVD risk (Framingham 10 year risk score). Subjects were followed for one year and were seen for quarterly assessments, which included evaluation of weight, BP, lipid, and glucose status. At each of the four quarterly visits, subjects were asked if their physician had discussed or made recommendations regarding life-style behaviors, specifically diet/weight loss and exercise.

Results: The average patient age was 61.3, average HgbA1C was 6.56, average cholesterol was 191. The average BMI was 31.7, and the average blood pressure was 135/78. Aside from a trend towards significance in systolic blood pressure (P=.076), only patients' BMI (P<.001) was found to be statistically significant with respect to provision of counseling.

Conclusion: The data indicates that patient weight/BMI is a major factor determining whether or not physicians provide patient counseling regarding weight loss and exercise. Physicians may be missing important opportunities to influence behavior in patients at high risk for CVD by limiting their focus to obese patients.

**Effects of Blood Pressure Self Measurement and Telemedicine Communication
on Physician Prescribing Habits**

Val Rakita, MD

Hypothesis and Purpose: Blood pressure control plays an integral role in the prevention of cardiovascular disease (CVD). Aside from lifestyle changes, pharmacotherapy is the physician's most effective method of lowering blood pressure. We hypothesize that patient involvement in a program centered on frequent self measurement of blood pressures and frequent reporting via telemedicine will bring about changes in physician prescribing habits.

Study Design and Methods: This was a secondary analysis of a telemedicine trial of 241 patients with uncontrolled hypertension, who were randomized to usual care or telemedicine. At the end of the study, patients' anti-hypertensive medications were compared to their baseline therapy.

Results: The average age of patients was 59 ± 13 years; initial average blood pressure was $155.9 \pm 13.7 / 88.9 \pm 11.2$. At baseline, 56.8% of patients were taking between 1-2 anti-hypertensives. There was a statistically significant change in the number of anti-hypertensive medications prescribed to patients in the Telemedicine group (2.20 ± 1.20 to 2.34 ± 1.15 , $p=0.004$), but not in the control group (1.95 ± 1.02 to 1.91 ± 1.21 , $p=0.468$). Multivariate analysis did not show any difference in results with respect to age, ethnicity, education, or income.

Conclusions: Patients in the telemedicine group were more likely to be prescribed more anti-hypertensive medications during the study. This may indicate that patient involvement in self-reporting via telemedicine changes the information available to the physician in such a way that leads to more appropriate and effective pharmacotherapy, better blood pressure control, and overall reduction in cardiovascular risk.