Department of Medicine Temple University School of Medicine



2014 Annual Fellows and Residents Research Symposium

Sol Sherry Awards for Excellence in Research

Wednesday, June 11, 2014

Medical Education and Research Building
Luo Commons

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. 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.

Distinguished Scientist Award and Lecture – 2014

"Platelets, Bleeding, Thrombosis....and More"

A. Koneti Rao, M.D.
Sol Sherry Professor of Medicine
Professor, Sol Sherry Thrombosis Research Center and Pharmacology
Director, Benign Hematology, Hemostasis and Thrombosis
Co-Director, Sol Sherry Thrombosis Research Center
Temple University School of Medicine



A. Koneti Rao, M.D. was born in Madras (Chennai) in India. After obtaining the M.B.B.S. degree in 1973 from the All India Institute of Medical Sciences, New Delhi, he came to Philadelphia and did his medical residency training at the Thomas Jefferson University (1975-1977). He was a fellow in hematology-oncology at Temple University School of Medicine (1977-78) and at the Cardeza Foundation for Hematologic Research of Jefferson University (1978-79). In 1979 he joined the faculty at Temple in the Department of Medicine (Hematology-Oncology) and the Thrombosis Research Center. He was promoted to Associate Professor with tenure in 1984 and became Professor of Medicine in 1991. In 2010, he became the Sol Sherry Professor of Medicine.

Dr. Rao has served in several leadership positions at TUSM – as the Associate Dean for the Temple MD-PhD program from 2001-2005, Director of the Sol Sherry Thrombosis Research Center (2005-2011) and the Chief of Hematology section (2005-2013).

With 190 original publications and invited reviews in major front-line journals including *Blood*, *Proceedings of the National Academy Sciences* (USA), *New England Journal of Medicine*, *Circulation*, *Journal of Thrombosis and Haemostasis*, Dr. Rao has made major contributions in the area of hemostasis and thrombosis. Dr. Rao's major research interest since 1979 has been in the area of platelets, on the molecular mechanisms of inherited disorders of platelet function. He has made major contributions in this

area in elucidating molecular and genetic mechanisms. Dr. Rao's studies have provided the first descriptions of human deficiencies in key platelet signaling proteins, including phospholipase C- $\beta 2$, GTP binding protein $G\alpha q$ and protein kinase C- θ . He was among the first to apply platelet expression profiling to studies into human platelet dysfunction. These studies established that hematopoietic transcription factor RUNX1 regulates platelet/megakaryocyte genes, myosin light chain, platelet factor 4, 12-lipoxygenase and protein kinase C- θ . His research has been continuously supported since the 1980s by grants from NIH and other foundations.

Dr. Rao has had a wide range of research interests, including in antithrombotic therapy, sickle cell disease, and cardiopulmonary bypass. An early collaborative study he spearheaded was on experimental human Rocky Mountain spotted fever. This study, published in the *New England Journal of Medicine*, documented activation of platelets and coagulation in very early disease. He has served on the executive and steering committees of the multicenter NIH-funded Thrombolysis in Myocardial Infarction (TIMI) trial-Phase I in the 1980's, and was one the first investigators to demonstrate systemic fibrinogenolysis with administration of tissue plasminogen activator. Dr. Rao's other studies have focused on the alterations in tissue factor and coagulation mechanisms in diabetes mellitus. In collaboration with Dr. Guenther Boden, these studies have provided major insights regarding activation of coagulation mechanisms in both health non-diabetic subjects and those with diabetes mellitus. He currently serves as a principal investigator together with Dr. Nina Gentile of the large NIH-funded multicenter trial (I-SPOT) on the effects of intensive glucose control on blood coagulation in patients with stroke and diabetes mellitus.

Dr. Rao is a member of several prestigious scientific societies. He is a member of the American Society for Clinical Investigation, and a fellow of the American College of Physicians, Society of Vascular Biology and Medicine, and the Council on Thrombosis (American Heart Association). He was elected to the Interurban Clinical Club in 1997 and served as its President in 2004. He has served on several Committees at Temple and outside, including at the NIH, American Society of Hematology and International Society of Thrombosis and Haemostasis (ISTH).

Dr. Rao has served as the Principal Editor for USA for the journal *Platelets* since 1989, and as guest editor for *Seminars in Thrombosis and Hemostasis* and the *Clinics in Hematology-Oncology*. He has been a member on the editorial boards of the *Journal of Cardiovascular Pharmacology and Therapeutics*, *Vascular Medicine*, *Clinical and Translational Science* and *Hem/Onc Today*, and is a contributing member of the *Faculty of 1000*.

Dr. Rao has received several awards including a NIH Academic Award in Vascular Diseases (1992), the Investigator Recognition Award from the International Society on Thrombosis and Haemostasis (1997) for contributions to the field of hemostasis and thrombosis, the Temple University Faculty Research Award (2001), Distinguished Career Award from the South Asian Society for Atherosclerosis and Thrombosis (2006), the Mario Toppo Distinguished Scientist award from the Association of Scientists of Indian origin in America (2009), and Faculty Member of the Year 2013 in Hematology by F1000 Prime. Dr. Rao has been recognized as an accomplished clinician and listed as one of *Best Doctors in America*® and as one of the *Top Doctors* by the Philadelphia Magazine.

Acknowledgements

The Temple University School of Medicine Department of Medicine gratefully acknowledges and thanks the following corporate exhibitors for their generous support of our program this year:

Platinum Level:







Gold Level:







Fellows and Residents Research Symposium Wednesday, June 11, 2014 Medical Education and Research Building

12:00 – 1:45 PM	Luncheon, Poster Viewing and Poster Discussions (Luo Commons)
2:00 – 5:30 PM	Oral Presentations
	Fellows – Room 217
	Residents – Room 219
5:45 PM	Distinguished Scientist Award and Lecture – 2014 (Room 217)
	"Platelets, Bleeding, Thrombosisand More"
	A. Koneti Rao, M.D.
	Sol Sherry Professor of Medicine
	Professor, Sol Sherry Thrombosis Research Center and Pharmacology
	Director, Benign Hematology, Hemostasis and Thrombosis
	Co-Director, Sol Sherry Thrombosis Research Center
	Temple University School of Medicine
6:15 PM	Presentation of Awards to Fellows and Residents (Room 217)
	Reception (Luo Commons)

<u>Poster Presentations – Fellows</u>

Chair: Nathanial Marchetti Judges: Marissa Blum, Wissam Chatila, David Essex, Avrum Gillespie, Sharon Herring, Victor Kim

Rebakah Sumalini Abel Boenerjous MD (Geriatrics) <i>How Well Are We Communicating?</i>	Poster Board #1 Abstract #2
Rebakah Sumalini Abel Boenerjous MD (Geriatrics) Elderly Nursing Home Resident with Head Drop	Poster Board #2 Abstract #3
Jason Krahnke D.O. (Pulmonary) FEF25-75 and FEV3/FVC as Predictors of Gas Trapping and Early Emphysema in Smokers without COPD	Poster Board #3 Abstract #11
Jason Krahnke D.O. (Pulmonary) Clinical Factors Associated with Frequent Exacerbations in Mild to Moderate COPD	Poster Board #4 Abstract #12
Jason Krahnke D.O. (Pulmonary) Residual Volume >225% Predicted is Associated with Higher Mortality after LVRS in the NETT Cohort	Poster Board #5 Abstract #13
Jason Krahnke D.O. (Pulmonary) Peripheral Neutrophil and Lymphocyte Counts as Biomarkers for Severity and Structural Lung Parenchymal COPD Phenotype	Poster Board #6 Abstract #14
Jason Krahnke D.O. (Pulmonary) Clinical Predictors of Severe Exacerbations in Patients with COPD	Poster Board #7 Abstract #15
Tatiana Gandrabura (Endocrinology) Hyperparathyroidism Unmasked: Acute Hypercalcemia from Immobilization and Unrecognized Normocalcemic Primary Hyperparathyroidism	Poster Board #8 Abstract #7
Diana Kolman (Pulmonary) Higher Prevalence of Gastroesophageal Reflux and Esophageal Dysmotility in IPF Patients Compared to COPD Patients	Poster Board #9 Abstract #9
Jennifer M. Matro, MD (Hematology/Oncology) Correlation of PET/CT and CT RECIST Response in GIST Patients with PDGFRA D842V Gene Mutations Treated with Crenolanib	Poster Board #10 Abstract #17
Dercio Mendonca (Pulmonary) Predictors for Lung Structural and Functional Abnormalities on	Poster Board #11 Abstract #18

CT Chest in Smokers Without Airflow Obstruction

Frederick Ramos MD (Pulmonary)

Computed Tomography Measurement of Small Pulmonary Vessels

in Chronic Obstructive Pulmonary Disease

Frederick Ramos MD (Pulmonary)

Hyperinflated and Gas Trapped COPD Patients: Emphysema

Versus Non-emphysema Predominant

Pankaj Sharda MBBS, MD (Endocrinology)

Effect of Pioglitazone on Severe Hypertriglyceridemia in Patients

with Diabetes: A Case Series

Kiley K. Walp, D.O. (Gastroenterology)

Liquid Nitrogen Spray Cryotherapy can be Used Safely in Retroflexion for Treatment of Lesions at the Esophagogastric

Junction and Gastric Cardia

Poster Board #12 Abstract #22

Poster Board #13 Abstract #24

Poster Board #14 Abstract #26

Poster Board #15

Abstract #29

<u>Poster Presentations – Residents</u>

Chair: Nathanial Marchetti
Judges: Susan Fisher, Nathanial Marchetti, Anuradha Paranjape,
Ajay Rao, Daniel Rubin, Howard Rudnick

Justin M. Darrah, MD (Internal Medicine) Obtaining Patient Feedback in the Patient-Centered Medical Home (PCMH)	Poster Board #16 Abstract #36
Andrew Friedman M.D. (Internal Medicine) Appropriateness of Brain MRIs at Temple University Hospital Based on the ACR Appropriateness Guidelines and Its Impact on Management	Poster Board #17 Abstract #38
Jonathan Galli (Pulmonary) Quantitative CT Patterns in Smokers without Airflow Obstruction and Their Effect on Severe Respiratory Exacerbations	Poster Board #18 Abstract #40
Harish Jarrett (Cardiology) An Unusual Cause of Acute Coronary Syndrome	Poster Board #19 Abstract #43
Harish Jarrett (Cardiology) Contemporary National Trends and Outcomes of Catheter Directed Thrombolysis in Patients with Proximal Lower Extremity Deep Vein Thrombosis	Poster Board #20 Abstract #44
Harish Jarrett (Cardiology) Atherosclerotic Cardiovascular Disease in African-Americans: More than LDL Lowering	Poster Board #21 Abstract #45
Asad Javed MD (Internal Medicine) A Paradox of Anticoagulation: Warfarin Induced Skin Necrosis	Poster Board #22 Abstract #46
Michael Lashner D.O. (Cardiology) Contemporary National Trends and Outcomes of Inferior Vena Cava Filter Placement in High Bleeding Risk Patients with Proximal Lower Extremity Deep Vein Thrombosis	Poster Board #23 Abstract #47
Meredith McFarland, MD (Cardiology/Endocrinology) A Case of Coronary Vasospasm Caused by Undiagnosed Hyperthyroidism	Poster Board #24 Abstract #49
Anand Patel, M.D. (Hematology/Oncology) Severe Thrombocytopenia Due to Macrophage Activation Syndromeborne from Adult Onset Still's Disease	Poster Board #25 Abstract #51

Poster Board #26

Abstract #53

Val Rakita, MD (Cardiology)

Behavioral Locus of Control and Reduction of Cardiovascular Risk

Jennifer Y. So, M.D. (Pulmonary)

COPD Patients with Greater Rate of Change in Daily Peak Expiratory Flow Have More Disease Instability

Poster Board #28 Abstract #56

Poster Board #27

Abstract #55

 $Lexi\ Zavitsanos,\ M.D.\ (Infectious\ Diseases)$

Strongyloides Hyperinfection Mimicking Endocarditis

<u>Poster Presentations – Medical Students</u>

Chair: Nathanial Marchetti
Judges: Susan Fisher, Nathanial Marchetti, Anuradha Paranjape,
Ajay Rao, Daniel Rubin, Howard Rudnick

Katherine Selman (Infectious Diseases)

Medical Students Learning Global Health through Service: Temple Emergency Action Corps Service Trip – Managua, Nicaragua, 2014

Poster Board #30

Poster Board #29

Abstract #57

Abstract #58

Daniel H. Shu, B.A., M.A. (Rheumatology)

Spontaneous MAVS Aggregation may Contribute to Excessive Type I Interferon in SLE Patients

Oral Presentations – Fellows Chair: A. Koneti Rao, M.D.

Judges: Peter Axelrod, Philip Cohen, Thomas Fekete, Crystal Gadegbeku, Daohai Yu

2:00 PM	Aaron Czysz, MD (Pulmonary) Predictors of COPD Stability	
2:15 PM	Rushang Patel, MD (Hematology/Oncology) A Long-term follow up Report on Autologous Stem Cell Transplantation for Mantle Cell Lymphoma – A Single Institution Experiences	Abstract #20
2:30 PM	Paul Chang, MD (Gastroenterology) Hospital Mortality in Cirrhotics Admitted with Esophageal Variceal Bleeding is Lower in the Community Setting	Abstract #4
2:45 PM	Mohamad Alkhouli, MD (Cardiology) National Trends and Comparative Outcomes of Catheter-Directed Thrombolysis Plus Anticoagulation Versus Anticoagulation Alone in the Treatment of Inferior Vena Cava Deep Vein Thrombosis	Abstract #1
3:00 PM	Diana Kolman (Pulmonary) Comparative Efficacy and Side Effects of Alemtuzumab Versus Basiliximab as Induction Agent in Lung Transplantation	Abstract #10
3:15 PM	Florence Momplaisir, MD MSHP (Infectious Diseases) Time of HIV Diagnosis and Engagement in Prenatal Care Impact Outcomes in Pregnant Women with HIV	Abstract #19
3:30 PM	Adam C. Ehrlich, MD, MPH (Gastroenterology) Measurement of Fractional Exhaled Nitric Oxide (FeNO) Does Not Predict Presence of Inflammatory Bowel Disease or Disease Activity	Abstract #6
3:45 PM	Giuseppe Guglielmello DO (Pulmonary) Using FEF25-75/FVC to Predict Early Lung Disease in Smokers without Airflow Obstruction	Abstract #8
4:00 PM	Varsha Pathak, MD (Nephrology) Validation of Molecular Observations Related to ADMA Dysregulation	Abstract #21
4:15 PM	Zubair Malik MD (Gastroenterology) EndoFLIP as a Novel Way to Evaluate the Pyloric Sphincter in Patients with Gastroparesis	Abstract #16

4:30 PM	Frederick Ramos MD (Pulmonary) Gastroesophageal Reflux Disease and Chronic Obstructive Pulmonary Disease in SPIROMICS	Abstract #23
4:45 PM	Rajeeve Subbiah, M.D. (Cardiology) Findings of Pulmonary Hypertension in ESRD Patients	Abstract #27
5:00 PM	Abhinav Sankineni MD, MPH (Gastroenterology) Practice Patterns in the Treatment of Achalasia: Results of a Nationwide Survey	Abstract #25
5:15 PM	Zael Vazquez, M.D. (Pulmonary) The Implementation of the Lung Allocation Score Improves Post-transplant Survival in Patients with Idiopathic Pulmonary Fibrosis	Abstract #28

$\underline{Oral\ Presentations-Residents}$

Chair: Henry Parkman, M.D.

Judges: Roberto Caricchio, Frank Friedenberg, Oleh Haluska,
Brian O'Murchu, Rafik Samuel

2:00 PM	Jeydith Gutierrez Perez, MD (Cardiology) A Case of Unrecognized May-Thurner Syndrome Leading to Recurrent Pulmonary Embolism	Abstract #52
2:15 PM	Lucy Salieb, M.D. (Gastroenterology/Pulmonary) Gastroesophageal Reflux and Dysmotility in End Stage Lung Disease Patients	Abstract #54
2:30 PM	Harish Jarrett, MBChB (Cardiology) Comparative Outcomes of Catheter Directed Thrombolysis Plus Anticoagulation Versus Anticoagulation Alone in the Treatment of Proximal Deep Vein Thrombosis in Patients with Chronic Kidney Disease	Abstract #42
2:45 PM	Natalya Iorio, MD (Gastroenterology) Post-Traumatic Stress Disorder is Strongly Associated with IBS in African Americans	Abstract #41
3:00 PM	Jasmin Desai, MD (Hematology/Oncology) High Baseline Joint Pain in Women Starting Aromatase Inhibitors for Breast Cancer	Abstract #37
3:15 PM	David Berman/Jonathan Gotfried (Internal Medicine) Identifying High Risk Patients and Reducing Emergency Room Visits and Hospitalizations: Experience in a Resident Clinic	Abstract #34
3:30 PM	Yuka Furuya, MD (Pulmonary) The Impact of Alemtuzumab and Basiliximab Induction on Graft and Recipient Survival in Orthotopic Lung Transplantation	Abstract #39
3:45 PM	Ovais Ahmed, M.D. (Gastroenterology) The Prevalence of Dental Disease in Inflammatory Bowel Disease	Abstract #30
4:00 PM	Meredith McFarland, MD (Endocrinology/Cardiology) The Effect of Thyroid Function on the Acute Heart Failure Exacerbation: A Retrospective Study	Abstract #48
4:15 PM	David Verbofsky, MD (Internal Medicine) Development of a Risk Prediction Tool for Likelihood of Missed Appointments	Abstract #33

4:30 PM	Peter Barth, MD (Hematology/Oncology) A Review of Interventional Clinical Trials (CTs) in Renal Cell Carcinoma (RCC): A Status Report from the ClinicalTrials.gov Website	Abstract #32
4:45 PM	Saraswathi Arasu, D.O. (Gastroenterology) Impaired Gastric Accommodation in Gastroparesis: Relationship to Gastroparesis Cardinal Symptom Index (GCSI) Severity Scores	Abstract #31
5:00 PM	Yevgeniy Brailovsky (Cardiology) Contemporary National Trends and Outcomes of Inferior Vena Cava Filter Placement in Cancer Patients with Proximal Lower Extremity Deep Vein Thrombosis	Abstract #35
5:15 PM	Scott M. Norberg, D.O. (Hematology/Oncology) Spontaneous Tumor Lysis Syndrome in Renal Cell Carcinoma - A Case Report	Abstract #50

National Trends and Comparative Outcomes of Catheter-Directed Thrombolysis Plus Anticoagulation Versus Anticoagulation Alone in the Treatment of Inferior Vena Cava Deep Vein Thrombosis

Mohamad Alkhouli, MD, Chad J. Zack, MD, Huaqing Zhao, PhD, Grayson Wheatley MD, Eric Choi, MD, Riyaz Bashir, MD

Background: The contemporary nationwide practice in the management of patients with inferior vena cava thrombosis and the safety of catheter-directed thrombolysis in these patients are unknown.

Methods: We used the Nationwide Inpatient sample database (2005 to 2011) to identify patients with a principal discharge diagnosis of inferior vena cava (IVC) thrombosis (ICD-9-CM 453.2). Among 2,674 patients admitted with IVC thrombosis, 26.9%(718) underwent catheter directed thrombolysis (CDT). We evaluated national trends in the utilization of CDT and performed comparative outcomes analysis using risk adjusted propensity scores between patients treated with CDT+anticoagulation (598 patients) versus anticoagulation alone (598 patients).

Results: The national CDT utilization rates increased from 16.0% in 2005 to 34.7% in 2011(p<0.001). The groups that were less likely to be treated with thrombolysis included females (22.4% versus 31.7%; p <0.001), and African-Americans (21.2% versus 29.1%; p<0.001). We observed a non-significant trend towards a higher In-hospital mortality in the CDT group compared with the anticoagulation alone group (2.5% versus 1.2%; p= 0.09). Also the CDT group had significantly higher rates of blood transfusion, pulmonary embolism, intracranial bleeding, and acute renal failure. The length-of-stay and hospital charges were also significantly higher in the CDT group.

Conclusions: In this nationwide observational study we found increasing utilization of CDT in the treatment of IVC thrombosis between 2005-2011. There was significantly higher morbidity and a trend towards higher In-hospital mortality in the CDT group compared with the anticoagulation alone group. CDT was associated with higher cost and resource utilization.

How Well Are We Communicating?

Rebakah S Abel Boenerjous MD, William Zirker MD, Suhas Masilamani A.B MS, DNB

Objective of the survey: To evaluate communications and flow of the information that medical specialists receive when consulting on a nursing home patient.

Method: A 12 question survey was sent out weekly to approximately 592 consulting physicians at Crozer Keystone Health System and Temple University Health System through Survey monkey from February-March 2014 evaluating flow of information and communication involved in the referral process.

Results: The survey showed that all 55 respondents saw some nursing home patients in their office practice but 90% of them never go to a nursing home to do consults.70% said they rarely or sometimes receive a clear referral question, 82% said that the patients come with a medication list most or all the time. Over 70 % of consultants said that patients rarely or only sometimes come with other pertinent clinical information like labs, imaging reports or physician progress notes.38% indicated that the patient or care giver rarely knew the reason for the visit. Only 25% of consultants contacted the referring physician to get the information they needed to do the consult. The most common form of communication back to the referring physicians; 67% was via handwritten notes.

Conclusion: The flow of information between consultants and nursing home physicians is often not good and there is a lot of room for improvement in the process.

Elderly Nursing Home Resident With Head Drop

Rebakah S Abel Boenerjous MD, William Zirker MD, Suhas Masilamani A.B MS,DNB

Introduction: Onset of pain, functional decline and musculoskeletal problems can present a diagnostic challenge in demented nursing home residents.

Case: We report the case of an 87 yr old African American female nursing home resident who was hospitalized for pneumonia and after returning to the nursing home was noted to be, unable to hold her head up .She could provide no history and was constantly moaning in pain. She was no longer able to feed herself without assistance and was losing weight. Her past medical history included Alzheimer's dementia with psychosis, hypertension, atrial fibrillation, rheumatoid arthritis. Her medications were diovan, risperidone, diltiazem, acetaminophen, and oxycodone. On exam she had normal vital signs and was alert and oriented to her name only. Her head was down with her chin resting on her chest; she could not lift it and had restricted range of motion. Neurologically no other focal deficits were noted. A recent CAT scan head showed no acute stroke. Cervical spine x-rays and CT scan did not show any acute abnormality. After reviewing all available data including medications we thought that her head drop could be late onset dystonia secondary to risperidone use. Risperidone was discontinued, the patient was given a soft neck collar and was treated with benztropine. Over the course of 1 to 2 weeks she was able to hold her head up, feed herself and communicate more clearly.

Discussion: This case illustrates an uncommon side effect, late onset dystonia from risperidone. Dystonia is defined as a slow, sustained muscular contraction or spasm. Drug induced dystonia's are classified as either acute and late onset. Acute dystonia's are more common and develop hours to days after initiation or increase in dose of an antipsychotic. Late onset dystonia's usually appear after months to years of antipsychotic administration. Atypical antipsychotic like risperidone are less likely to cause dystonia when compared to typical antipsychotics.

Conclusion: Health care providers need to be aware of late onset side effects of atypical antipsychotics. Even though its uncommon it's important to consider drug induced dystonia's in evaluating the patients with head drop and neck pain.

Hospital Mortality in Cirrhotics Admitted With Esophageal Variceal Bleeding is Lower in the Community Setting

Paul Chang, MD, Adam C. Ehrlich, MD, MPH, Joseph Yoo, Frank Friedenberg, MD, MS(Epi)

Background: Esophageal variceal bleeding is a leading cause of mortality in patients with cirrhosis. Prior studies have indicated the in-hospital mortality to be 15-20%. The mortality rate has also decreased over time. To investigate the mortality rate for patients admitted to community hospitals with esophageal variceal bleeding.

Methods: Data from the Nationwide Inpatient Sample (NIS) was examined from 2008-2011. The NIS is an inpatient care database containing data from approximately 8 million stays, from 1000 hospitals sampled to approximate a 20 percent stratified sample of US community hospitals. After appropriate sample weighting, patients were identified using the ICD-9 code 456.0 (representing esophageal varices with bleeding). These patient records were examined for in-hospital mortality and if patients had endoscopy during admission. A multivariate analysis was performed using SPSS adjusting for age, sex, and race effect on mortality.

Results: A total of 34,911 patients met a diagnosis of 456.0. The average age was 57 ± 14 years, 23,430 (68%) were male, 29,097 (83.3%) had an endoscopy, and 3,135 (9%) died during hospitalization. The majority of patients, 90.5%, had an endoscopy during the first 4 days of admission. Mean time to EGD was 1 day after admission (IQR: 0-2 days after admission). Average length of stay was a mean of 6.13 ± 8.2 days. Mortality rates decreased the longer the time to EGD (Table 1), with mortality rates of 7.9%, 4.9%, 3.7%, and 2.2% at day of admission, 1 day after admission, 2 days after admission, and 3 days after admission respectively. In multivariate analysis, Hispanic patients had a higher mortality after adjusting for age and sex compared to Caucasian patients (OR=1.3, 95% Cl=1.1-1.4). African Americans had an odds ratio of 2.2 with a lower 95% confidence interval of 1.9 adjusted for age, and sex compared to whites. Hispanics had a 1.3 odds ratio with a lower 95% confidence interval of 1.1.

Conclusions: Despite advancements in endoscopic treatment and availability of endoscopic and medical treatment for esophageal variceal bleeding, mortality remains high. In this analysis of patients with variceal bleeding in the community hospital setting, the in-hospital mortality is 9%, far lower than previous reports. Additionally, patients with earlier endoscopy had higher mortality rates. These results may be due to more severely ill patients getting their endoscopy earlier, the lower mortality rates seen in this study may be due to prior studies looking at patients at referral centers whereas this study targeted community hospitals. Minorities (Hispanics and African Americans) seem to have a higher rate of in-hospital mortality compared to Caucasians when admitted for variceal bleeding. It is unclear why this disparity exists and further study is indicated to determine if this finding is related to access to care versus overall worse disease.

Predictors of COPD Stability

A Czysz, MD, H Zhao, F J Martinez, G J Criner, MD & the SPIROMICS Research Group

Purpose: SPIROMICS is a prospective cohort study that will enroll approximately 3200 subjects across four strata (Never smokers, Smokers without COPD, Mild/Moderate COPD, and Severe COPD) with the goals of identifying new COPD subgroups and intermediate markers of disease progression. Various demographic, physiologic and scoring systems predict mortality in COPD, including a history of acute exacerbations of COPD (AECOPD). It is unclear why certain patients of similar disease severity are more symptomatic and unstable, with more AECOPD, thereby predicting higher mortality.

Methods: 1648 subjects from SPIROMICS strata 2, 3 and 4 were characterized with various demographic, physiologic, radiographic, biologic and symptomatic indices. 1298 subjects had inspiratory and 1301 had expiratory CT scans. Emphysema and gas trapping burden were correlated to symptoms via the previously validated MRC and SGRQ scores. Two groups of no vs. 1+ AECOPD (total and severe) in the prior year were compared using Chi-square, t-test and Pearson correlations.

Results: Preliminary results of data available at the time of analysis showed 1648 subjects were 54% male, 78% white, age 64.4+/-8.9, had FEV1% 74.5+/-25.9%, emphysema 7.9+/-10.1% with gas trapping 4.0+/-7.4%, BMI 27.6+/-5.1, MRC 1.0+/-1.0, SGRQ 31.4+/-19.9, with cardiac disease in 35% and psychiatric disease in 68%. Women had 28% total AECOPD vs. 19% in men; however severe AECOPD was similar (11% vs. 9%). Total AECOPD occurred in 31% of African Americans, but only 21% of white and 22% of others. Total AECOPD occurred in age 63 vs. 65 years, FEV1% 61% vs. 79%, 6MWT 377m vs. 420m, BODE 2.2 vs. 1.1, total emphysema 11% vs. 7%, gas trapping 34% vs. 23%, MRC 0.9+/-1.4 and SGRQ 46 vs. 27. MRC, SGRQ Activity and Total scores correlated with total emphysema and gas trapping of 0.33 & 0.33, 0.41 & 0.39, and 0.34 & 0.34, respectively.

Summary: Women have more total, but similar severe AECOPD as men. African Americans have more AECOPD. AECOPD subjects had worse FEV1%, lower 6MWT distance, were slightly younger, had more anxiety, depression and angina, worse BODE, MRC and SGRQ, more emphysema and more gas trapping. Total emphysema and gas trapping correlate moderately with MRC and SGRQ Activity and Total scores.

Conclusions: COPD subjects vary greatly by phenotype and certain groups have more AECOPD. Further prospective analysis of this population and subdivision into GOLD staging may help elucidate those specific characteristics driving frequent AECOPD from more stable subjects. Emphysema and gas trapping correlate with symptom burden.

Measurement of Fractional Exhaled Nitric Oxide (FeNO) Does Not Predict Presence of Inflammatory Bowel Disease or Disease Activity

Adam C. Ehrlich, MD, MPH; Erkanda Ikonomi, MD; Vikram Bathula, MD; Ovais Ahmed, MD; Robin Rothstein, MD; Frank Friedenberg, MD, MS(Epi)

Purpose: Active inflammation in IBD is frequently estimated through readily available markers such as C-reactive protein, erythrocyte sedimentation rate, and the leukocyte and platelet count. Small studies have shown that levels of exhaled nitric oxide levels are elevated in patients with IBD and correlate with disease. Our purpose was to use data from the National Health and Nutrition Examination Survey (NHANES) to identify whether a relationship indeed exists between fractional exhaled nitric oxide (FeNO), presence of IBD, and IBD severity.

Methods: Two years of NHANES data were combined (2009-2010) for analysis. After weighting using the Complex Samples module of SPSS 20.0, the age range was restricted to 18-65 y. Subjects were self-identified as having Crohn's Disease (CD) or Ulcerative Colitis (UC). We created a 4-point disease activity index using variable available from the database and assigned one point for each of the following: iron deficiency, hypoalbuminemia, elevated CRP, and diarrhea. A random sample of control subjects in 2:1 ratio was identified. FeNO was measured using the Aerocrine NIOX MINO® analyzer (Aerocrine AB, Sweden). The NHANES protocol required two valid FeNO measurements that were reproducible. Overall, 89.1% of all subjects underwent FeNO testing. Normal FeNO levels are ≤ 25 ppb.

Results: After exclusions, the weighted sample contained 1,603,958 patients with IBD and 3,655,294 control patients. Mean FeNO levels in those with IBD and those without were within the normal range. FeNO had a poor ability to predict the presence of IBD with an area under the receiver-operator curve of 0.49 (95% CI=0.38-0.59) compared to CRP (AUROC=0.62; 95% CI=0.51-0.72). Of those patients with IBD, FeNO was elevated in patients with diarrhea (30 ppb vs. 16 ppb in patients without diarrhea, p<0.01); however, patients with abnormal labs had lower FeNO (all p<0.01).

Conclusions: FeNO levels in subjects with and without IBD were, on average, within the normal range. Although IBD patients with diarrhea had higher FeNO, this did not hold when comparing IBD patients with abnormal labs. FeNO does not appear to be a good standalone test for predicting IBD or predicting disease activity in already established patients.

Hyperparathyroidism Unmasked: Acute Hypercalcemia From Immobilization and Unrecognized Normocalcemic Primary Hyperparathyroidism

Tatiana Gandrabura, MD; Charis Gn; Cherie Vaz, MD

Introduction: Immoblization is a known cause of hypercalcemia (1) and has been implicated in the etiology of hyperparathyroidism by mechanisms which are not fully understood (2).

We describe a case of acute hypercalcemia diagnosed during 3 weeks hospitalization in a patient with an underlying normocalcemic primary hyperparathyroidism.

Case: A 65 y/o female was admitted with T5-T6 fractures of spine after a fall from syncope due to complete heart block. She had a diagnosis of osteoporosis at L4 and was taking weekly alendronate since 2011. She had no prior history of elevated calcium, and was ambulatory prior to hospitalization. She received permanent pacemaker but had a complicated hospital course requiring mechanical ventilation.

At 3 weeks of hospitalization, she was found to have serum calcium of 11.0 mg/dl, corrected calcium of 12.4 mg/dl, iCa 6.8 mg/dl, iPTH 206 pg/ml,(10-65), creatinine 1.6 mg/dl (eGFR 60), Vit. D 25-OH 17 ng/ml(30-100) ,1,25D2OH 23 pg/ml(18-72), Phosphorous 3.1 mg/dl, and TSH of 2. Despite receiving IV hydration (100 ml/h) for 4 days, her corrected calcium rose to 13.5mg/dl. Next, patient received IV pamidronate 60 mg, and calcitonin 250IU x 4 doses in addition to IV fluids. Her corrected calcium improved from 13.5 mg/dl to 10.8 mg/dl over the next 24 hours. A repeat PTH was 216 pg/ml. Calcium remained within normal range during the rest of hospitalization and at the time of discharge. Thyroid ultrasound showed a solid nodule in the right thyroid lobe 10x9x9 mm. A parathyroid sestamibi scan was negative for any adenoma.

Discussion: This case discusses an acute unmasking of normocalcemic hyperparathyroidism following a short period of relative immobilization. Immobilization causes uncoupling of bone turnover with a reduction in bone formation and increase in bone resorption (3) with a rapid efflux of calcium from bone into the circulation causing hypercalcemia with appropriate suppression of PTH. Persistent elevation of PTH despite hypercalcemia favored a diagnosis of underlying primary hyperparathyroidism. Immobilization possibly contributed to patient's hypercalcemia in the acute setting. One should be vigilant for acute hypercalcemia in an immobilized patient with normocalcemic hyperparathyroidism.

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Using FEF₂₅₋₇₅/FVC to Predict Early Lung Disease in Smokers Without Airflow Obstruction

Guglielmello G, Kim V, Zhao H, Criner GJ

Rationale: Small airway narrowing is associated with dyspnea and precedes the development of airflow obstruction in COPD. Dysanapsis represents variance in proportional dimensions between the small airways and lung parenchyma. A lower FEF₂₅₋₇₅ /FVC ratio may indicate the presence of dysanapsis. We aimed to characterize subjects with a lower FEF₂₅₋₇₅/FVC and hypothesized that subjects with a lower FEF₂₅₋₇₅/FVC may be predisposed to hyperinflation and gas trapping.

<u>Methods</u>: A retrospective investigation of the COPDGene data set was performed in 4,040 subjects without evidence of obstruction by ATS criteria. Utilizing 79 non-smoking subjects as controls, a mean FEF₂₅₋₇₅ /FVC of 0.70 was determined to pinpoint a cutoff value for this parameter. Subjects were then placed in two groups of either high or low FEF₂₅₋₇₅ /FVC based on the mean. Statistical analysis was performed using student's t-test and Chi–square test to determine differences in gender, race, age, associated risk factors and computed tomography (CT) indices of gas trapping and emphysema.

<u>Results</u>: Subjects with a lower FEF_{25-75}/FVC were more likely to be older, male and Caucasian. In addition, these subjects were more likely to have smoked for more pack-years, exposed to second hand smoke, more likely to have a mother who smoked during pregnancy, or have a father with a diagnosis of COPD.

On chest CT, patients with a lower FEF_{25-75} /FVC had more gas trapping, emphysema and increased calculated total lung capacity and functional residual capacity.

<u>Conclusions</u>: A lower FEF₂₅₋₇₅ /FVC in subjects without evidence of airflow obstruction by conventional physiologic measures is associated with older age, Caucasian race, and male gender. In addition, these subjects have more gas trapping, emphysema, and hyperinflation.

Higher Prevalence of Gastroesophageal Reflux and Esophageal Dysmotility in IPF Patients Compared to COPD Patients

D. Kolman, L. Salieb, M. Smith, H. Zhao, F.C. Cordova, Y. Toyoda, A. Shiose, M. Butler-LeBair, G.J. Criner, N. Patel

BACKGROUND: Gastroesophageal reflux (GER) has been thought to have a role in pathogenesis of idiopathic pulmonary fibrosis (IPF), but the prevelance has not been well established. In addition, the role of epithelial damage that may occur due to aspiration from esophageal dysfunction (ED) remains unclear.

PURPOSE: To determine prevalence of GER and ED in patients with IPF as compared with those with COPD.

METHODS: Retrospective records review was conducted for patients with IPF and chronic obstructive pulmonary disease (COPD) undergoing evaluation for lung transplant between January 2009 to July 2013 at our institution. Initially, selected patients with IPF and COPD with gastrointestinal (GI) symptoms underwent evaluation with testing such as barium esophagram, high resolution esophageal manometry and pH testing (48 hour BRAVO capsule or 24 hour pH-impedance). In 2010 there was a protocol transition toward testing all patients with IPF regardless of symptoms with pH testing unless medically contraindicated.

RESULTS: 102 patients (55 IPF, 47 COPD) had at least one GI test. Prevalence of reflux, defined as a positive pH study or GER on esophagram, was higher in IPF (32/55, 58%) than COPD (13/47, 27%), p < 0.05. Abnormal impedance was seen in 14/26 (54%) IPF patients versus 1/7 (14%) in COPD patients, p = 0.06. Similarly, esophageal dysmotility was noted on esophagram in more IPF (30/53, 57%) than COPD patients (11/45, 24%), p=0.007. Manometric testing suggested IPF patients may have a greater prevalence of weak peristalsis (26.3%, 11/40), compared to COPD patients (6.6%, 1/16), p = 0.07. A higher percentage of IPF patients had low or low-normal resting lower esophageal sphincter pressures than COPD patients (11/40, 27.5% vs. 1/16, 6.2%), p = 0.07.

CONCLUSION: In the pre-transplant population, there is a higher prevalence of GER and esophageal dysfunction in IPF versus COPD patients. This increased prevalence of GER and ED maybe be implicated in causing epithelial damage leading to fibrosis in patients with IPF.

Comparative Efficacy and Side Effects of Alemtuzumab Versus Basiliximab as Induction Agent in Lung Transplantation

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INTRODUCTION: Induction immunosuppression therapy decreases acute cellular rejection (ACR) in organ transplantation. Comparative efficacy of the different agents is not well studied.

PURPOSE: To evaluate the comparative efficacy of Alemtuzumab and Basiliximab in reducing ACR after lung transplantation.

METHODS: Retrospective review of medical records was conducted in patients who underwent single, double lung transplant, and combined heart - lung transplant between period of January 2010 and September of 2013 at Temple University Hospital. All patients received either Alemtuzumab or Basiliximab followed by three drug immunosuppression regimen including cyclosporine, mycophenolate and corticosteroids. Between January 2010 and December 2011, all patients were given Basiliximab as an induction agent. After January 2012, patients with history of malignancy or cytomegalovirus (CMV) mismatch received Basiliximab and all others received Alemtuzumab. Surveillance bronchoscopy with transbronchial biopsies were performed at 1, 2, 4, 6, and 12 months, or as clinically indicated unless deemed high risk. Infection was defined by isolation of pathogenic organisms on bronchioalveolar lavage and treatment with antimicrobial agents. Acute rejection was defined based on ISHLT criteria. All patients received antifungal prophylaxis for 6 months and CMV prophylaxis for 12 months.

RESULTS: 48 lung transplant (5 single, 43 double, 4 heart lung transplants) recipients were studied. 20 patients received Alemtuzumab and 28 patients received Basiliximab as induction agents. They were followed for 394 ± 175 days and 122 biopsies were performed (32 for Alemtuzumab and 90 for Basiliximab). Frequency of ACR with grade A1 or higher was significantly less in the Alemtuzumab cohort (3, 23%) as compared to the Basiliximab cohort (18, 78%), p < 0.01. There were fewer abnormal biopsy results in the Alemtuzumab group, which remained significant when adjusted for the number of biopsies performed (18 \pm 32 vs 44 ± 30 , p = 0.02). In double lung transplant recipients, post-transplant FVC% was ($66\pm12\%$ vs $69\pm7\%$, p = 0.44) and FEV1% ($72\pm16\%$ vs $70\pm16\%$, p= 0.71), which was not statistically different. There was no difference in the number of infections 8 (40%) vs 17 (61%), (OR 2.3, CI 0.52, 10.5; p = 0.24), leukopenia 14 (70%) vs 17 (60.7%), p = 0.55 and thrombocytopenia 17 (85%) vs 20 (71.4%), p = 0.32 in the Alemtuzumab and Simulect groups respectively.

CONCLUSION: Induction therapy using Alemtuzumab appears to significantly lower frequency of acute cellular rejection compared to Basiliximab in lung transplantation. There was no significant difference in rates of infection, leukopenia or thrombocytopenia between the two induction agents.

FEF₂₅₋₇₅ and FEV₃/FVC as Predictors of Gas Trapping and Early Emphysema in Smokers Without COPD

Jason S. Krahnke, DO, Victor Kim, MD, Huaqing Zhao, PhD, Christopher B. Cooper, MD, Fernando J. Martinez, MD, Gerard J. Criner, MD for SPIROMICS

Forced expiratory flow 25-75% (FEF $_{25-75}$) and forced expiratory ratio after 3 seconds (FEV $_3$ /FVC) have been proposed as measures to evaluate small airways function. Their role in the diagnosis and management of COPD is unclear, and their utility in those at risk for airflow obstruction is poorly defined.

Methods: We analyzed data from 444 subjects with at least a 20 pack-year history of smoking without airflow obstruction (FEV₁/FVC>0.7) from the SPIROMICS study. The subjects underwent clinical characterization, spirometry, and had CT scans where %gas trapping and %emphysema were quantified. We divided subjects into low and high groups, based on the median value of the FEF₂₅₋₇₅ and the FEV₃/FVC. Differences between groups were assessed using t-test, chi-squared test, and Wilcoxon rank-sum test (median, inter-quartile range). The log of %emphysema and %gas trapping was calculated since the data were not normally distributed. Univariate analysis with FEF₂₅₋₇₅ and FEV₃/FVC as continuous variables was performed using Pearson correlations. Multivariable linear regression for %emphysema, and %gas trapping was performed with FEV₁, FEF₂₅₋₇₅, FEV₃/FVC, age, smoking history, gender and race as covariates.

Results: Both the low FEF $_{25-75}$ and low FEV $_3$ /FVC groups were older and had a greater smoking history but were more likely to have quit smoking. The low FEF $_{25-75}$ group, had more %gas trapping whereas the low FEV $_3$ /FVC group had more %gas trapping and more %emphysema. In univariate analysis, there were significant inverse correlations between FEF $_{25-75}$ and %gas trapping, and between FEV $_3$ /FVC with %emphysema and %gas trapping. In multivariate analysis, FEF $_{25-75}$ was only associated with %gas trapping (odds ratios 0.83, p=0.001). FEV $_3$ /FVC was not associated with %gas trapping or %emphysema after controlling for demographics and lung function.

Conclusions: In the SPIROMICS cohort, older patients without a diagnosis of COPD (FEV $_1$ /FVC>0.7) but with greater smoking histories had worse small airways function evidenced by lower FEV $_{25-75}$ and FEV $_3$ /FVC. FEV $_{25-75}$ is only associated with % gas trapping whereas FEV $_3$ /FVC is not associated with % emphysema or % gas trapping . FEF $_{25-75}$ is a better predictor of %gas trapping than FEV $_3$ /FVC in this cohort. These findings provide important insight into structure-function relationships in smokers, and FEV $_{25-75}$ may be a useful physiologic parameter to assess for the early development of obstructive lung disease.

Clinical Factors Associated With Frequent Exacerbations in Mild to Moderate COPD

Jason S Krahnke DO, Huaqing Zhao PhD, Victor Kim MD, Nathaniel Marchetti DO, Marilyn G Foreman MD, Barry J Make MD, Gerard J Criner MD and the COPDGene Investigators

Acute exacerbations of chronic obstruction pulmonary disease (AECOPD) profoundly impact quality of life, lung function decline, healthcare utilization and cost and overall prognosis. A reduced FEV1 and a previous exacerbation history have been shown to be predictors of exacerbation frequency. Limited data exists on identifying clinical factors associated with frequent exacerbations in subjects with mild to moderate COPD.

Methods: We analyzed data obtained from the COPDGene Study. Subjects included had a diagnosis of COPD confirmed by spirometry (GOLD Stage I-II, n=2,716) and were subdivided into three groups based on exacerbation history over the 12 months prior to enrollment: frequent exacerbators (≥2 exacerbations, n=290), infrequent exacerbators (1 exacerbation, n=388) and non-exacerbators (n=2,038). A severe exacerbation was defined as requiring assessment in the emergency department or admission to the hospital. Demographic data, pulmonary function testing, CT scan analysis, past medical and social history, symptom history, health status by survey instruments were analyzed. Differences between groups were assessed using t test or chi squared test. Logistic regression was performed using demographic data as predictors of exacerbation frequency.

Results: Logistic regression analysis revealed that the clinical factors associated with the infrequent exacerbation group compared to the non-exacerbator group were a history of severe exacerbation, chronic bronchitis, diabetes, older age, African American race, female gender, greater percent emphysema, a higher SGRQ Total score. Clinical factors associated with the frequent exacerbator group compared to the non-exacerbator group were a history of severe exacerbation, chronic bronchitis, asthma, wheezing, GERD, a lower FEV1/FVC ratio, exsmoker, African American race, female gender, an older age starting to smoke, a higher SGRQ Total score. Clinical factors associated with the frequent exacerbation group compared to the infrequent exacerbation group were a history of asthma, ex-smoker, younger age, older age when starting to smoke a lower FEV1/FVC ratio, a higher SGRQ Total score.

Conclusion: Subjects with mild to moderate COPD who experience frequent exacerbations are more likely to have a history of severe exacerbations, be female, African American, ex-smokers, have a later smoking debut, have a lower FEV1/FVC ratio, have a history of asthma, chronic bronchitis, GERD, higher SGRQ scores and report wheezing compared to subjects without exacerbations. When compared to infrequent exacerbators, frequent exacerbators are younger, are ex-smokers, and have lower FEV1/FVC ratios, an older smoking debut, a history of asthma and higher SGRQ scores. Having a history of a severe exacerbation is not a clinical factor associated with the frequent exacerbation group when comparing to the infrequent exacerbation group.

Residual Volume >225% Predicted is Associated With Higher Mortality After LVRS in the NETT Cohort

Jason S. Krahnke DO, Jonathan Galli MD and Gerard J. Criner MD for the National Emphysema Treatment Trial Research Group

Emphysema is an irreversible and disabling disease. Lung volume reduction surgery has been shown to improve lung function, quality of life and survival in select patients. Results from BLVR trials suggests that patients with a RV>225% have greater improvements in FEV1 and exercise tolerance post procedure compared to patients with a RV≤225%. To our knowledge no lung reduction study has evaluated the affect that a RV>225% has on survival.

Methods: 1218 subjects (610 Medical Group, 608 LVRS Group) enrolled in NETT were divided into two groups based on their RV% predicted (≤225% and >225%). Demographic, pulmonary function, exercise testing, and CT scan analysis data were analyzed. The difference between pulmonary function and exercise testing result values from randomization to the 24-month follow-up visit were calculated. Data analysis was performed using t test and chi square test. Kaplan Meier analysis was used to calculate survival data.

Results: 505 subjects in NETT had a RV % predicted >225%. Subjects with a RV % predicted >225% were younger in age (65.3±6.5 vs. 68.5±5.5 yrs, p<0.0001), male gender (71% vs. 54%, p<0.0001), had lower FEV1% pred (22.7±6.0 vs. 29.5±6.6, p<0.0001), higher TLC % pred (138.8±13.6 vs. 120.8±11.1, p<0.0001), lower DLCO% (26.3±9.5 vs. 29.7±9.6, p<0.0001), lower PaO2(63.6±10.6 vs. 64.8±10.1 mmHg, p<0.05), higher PCO2 (44.5±6.3 vs. 42.3±5.3 mmHg, p<0.0001), and lower maximum work (34.8±20.7 vs. 41.8±21.8 Watts, p<0.0001). Follow-up exercise and pulmonary function testing in the LVRS group revealed a statistically significant decline in the 6month exercise test results in the RV>225% compared to RV≤225% group (-7.9±14.7 vs. -4.1±14.4 Watts, p=0.006) only and no difference in FEV1 over a 24month follow up period. There was no difference in FEV1 and exercise test results in the medical group over the 24month follow up period. Kaplan Meier analysis revealed a higher mortality in subjects randomized to LVRS with a RV >225% compared to RV ≤ 225%. There was no difference in mortality in subjects randomized to the medical group.

Conclusion: Subjects in the LVRS group of NETT with a RV % predicted >225% had a higher mortality compared to subjects with an RV ≤ 225%. There was no mortality difference in the Medical group when dividing subjects by RV % predicted.

Peripheral Neutrophil and Lymphocyte Counts as Biomarkers for Severity and Structural Lung Parenchymal COPD Phenotype

Jason S. Krahnke, DO, Eric T. Wang, BA and Gerard J. Criner, MD

COPD is a chronic, inflammatory disease that progresses over time. Smoking causes peripheral airway remodeling and emphysema, factors that are associated with airway inflammation and altered pulmonary vasculature. Prior studies have shown that the airways in COPD patients have increased numbers of neutrophils, macrophages and CD8+ T cells. We propose that peripheral neutrophil, lymphocyte and monocyte counts will vary in COPD subjects based on the severity of airflow obstruction and presence and magnitude of emphysema.

Methods: This is a retrospective analysis of 109 subjects with COPD followed at Temple University Hospital pulmonary clinic from June 2008 to April 2011. Thoracic CT scans were analyzed using SLICER (http://www.slicer.org) to assess the severity of emphysema. Subjects were divided into three groups based on % emphysema (<5%, 5-25%, and >25%). Complete blood count data collected closest to the CT scan date was included in the analysis. Complete blood count with differential data was compared in subjects across GOLD Stages and % emphysema groups. Data analysis was performed using ANOVA and Wilcoxon rank-sum test. Data is presented as percent of population, mean ± SD and median (inter-quartile range).

Results: 109 Subjects, Age 60.3 ± 7.9 years, 56 Male, BMI 26.6 ± 6.5 kg/m2, FEV1 %predicted 41.4 ±22.7 , and a 51.5 ±29.9 pack-year history of smoking. GOLD Stage I-IV respectively, had greater % of peripheral neutrophils (57.2% vs. 56.0% vs. 61.4% vs. 71.5%, p<0.0001, GOLD Stage I-IV respectively) and lowest % of peripheral lymphocytes (29.6% vs. 32.0% vs. 26.9% vs. 17.7%, p<0.0001, GOLD Stage I-IV respectively). There was no difference in total white blood cell count (p=0.41), hemoglobin (p=0.08), % monocytes (p=0.10) and % eosinophils (p=0.75) across GOLD Stages.

Conclusion: COPD patients with lower FEV1 and greater percent emphysema have a higher percentage of neutrophils and lower percentage of lymphocytes in peripheral blood. These results show that data from a complete blood count may be an inexpensive test to screen for both the severity and structural lung parenchymal phenotype of COPD.

Clinical Predictors of Severe Exacerbations in Patients With COPD

Jason S Krahnke DO, Huaqing Zhao PhD, Victor Kim MD, Nathaniel Marchetti DO, Marilyn G Foreman MD, Barry J Make MD, Gerard J Criner MD and the COPDGene Investigators

Acute exacerbations of chronic obstruction pulmonary disease (AECOPD) profoundly impact quality of life, lung function decline, healthcare utilization and cost and overall prognosis. Limited data exists on identifying clinical factors associated with severe exacerbations.

Methods: We analyzed data obtained from the COPDGene Study. Subjects included had a diagnosis of COPD confirmed by spirometry (GOLD Stage I-IV, n=4,484) and were subdivided into two groups based on their history of severe exacerbation over the 12 month period prior to enrollment. A severe exacerbation was defined as requiring assessment in the emergency department or admission to the hospital. Demographic data, pulmonary function testing, CT scan analysis, past medical and social history, symptom history, health status by survey instruments were analyzed. Differences between groups were assessed using t test or chi squared test. Logistic regression was performed using demographic data as predictors of severe exacerbation.

Results: 876 subjects reported a severe exacerbation prior to study enrollment. Subjects with a history of severe exacerbation were younger (61.4 \pm 8.6 vs. 63.4 \pm 8.6 years, p<0.0001), on LTOT (41% vs. 20%, p<0.0001), ex-smokers (60% vs. 56%, p=0.02), have lower FEV1% (45.3 \pm 19.8 vs. 60.4 \pm 22.5, p<0.0001), lower FEF₂₅₋₇₅ (0.51 \pm 0.4 vs. 0.75 \pm 0.5, p<0.0001), lower 6MWD (1041 \pm 396.8 vs. 1278.8 \pm 397.1, p<0.0001), history of asthma (39% vs. 22%, p<0.0001), chronic bronchitis (33% vs. 24%, p<0.0001), wheezing (86% vs. 66%, p<0.0001), higher SGRQ Total (53.9 \pm 19.3 vs 32.8 \pm 21.8, p<0.0001) MMRC dyspnea score (2.77 \pm 1.2 vs 1.69 \pm 1.4, p<0.0001), greater % emphysema (14.6 \pm 13.6 vs. 10.9 \pm 11.7, p<0.0001) and % gas trapping (42.6 \pm 21.2 vs. 34.2 \pm 20.4, p<0.0001) on CT analysis. Logistic regression analysis revealed younger age, Caucasian race, lower resting oxygen saturation, LTOT, lower FEV1 % predicted, lower 6MWD, ex-smoker, and history of wheezing and chronic bronchitis were predictors of severe exacerbations.

Conclusion: Twenty percent of the cohort experienced a severe exacerbation in the year prior to enrollment. Subjects who experienced a severe exacerbation are more likely to be treated with LABA, LAMA, ICS, or ICS/LABA therapy compared to subjects without a history of severe exacerbation. A history of wheezing, chronic bronchitis, LTOT, ex-smoking, younger age, Caucasian race, lower resting oxygen saturation, 6MWD and FEV1 % predicted were predictors of severe exacerbations in this cohort of COPD subjects.

EndoFLIP as a Novel Way to Evaluate the Pyloric Sphincter in Patients With Gastroparesis

Zubair Malik MD; Abhinav Sankineni, MD, MPH; Henry Parkman MD

Endoscopic Functional Luminal Imaging Probe (EndoFLIP) is a technology that has been used to evaluate the LES. EndoFLIP uses 16 sensors inside a balloon that is inflated inside a sphincter and measurements are obtained. Prior studies have assessed pyloric sphincter pressures using water perfused or high resolution manometry.

Aim: To measure the cross-sectional area (CSA), shape, pressure, length, and distensibility of the pylorus using EndoFLIP in patients with gastroparesis.

Methods: EndoFLIP was performed in 16 patients (9 idiopathic gastroparesis [IG], 7 diabetic gastroparesis [DG]). An EndoFLIP catheter was passed into the pylorus under direct endoscopic visualization. CSA, shape, pressure, and diameter of pylorus was measured at different balloon volume distensions. Distensibility was calculated as minimum CSA divided by pressure. Length of the pylorus was assessed visually.

Results: The pyloric contour was seen best at 40cc balloon distension (diameter 13.0±0.9mm, CSA 144.6±19.8mm2, pressure 16.8±2.3mmHg, length 1.7±0.8cm, distensibility 13.6±3.4mm2/mmHg). There was a wide range seen in diameter (5.6-20.6mm) and distensibility (1-55 mm2/mmHg); low distensibility suggesting a "stiff" pylorus whereas high distensibility suggesting an "open" pylorus. DG tended to have a smaller diameter pylorus (11.6±1.3mm vs 14.3±2.6mm; p=0.16) with less distensibility (10.4±4.6mm2/mmHg vs 16.9±5.8mm2/mmHg; p=0.20) compared to IG.

Conclusions: EndoFLIP is a novel technique that can be used to assess pyloric parameters. No significant differences were seen when comparing DG and IG, but this may be due to the small study size of this preliminary trial. Further studies are needed to characterize these findings in normal subjects and in different etiologies of gastroparesis.

Correlation of PET/CT and CT RECIST Response in GIST Patients With PDGFRA D842V Gene Mutations Treated With Crenolanib

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Background: Crenolanib (CP-868,596) is an orally bioavailable, selective inhibitor of platelet derived growth factor receptor (PDGFR) tyrosine kinase, with in vitro studies demonstrating activity against PDGFRA D842V mutant cell lines. A phase II study evaluated antitumor efficacy of crenolanib in patients (pts) with advanced gastrointestinal stromal tumor (GIST) with PDGFRA D842 related mutations and deletions. An exploratory objective evaluated metabolic response after 1 cycle of therapy as a predictor of RECIST response, so positron emission tomography/computerized tomography (PET/CT) data was available for a majority of pts. We present the results of this exploratory objective.

Methods: Pts with advanced GIST with PDGFRA D842 related mutations and deletions, including D842V, with residual measurable disease were eligible for enrollment at 1 of 2 study sites. Pts with a baseline PET/CT and a follow-up PET/CT after 1 cycle were included in this analysis. One nuclear medicine specialist interpreted the scans and provided SUV estimates for index lesions at baseline and after 1 treatment cycle. RECIST measurements were provided by the local interpreting radiologist.

Results: 12 pts treated with crenolanib had both a baseline and follow-up PET/CT after 1 cycle. Baseline FDG avidity was lower than expected for GIST based on published reports, with the exception of 1 pt who had average initial standardized uptake value (SUV) of 33. Average SUV excluding this pt was 4.6. The table shows PET metabolic response after 1 cycle and CT RECIST best response. 7 of 12 (58%) pts had non-concordant PET and CT responses, including one with partial response (PR) on PET but progressive disease (PD) on CT.

Conclusions: In this small exploratory analysis, pts with PDGFRA D842 related mutations had lower than expected SUV activity on PET, and metabolic response did not predict response by RECIST. These results suggest that PET/CT may not be an optimal method for predicting, evaluating and following response among GIST pts with PDGFRA D842 related mutations.

Radiographic Response			
# of patients	PET Metabolic	CT RECIST	
	Response		
3	SD	SD	
2	PD	PD	
2*	PD	SD	
2*	SD	PD	
1*	PR	SD	
1*	PR	PD	
1*	SD	PR	

SD = Stable disease

^{*}Indicates non-correlation

Predictors for Lung Structural and Functional Abnormalities on CT Chest in Smokers Without Airflow Obstruction

D. Mendonca MD; N. Marchetti DO; H. Zhao PhD; J.A. Mamary MD; G.J. Criner MD

Rationale: Little is known about the clinical characteristics of smokers with no airflow obstruction and abnormal radiographs. Our objective is to characterize smokers without airflow obstruction who have abnormal chest CT findings.

Methods: Our study population was the group of smokers without airflow obstruction (FEV1/FVC > 0.7) from COPDGene as measured by spirometry. We divided the group into those with normal vs. abnormal chest CTs (%emphysema > 6.7% and/or %Gas trapping > 28.4%). The data were analyzed using chi-square, t-test and multivariate logistic regression analyses.

Results: 356 subjects without airflow obstruction had abnormal chest CT scans. This group was older (59.9 +/- 8.9 vs. 56.5 +/- 8.1), predominantly male (70% vs. 50%), caucasian (70% vs. 59%), had lower BMI (26.5 vs. 29.2). There was no statistically significant difference in total rate of exposure to smoking. They were however much less likely to be current smokers (38% vs. 60%). TLC% was higher in this group as well (99% vs 91%, p: 0.0001). Logistic regression analysis showed that the two strongest associations with having an abnormal CT scan were male gender (OR 3.8, CI 2.9-5.0) and being a current smoker (OR 0.29, CI 0.22-0.39); both p<0.0001.

Conclusion: We found radiographic abnormalities in about 9% of a population of smokers without airflow obstruction. These subjects were more likely male and not current smokers. Radiographic imaging may identify the presence of lung structural abnormalities before the development of airflow obstruction.

Time of HIV Diagnosis and Engagement in Prenatal Care Impact Outcomes in Pregnant Women With HIV

Florence Momplaisir, Kathleen Brady, Dana Thompson, Thomas Fekete, Baligh Yehia

Background: Little is known about how the care continuum of HIV positive women during pregnancy relates to viral suppression at the time of delivery. In this study, we investigate the association between time to HIV diagnosis, quality of prenatal care and viral suppression among pregnant women with HIV.

Methodology: Retrospective analysis of 836 pregnancies, involving 656 HIV-infected women, in Philadelphia in 2005-2013. Multivariable logistic regression examined associations between time of HIV diagnosis, engagement in prenatal care, and the outcomes (ART use and viral suppression), adjusting for sociodemographic factors and year of pregnancy.

Results: Women were adequately engaged in care in 39% of pregnancies, intermediately engaged in 38%, and inadequately engaged in 23%. Outcomes significantly (p<0.05) varied by time of HIV diagnosis and engagement in prenatal care. Overall, 89% of women diagnosed with HIV before pregnancy were prescribed ART and 46% achieved viral suppression compared to 73% and 31% for women diagnosed with HIV during pregnancy. Similarly, 92% of women with adequate engagement in prenatal care were prescribed ART and 43% achieved viral suppression compared to 55% and 26% for women with inadequate engagement. Multivariate model confirmed that HIV diagnosis during pregnancy (vs. before) and intermediate or inadequate engagement in prenatal care (vs. adequate) were negatively associated with use of ART and viral suppression (p<0.05).

Conclusions: Outcomes varied by time of HIV diagnosis and engagement in prenatal care. Targeted interventions to diagnose women early and improve engagement in prenatal care are needed and have the potential to improve outcomes for mothers and infants.

A Long-term Follow Up Report on Autologous Stem Cell Transplantation for Mantle Cell Lymphoma – A Single Institution Experiences

Nasheed Hossain MD; Matthew Zibelman MD; Richard Fisher MD; Nadia Khan MD; Thomas Klumpp MD; Mary Ellen Martin MD; Michael Millenson MD; Rushang Patel MD; Henry Chi Hang Fung MD; Patricia Kropf MD

Background: Mantle cell lymphoma (MCL) is a type of B cell non-Hodgkin's lymphoma with an often-aggressive clinical course. Treatment generally consists of conventional induction chemotherapy followed by consolidation with autologous stem cell transplant (ASCT).

Methods: We queried our core database to analyze the clinical cases of the 24 consecutive patients with a diagnosis of MCL, all of whom underwent ASCT, between August 1995 and December 2013.

Results: The median age at transplant was 57.5 (range 24-68) with a male predominance (70.1%), reflecting historical observations in MCL. Fifty percent of patients were transplanted in CR1. The most common conditioning regimen was cyclophosphamide with total body irradiation [75.0% of cases]. At the time of data collection, 14/24 (58.3%) of patients were still living, 13/24 (54.2%) without disease. Furthermore, 13/24 (54.2%) were disease free at two-year post-transplant, but 5/13 (38.5%) died prior to the five-year post-transplant mark. Eight patients died of disease (33.3%), one of toxicity (pneumonitis) and one of unrelated causes (metastatic melanoma). For the remaining patients, median follow-up was 1048 days (2.9 years) with four patients alive past the six-year post-transplant mark. The five-year actuarial overall survival was 59.2%. Progression free survival at five years was 50.2%. The transplant-related toxicity profile was manageable, similar to other institutions' experiences. Toxicities of grade 3-4 or higher were seen in only three patients (diarrhea, mucositis), and one patient had grade 5 pneumonitis.

Conclusions: Overall, these data support ASCT as an effective and tolerable option for transplant eligible patients with MCL.

Validation of Molecular Observations Related to ADMA Dysregulation

Varsha Pathak, WenJun Ju, Viji Nair, Matthias Kretzler, Huaquing Zhoo, Crystal Gadegbeku

Background: Plasma ADMA levels are uniquely high in patients with chronic kidney disease and associated with cardiovascular mortality. Previously, we demonstrated associations between renal function and gene expression of enzymes of ADMA metabolism in the tubulo-interstitium of renal biopsy samples. The goal of the present study was to validate these findings and characterize glomerular compartment gene expression.

Methods: Gene expression analysis was performed using Affymetrix 133 plus GeneChips on renal biopsy tissue obtained from consented individuals in a European kidney disease cohort. Steady state gene expression levels of PRMT 1, DDAH and oxidative stress markers were measured from the microdissected tubule-interstitial (n=162) and glomerular (n= 143) renal cortical samples. To explore relationships between molecular markers and eGFR, Pearson correlations were used with adjustment for multiple comparisons.

Findings: In the tubulo-interstitial compartment, PRMT1 was inversely correlated with DDAH1 (R=-0.40, p<0.0001) and positively correlated with the oxidative stress markers, NADPH oxidase subunits and mitochondrial superoxide dismutase (R=0.4 - 0.44, p<0.0001). These oxidative stress markers were inversely correlated with DDAH1 (R = -0.4 - 0.52, p< 0.001). Further, eGFR correlated positively with DDAH1 (R=0.3) and negatively with PRMT1 (R=-0.37), and oxidative stress markers (R= -0.43 - 45) (all p<0.001).

In the glomerular tissue, only the oxidative stress markers demonstrated significant associations and were inversely correlated with eGFR.

Conclusion: Here, we validate the relationships between renal function, and expression of ADMA enzymes and oxidative stress markers in human renal biopsy samples. These findings provide further molecular evidence of the kidney's role in ADMA dysregulation.

Computed Tomography Measurement of Small Pulmonary Vessels in Chronic Obstructive Pulmonary Disease

Frederick L Ramos, Nathaniel Marchetti, Michael R Jacobs, Chandra Dass, Huaqing Zhao, and Gerard J Criner, for the COPDGene Investigators

Rationale: A retrospective study of patients in the National Emphysema Treatment Trial who had right heart catheterization (RHC) data reports that the mean pulmonary arterial pressure (PAP) in severe emphysema is correlated to a decrease in the percentage of total lung area taken up by the cross-sectional area of pulmonary vessels less than 5 mm² (total %CSA_{<5}). Estimation of systolic PAP by echocardiography is frequently inaccurate in advanced lung disease and leads to considerable over diagnosis of pulmonary hypertension (PH). Right heart catheterization (RHC) is recommended by guidelines to measure mean PAP and diagnose PH. An alternative noninvasive technique to estimate pulmonary hypertension in COPD patients is needed. Our hypothesis is that %CSA_{<5} is negatively correlated to mean PAP and that this correlation is strongest in those with PH by RHC.

Methods: Preliminary retrospective data collection involves 25 subjects in the COPDGene study recruited from Temple University Hospital who have computed tomography (CT) and RHC data. Three CT image slices are selected: 1 cm above the upper margin of aortic arch, 1 cm below the carina, and 1 cm below the right inferior pulmonary vein. K-PACS (V1.6.0) software is used to convert the image to a DICOM format and Image J software to obtain the total %CSA_{<5}. JMP Pro V10 pairwise correlation is used to correlate total %CSA_{<5} and Pulmonary Hemodynamics, Lung Function, and CT Measurements. Correlation data is presented in parenthesis as coefficient and p-value.

Results: 25 patients with CT and RHC data were identified. 7(28%) had RHC data in the same year as CT scan and the remainder have RHC within 1 to 6 years. Refer to the table for demographics, clinical characteristics, and CT and RHC measurements. Total %CSA $_{<5}$ is inversely correlated to CT measurements of %Emphysema (-0.92, p=0.0013) and %Gas trapping (-0.75, p=0.03) but not to pulmonary artery systolic (0.15, p=0.48), diastolic (0.12, p=0.57), and mean pressures (0.0017, p=0.99), pulmonary vascular resistance (-0.1, p=0.64), forced expiratory volume in one second (0.38, p=0.06), forced vital capacity (0.08, p=0.7), and other CT measurements of functional residual capacity (-0.17, p=0.68) and total lung capacity (-0.3, p=0.46).

Conclusion: Preliminary analysis reveals that %CSA_{<5} is inversely correlated to the amount of emphysema and gas trapping by CT scan but not to selected pulmonary hemodynamics or lung function measurements.

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Gastroesophageal Reflux Disease and Chronic Obstructive Pulmonary Disease in SPIROMICS

Frederick L Ramos, Huaging Zhao, Fernando Martinez, and Gerard J Criner

Rationale: SPIROMICS is a prospective cohort study that will enroll approximately 3,200 participants across four strata (Never smokers, Smokers without COPD, Mild/Moderate COPD, and Severe COPD) with the goals of identifying new COPD subgroups and intermediate markers of disease progression. Retrospective and prospective studies indicate that a history of gastroesophageal reflux disease (GERD) is associated with a higher frequency of COPD exacerbations. We aim to establish a COPD/GERD phenotype and thus extensively describe this subgroup via analysis of the Subpopulation and Intermediate Outcome Measures in COPD Study (SPIROMICS).

Methods: Preliminary data from SPIROMICS is analyzed. To account for potential misclassification of subjects, GERD is defined by both subject-reported history of GERD or heartburn (definition by history) and by subject-reported history of GERD or heartburn or GERD therapy with proton pump inhibitors, histamine2 receptor blockers, or antacids (definition by history or therapy). Subjects in the GERD group have either a subject-reported history of GERD and/or are receiving GERD therapy.

Results: Results shown are representative of data available at the time of analysis. Of the 1801 subjects in SPIROMICS cohort, 1651 are smokers (>20 pack-years) or have COPD. Based on definition by history, 479 subjects have GERD, 1155 have no GERD, and 17 could not be classified due to missing data. Based on definition by history or therapy, 587 subjects have GERD, 1052 have no GERD, and 12 could not be classified due to missing data. GERD group have less males (50% vs. 56%, p=0.02) on definition by history and more whites (81% vs. 77%, p=0.04; 82% vs. 76%, p=0.0006) and higher BMI (29±5 vs. 27±5, p<.0001; 28±5 vs. 27±5, p<.0001), on definition by history and history or therapy, respectively. Six minute walk distance (6MWD) in meters (402±109 vs. 414±106, p=0.04; 399±110 vs. 417±105, p=0.002) quality of life (34±20 vs. 30±20, p=0.001; 34±20 vs. 30±19, p<.0001) and sleep (7±4 vs. 6±4, -<.0001; 7±4 vs. 6±4, p<.0001) and total exacerbations (0.47±0.97 vs. 0.36±0.86, p=0.03; 0.47±0.96 vs. 0.35±0.85, p=0.009) are worse in the GERD groups in definitions by history and history or therapy, respectively. Refer to the included table.

Conclusions: Preliminary analysis of SPIROMICS show that COPD subjects with GERD have worse 6MWD and quality of life and sleep and have more COPD exacerbations. We propose more recognition of this COPD/GERD phenotype of disease and its potential for targeted therapy.

Hyperinflated and Gas Trapped COPD Patients: Emphysema Versus Nonemphysema Predominant

Frederick L Ramos, Nathaniel Marchetti, Huaqing Zhao, Craig P Hersh, George R Washko, Barry J Make, Edwin K Silverman, David Lynch, James D Crapo, and Gerard J Criner, for the COPDGene Investigators

Rationale: Lung hyperinflation is common in chronic obstructive pulmonary disease (COPD) and is associated with exercise intolerance, poor quality of life (QOL), and mortality. Small airways disease and emphysema both contribute to hyperinflation and gas trapping. Quantitative measures based on paired inspiratory and expiratory chest computed tomography (CT) scans are used as markers of small airway disease in smokers with and without COPD. Whether hyperinflation and gas trapping due to either emphysema or small airways disease has different clinical characteristics is unclear.

Methods: The sample was derived from the 10,192 smokers with and without COPD and 108 non-smokers without COPD from COPDGene study. CT lung volumes were calculated by 3D slicer software at full inspiration (total lung capacity $[TLC_{CT}]$) and relaxed exhalation (functional residual capacity $[FRC_{CT}]$). CT lung volumes were used to calculate FRC/TLC_{CT} ratio. %Emphysema was defined as %lung <-950 HU at full inspiration and %gas trapping as %lung <-856 at relaxed expiration. Dividing the group into quartiles and studying those in the 4th quartile for both variables identified subjects with more severe hyperinflation and gas trapping. The %gas-trapping variable was converted to square root to construct a normal distribution. Only COPD patients ($FEV_1/FVC<0.7$) were included in the final analysis. An emphysema predominant phenotype was defined as %emphysema >=15% and the remainder were defined as non-emphysema predominant (i.e. hyperinflation and gas trapping from small airway disease).

Results: 7446 subjects remained after 1602 were excluded due to incomplete CT data, 1183 due to incorrect CT breathing instructions (forced exhalation instead of relaxed exhalation), and 69 who were normal controls. 1187 subjects of 7446 were in the 4th quartile for FRC/TLC_{CT} (>=0.68) and square root of %gas trapping (>=5.79). 3 subjects missed spirometry and were excluded from the final study population. The final study population includes 1092 of 1187 subjects who had airflow limitation (FEV₁/FVC<0.7). 640 subjects had predominantly emphysema phenotype (%emphysema >=15%) and the remaining 452 had a non-emphysema predominant phenotype. Subjects in the emphysema predominant group were older and mostly white and had higher BMI and more oxygen usage. The emphysema predominant group had worse lung function, 6MWD, and QOL, more exacerbations, and a higher BODE score.

Conclusion: Severely hyperinflated and gas trapped COPD patients due to emphysema, compared to small airway disease, have worse lung function, QOL, and walk distance, more exacerbations, and a higher BODE score.

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Practice Patterns in the Treatment of Achalasia: Results of a Nationwide Survey

Sankineni A, Maranki JL, Smith MS, Klebanov N, Friedenberg FK, Haluszka O, Parkman HP

Aims: To determine practice patterns among US gastroenterologists in the treatment of achalasia, and to identify physician characteristics that influence choice of treatment.

Methods: A 16-question online questionnaire was distributed to 8570 email addresses of members of the ACG and AGA.

Results: Response rate was 11%.

Of the respondents, first line treatment was Heller Myotomy (HM) for 50% of physicians, pneumatic dilation (PD) 29%, botulinum toxin (BoNT) 15%, and medical treatment in 2%. If all proposed modalities were readily available, HM was preferred most frequently (56%) compared to PD(33%) and BoNT(11%).

Respondents who have been in practice more than 20 years were more likely to personally perform PD (46%) than those with less than 20 years of experience (32%), p < 0.001.

Respondents who see fewer than 10 cases annually were less likely to prefer PD (29%) and more likely to prefer Heller myotomy (60%) than those who see a higher volume(p<0.005).

Years in practice was an independent predictor of preferred modality, as respondents practicing less than 20 years were 1.8 times more likely to prefer HM(Cl 1.32 – 2.44). Personal performance of PD was also an independent predictor of preferred modality, as those performing it were 1.6 times more likely to prefer PD (Cl 1.19 – 2.22). The most common reasons for not preferring PD were preference for surgery (37%) and fear of complications (32%).

Conclusions: Heller myotomy is the preferred modality for treatment of achalasia among practicing gastroenterologists. Years in practice is an independent predictor of preferred modality.

Effect of Pioglitazone on Severe Hypertriglyceridemia in Patients With Diabetes: A Case Series

Pankaj Sharda, MD; Elias Siraj MD, FACP, FACE

Objectives: Studies show that pioglitazone improves triglyceride(TG) levels in addition to glycemic control. Most studies were done in patients with average TG levels. Therefore, effect on individual cases of severe hypertriglyceridemia (HTG) remains inadequately documented.

Cases:

<u>Case 1:</u> 53-year-old woman with type 2 DM(T2DM) and HTG managed with insulin, glipizide and sitagliptin. HbA1c ranged 7.8-8.8%. TG levels ranged 730-810mg/dL (normal <150mg/dL) despite treatment with statins, ezetimibe and fish oil. We started pioglitazone 15mg daily and TG levels dropped from 806 to 260mg/dL. Follow-up TG dropped to156mg/dL after 1-year.

<u>Case 2:</u> 30-year-old woman with T2DM and HTG managed insulin, metformin and rosiglitazone. HbA1c ranged 5.9-7.5%. TG level ranged 500-2000mg/dL despite treatment with fibrates and niacin. We continued fenofibrate she was taking (160mg daily) and replaced rosiglitazone with pioglitazone 15mg daily. TG levels dropped from 667 to 163mg/dL. Follow-up TG levels remained <200mg/dL after 1-year.

<u>Case 3:</u> 63-year-old woman with T2DM presented for severe HTG ranging 650-2000mg/dL. HbA1c ranged 5.1-6.8%. Pioglitazone 15mg daily added to her regimen of gemfibrozil 600mg BID. TG levels dropped from 800 to 227mg/dL. Increasing pioglitazone to 30 mg daily further dropped TG level to 156mg/dL. Follow-up TG levels stayed <160mg/dL after 2-years.

Discussion: Pioglitazone effectiveness could be due to induction of increased lipoprotein lipase activity, leading to increased fractional clearance rate of VLDL-TG. Also, insulin sensitizing effects of pioglitazone may help restore hypertriglyceridemia and postprandial lipemia.

Conclusions: Our cases demonstrate that pioglitazone can lead to dramatic drop and near-normalization of TG in patients with very high TG levels.

Findings of Pulmonary Hypertension in ESRD Patients

Rajeeve Subbiah and Brian O'Murchu

Introduction: Among patients undergoing chronic hemodialysis, pulmonary hypertension (PH) (defined as pulmonary artery systolic pressure [PASP] ≥35mmHg) 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) ≥25mmHg.

Methods: Hemodynamic data from 104 stable chronic hemodialysis 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 391% were women. Eighty nine (86%) were dialyzed through an arteriovenous fistula or graft. Of those patients forty two (47%) had PH (MPA>25mmHg). 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). Pulmonary arterial hypertension[PAH] (defined as MPA > 25 mm Hg and PCWP < 15 mm Hg) was observed in twelve (13.5%) of patients with AV fistula or grafts.

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. Hemodialysis through an AVF should be considered a risk factor for the development of pulmonary arterial hypertension.

The Implementation of the Lung Allocation Score Improves Post-transplant Survival in Patients With Idiopathic Pulmonary Fibrosis

Zael Vazquez MD, Francis Cordova MD, Huaqing Zhao PhD, Sharven Taghavi MD, Jayarajan Senthil MD, Yoshiya Toyoda MD, Gerard J. Criner MD

Background: Idiopathic pulmonary fibrosis (IPF) is the most common indication for lung transplantation since the institution of the Lung Allocation Score (LAS). The effect of LAS on post-transplant survival has not been evaluated in a large cohort of patients with IPF.

Methods: Lung transplant recipients with a primary diagnosis of IPF were identified in the United Network of Organ Sharing registry from 1987 to 2012. Those receiving transplantation prior to the institution of LAS were compared to those transplanted in the LAS era. Statistical analysis was performed using Chi-square, T-test, and Cox proportional hazard. Post-transplant survival and length of stay were used as endpoints.

Results: There were 6158 lung transplants meeting study criteria. There were 2207 patients in the pre-LAS cohort and 3951 patients in the post-LAS era. Patients in the LAS era were older $(60.2\pm8.9 \text{ vs.} 53.3\pm11, \text{ p}<0.001)$, had higher BMI (27.1 vs. 26.8, p<0.0001) and a significantly higher number of double lung transplants (DLT) performed (2034 vs. 634, p<0.0001). Univariate analysis showed that factors affecting survival were DLT, age, gender, ischemic time, and post-LAS era (Table 1). On multivariate analysis, increasing age was associated with higher mortality [HR $(95\%\text{Cl})\ 1.014\ (1.009-1.018), \text{ p}<0.0001]$. Variables associated with survival on multivariate analysis included DLT [HR $(95\%\text{Cl})\ 0.792\ (0.730-0.858), \text{ p}<0.0001]$, and transplant after the institution of the LAS [HR $(95\%\text{Cl})\ 0.773\ (0.710-0.841), \text{ p}<0.0001)$ respectively. Factors associated with length of stay included lower FVC [Estimate (SE) -0.108 (0.03), p<0.0001], longer ischemic time [Estimate (SE) 1.686 (0.27), p<0.0001), and DLT [Estimate (SE) 7.55 (0.88), p<0.0001].

Conclusion: The institution of lung allocation score has improved post-transplant survival in patients with idiopathic pulmonary fibrosis. While double lung transplantation results in longer length of stay for patients with IPF, it improves long term survival and should be the preferred transplant procedure for IPF patients.

Liquid Nitrogen Spray Cryotherapy can be Used Safely in Retroflexion For Treatment of Lesions at the Esophagogastric Junction and Gastric Cardia

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Background: Endoscopic ablation of neoplastic tissue distal to the tubular esophagus presents a challenge. Liquid nitrogen spray cryotherapy (LN2SC) is a technique which has been used to treat Barrett's esophagus (BE), esophageal cancer and non-esophageal diseases. We describe the feasibility and safety of treating lesions at the esophagogastric junction (EGJ) and gastric cardia with retroflexed LN2SC.

Methods: We performed a retrospective study of subjects treated with LN2SC in retroflexion at 4 U.S. tertiary care centers. Eligible subjects were treated for dysplastic BE or adenocarcinoma with either curative or palliative intent.

Results: In total, 13 patients underwent 18 retroflexed LN2SC administrations. While 9 patients had 1 retroflexed session, 4 had at least 2 sessions of treatment. Histologic grading of lesions included 4 cases of invasive adenocarcinoma, 4 of intramucosal adenocarcinoma, 4 of BE with high grade dysplasia and 1 of BE with low grade dysplasia. Lesions targeted for treatment included 3 EGJ nodules/masses, 3 cardia nodules/masses, 1 area of nodularity including the EGJ and cardia and 6 flat EGJ lesions. Retroflexed LN2SC was chosen either for lesions extending beyond the EGJ that were not fully visible en face or due to concerns for incomplete treatment with prior ablation.

Conclusion: Experience to date demonstrates the feasibility and safety of LN2SC in retroflexion for treatment of lesions at the EGJ and cardia. The ability to use LN2SC in both en face and retroflexed positions expands the treatment options available for lesions in the upper gastrointestinal tract, especially those previously unreachable by other methods.

The Prevalence of Dental Disease in Inflammatory Bowel Disease

Ovais Ahmed, MD; Sherri Gampel, DO; Vikram Bathula, MD; Erkanda Ikonomi, MD; Adam Ehrlich, MD, MPH; Robin Rothstein, MD; Frank Friedenberg, MD, MS Epi

Inflammatory bowel disease (IBD) is a chronic inflammatory intestinal disorder, which has been associated with an increased prevalence of dental caries and periodontitis. Small studies have shown that patients with IBD often have poor oral health secondary to select nutritional deficiencies and immune suppression therapy while other research suggests that treatment for IBD may actually improve oral health. Our purpose was to clarify whether there is an association between IBD and the prevalence of dental and oral soft tissue disease at a population level.

The 2009-2010 NHANES database was utilized for data analysis. After weighting (variable WTINT2YR) using the Complex Samples module of SPSS 20.0 the age range was restricted to 18-65 y. All survey participants 3-19 and 30 years and older were eligible for the oral examination.

Of a weighted sample size of 199,283,214 NHANES participants, there were 2,054,131 individuals (1.03%) with IBD. For all 32 teeth, the prevalence of an absent tooth at nearly all sites was higher in the group without IBD. Only for the upper left 3^{rd} molar and the lower left 2^{nd} molar, was the absence of a tooth > 10% higher in the IBD group. The prevalence of some level of gum/soft tissue disease was lower in the group with IBD (16.1 vs. 17.0%; P < 0.001).

Although slight differences existed in dental health between those with and without IBD, the overall oral condition for both groups appeared comparable. The results are limited by inability to adjust for disease activity, nutritional status, and medications.

Impaired Gastric Accommodation in Gastroparesis: Relationship to Gastroparesis Cardinal Symptom Index (GCSI) Severity Scores

Saraswathi Arasu, Henry Parkman, Alan Maurer

Impaired gastric fundic accommodation (GFA) to a solid meal in patients with functional dyspepsia may explain postprandial symptoms.

Aim: To assess impaired GFA as a part of a routine solid-meal gastric emptying scintigraphy (GES) and to identify symptoms associated with impaired GFA.

Methods: Patients completed the Patient Assessment of Upper GI Symptoms (PAGI-SYM) which includes the nine symptom Gastroparesis Cardinal Symptom Index (GCSI) in addition to upper abdominal pain between August 2011 to December 2013. GES was performed using the standardized 4-hour liquid, egg-white protocol. Normal fundic accommodation was defined as seeing greater than 50% of the radiolabeled solids in the upper half of the stomach in the image immediately post meal ingestion (zero minute time point).

Results: The Gastroparesis (GP) group included 70 patients (19 diabetic, 47 idiopathic, 4 post-surgical) with delayed gastric emptying. 24 (4 diabetic, 19 idiopathic, 1 post-surgical) had impaired fundic accommodation. Of the 60 patients with normal gastric emptying, 19 (8 diabetic, 0 post-surgical) had impaired fundic accommodation. Symptoms of stomach fullness and upper abdominal pain were significantly higher in the GP/impaired fundic accommodation group compared to GP/normal fundic accommodation. In the normal GES group, symptom severity scores were higher for early satiety with impaired fundic accommodation compared to normal fundic accommodation.

Conclusions: Impaired GFA can be assessed visually using current standardized solid-meal GES. Impaired GFA is associated with: stomach fullness and upper abdominal pain in patients with delayed gastric emptying and may explain early satiety in patients with normal GES.

A Review of Interventional Clinical Trials (CTs) in Renal Cell Carcinoma (RCC): A Status Report from the ClinicalTrials.gov Website

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Background: CTs in RCC have rapidly evolved with the introduction of targeted therapy (TT) and more recently novel immunotherapy. The objective of this study was to assess the current landscape of CTs in RCC to identify areas of strength and opportunities for improvement.

Methods: ClinicalTrials.gov was queried on September 24, 2013 using pre-specified search criteria. Only open, RCC-dedicated, interventional CTs in adult patients were included. Descriptive statistics and Fisher's exact tests were used to compare features of CTs.

Results: Of the 169 CTs analyzed, 42 were phase I or I/II (25%), 67 phase II (40%), 15 phase III (9%), and 45 other (26%). Overall, 27% were randomized, 65% were single-arm. Of the CTs evaluating patients with metastatic disease, 30% were for 1st line therapy, 40% for 2nd line or beyond and 30% for any line. 57% of all CTs included at least one TT. Immunotherapy was tested alone or in combination in 8%. Biomarkers were more frequently examined in TT and immunotherapy CTs (54% and 64%) than in surgery and other CTs (22% and 28%) (P=0.002). Sponsorship differed by therapy type (P=0.003), with immunotherapy CTs most commonly sponsored by industry (36%), and academic sponsorship more common for TT (46%), surgery (89%) and other (63%) CTs.

Conclusions: CTs in RCC are largely non-randomized, single arm, with minimal focus on non-clear cell RCC and evaluating primarily patients with AD. TT is the predominant systemic therapy evaluated. Significant differences were noted in the primary endpoint, sponsorship and biomarker assessment between therapy types.

Development of a Risk Prediction Tool for Likelihood of Missed Appointments

David Verbofsky, MD; Akilah Bates, MD; Kristi Holmes, MD; Regina Szczesniak, MD; Ryan Schmidt, MD

About twenty percent of patients miss appointments in primary care clinics. Missed appointments disrupt care, waste resources and may be associated with utilization of emergency departments. Certain factors are associated with missed appointments. Developing a risk tool that can predict which patients are likely to miss an appointment would allow for directing interventions to those patients who score high.

In prior research we determined demographic variables that were associated with missed appointments at an Internal Medicine Clinic. Age (18-29, 30-59, 60-89), gender (male, female), status (new, established), and insurance (Medicaid, Self-Pay, Medicare) correlated with missed appointments. Odds and likelihood ratios were determined for these variables. A qualitative comparison of these ratios was then used to assign variables specific point values within a risk prediction tool. A score of 0-5 was assigned, with higher scores indicating higher likelihood of missed appointments. A score of 3 was associated with 37% risk of missed appointments and was chosen to indicate high risk. We validated our risk tool by determining scores for scheduled visits to our clinic from August-November 2013.

A total of 276 patients were scored. As the score increased from 1 to 5, the rate of missed appointments increased. A patient who had a score of 1 had a missed appointment rate of 0.15 vs. 0.43 in a patient who scored 3.

A risk prediction tool can be used to determine a patients' likelihood of missing an appointment. Interventions can be directed at those patients who score high on our risk tool.

Identifying High Risk Patients and Reducing Emergency Room Visits and Hospitalizations: Experience in a Resident Clinic

Berman DE, Gotfried JI, McFarland M, Jarrett H, Schorpion AM, Yan D, Lashner M, Gordon M, Shapiro W, Norberg S, Peters A, Li SK, Malamood M, Chisty A

Introduction: Decreasing unnecessary emergency room visits and hospitalizations is a universal goal for primary care practices. These two principles are the target of scrutiny when developing a patient centered medical home. Significant costs savings may result from identifying patients at high risk of overutilization of health care resources.

Methods: Our resident clinic sought to identify patients at risk for over- or unnecessary utilization of health care resources. We identified high risk patients as those with over three emergency department visits, hospitalizations, or outpatient 'No-Shows' in one year. Invited patients were enrolled and seen at a first intensive visit. A comprehensive care plan was developed and barriers to care identified after meeting with primary care physician, nursing staff, pharmacy, social worker, and community health worker. Additional data was gathered including Hemoglobin A1C, LDL, and other biomarkers before enrollment. Enrolled patients were seen on an as-needed basis, provided a CHW for external barriers to care, and received weekly nursing student phone calls.

Results: We enrolled 16 patients into our study. The mean ED visits in year prior to enrollment was 3.8 visits per patient, mean hospitalizations of 1.8, mean no shows 3.9. Monitoring will continue until May 1 followed by post-intervention analysis.

Conclusions: At the completion of our study, we hope to disseminate risk factors for overutilization of health care. Identifying high risk patients is easily accomplished in a resident internal medicine practice, especially in the setting of EHRs. We anticipate there is a significant cost savings by identifying high risk patients and implementing more intensive counseling, outreach, and communication in addition to usual care in this cohort.

Contemporary National Trends and Outcomes of Inferior Vena Cava Filter Placement in Cancer Patients with Proximal Lower Extremity Deep Vein Thrombosis

Yevgeniy Brailovsky DO, Chad J. Zack MD, Harish Jarrett MD, Huaqing Zhao Ph.D, Eric Choi MD, Grayson Wheatley MD, Riyaz Bashir MD

Background: The role of inferior vena cava (IVC) filter placement in cancer patients with proximal lower extremity Deep vein thrombosis (DVT) is unknown.

Methods: We used the Nationwide Inpatient Sample (NIS) database from 2005 to 2011 to identify all patients admitted with a principal discharge diagnosis of proximal lower extremity or caval DVT (ICD-9-CM 453.41, 453.2). Among a total of 25,218 cancer patients, 23.7% (5,977) underwent IVC filter placement. We evaluated the national trends in the utilization rates of IVC filter placement using unmatched patients. The comparative outcomes analysis was performed using propensity scores and Elixhauser comorbidity index to match the two treatment groups. After 1:1 matching we compared in-hospital outcomes between 5,679 matched pairs of patients treated with (Group A) and without IVC filter placement (Group B).

Results: The national IVC filter placement rates have been steady at 22.5% to 23.2% (p=0.255) in these patients during the seven-year study period. The comparative outcomes analysis of the matched groups showed that in-hospital mortality was not significantly different between the two groups (Group A 2.1% vs. group B 2.2%; p=0.746). The rates of blood transfusion (Group A 19.9% vs. group B 13.6%; p=0.0001) and pulmonary embolism (Group A 21.3% vs. group B 15.1%; p=0.0001) were significantly higher in group A. The filter group also had increased length of stay (Group A 6.7 \pm 6.9 vs. Group B 5.5 \pm 4.7 days; P<0.0001) and hospital charges (Group A \$ 50,077 \pm 57000 vs. Group B \$29159 \pm 41609; p<0.0001).

Conclusions: In this nationwide observational study we found that in-hospital morbidity with IVC filters remains higher in cancer patients, however the in-hospital mortality was not significantly different between the two groups. We also found that IVC filter placement was associated with increased costs and healthcare resource utilization.

Obtaining Patient Feedback in the Patient-Centered Medical Home (PCMH)

Justin Darrah, Brittney Katsoff, Saras Arasu

Introduction: The patient-centered medical home is a medical model focused on comprehensive care of patients, and is a widely accepted model for how primary care should be organized and delivered. The term patient-centered refers to the fact that patients are involved in the decision making of the medical home. Therefore, a requirement for becoming a patient-centered medical home is to have a way for patients to provide feedback to the medical home about their preferences. To that end, we worked to establish a system for obtaining patient feedback in our practice.

Methods: Prior attempts at using telephone surveys were unsuccessful. Therefore, paper-based surveys were used in a pilot study to obtain patient demographics. The surveys were distributed to patients at the time of check in, filled out in the waiting room, and then collected at the time of triage.

Results: Surveys were distributed over a 3 month period; a total of 61 surveys were returned. Numerous problems were identified with this method that made it inefficient. Less than half (46%) of patients had access to a computer; only 2% of patients wanted to be contacted by computer/email.

Conclusions: Paper-based surveys proved to be time intensive and inefficient, and will likely need to be replaced by another model in the future in order to be sustainable. In our patient population, computer-based surveys would be difficult to implement due to poor computer access. Possible future methods include electronic surveys in the waiting room or forming representative patient panels.

High Baseline Joint Pain in Women starting Aromatase Inhibitors for Breast Cancer

Jasmin Desai MD, Aruna Padmanabhan MD

Joint pain is a common complaint in medical practice. Aromatase inhibitors (AI) are commonly used to treat hormone positive breast cancer to reduce recurrences. 45% of patients taking AI have joint pain/ stiffness leading to AI discontinuation. This survey was initiated to understand baseline arthralgia/myalgia scores for patients starting AI therapy and throughout treatment.

The study was initiated at Temple Hospital Cancer Center in August 2013. Eligible patients were surveyed at baseline regarding site and severity of joint pain, fatigue, stiffness and co-morbid conditions. Follow-up questionnaires are being collected at 2, 4 and 6 month intervals.

The results of the baseline survey on 20 patients have been described: 55% (11) African American, 20% (4) Hispanic and 25% (5) Caucasian. 30% (6) of patients were overweight and 55% (11) obese by BMI. 90% (18) of patients had \geq 2 co-morbid conditions. 40% (8) of patients had osteoarthritis and 70% (14) had joint pain prior to initiation of AI. 50% (10) of patients were followed out to two months of AI use when 10% (1) patients had new complaints of myalgia and zero complained of arthralgia.

These preliminary results highlight the importance of assessing joint pain in patients eligible for AI therapy. We have a large minority, overweight population with pre-existing co-morbid conditions placing them at a higher risk for joint pains. Assessing increments in pain attributable to AIs will be challenging. We plan to follow results over time to evaluate worsening pain and its impact on discontinuation rates during AI therapy.

Appropriateness of Brain MRIs at Temple University Hospital Based on the ACR Appropriateness Guidelines and its Impact on Management

Andrew Friedman, Alexander Lane, Jeydith Gutierrez-Perez, Eduardo Castillo Dominguez, Swati Rao, John Davidyock, Darilyn Moyer, Ji Hoon Baang

The United States has the highest expenditure per capita and fastest growth when it comes to health care. Imaging is one of the fastest growing services in medicine reaching approximately \$100 billion annually. There have been criticisms that often imaging studies are over utilized and inappropriate which results in unnecessary costs and waste.

We reviewed brain MRIs done at Temple University Hospital during the period of January 2012 through May 2012 (n=315) to assess how appropriate they were based on the American College of Radiology (ACR) appropriateness guidelines and to see what the impact of brain MRIs were in terms of management. We were able to find that 63% of brain MRIs were "usually appropriate". Of these 67% lead to a change in management. Of note 28% the brain MRIs done during this period were categorized as "unclassified" which were clinical situations that was outside the scope of the ACR guidelines. Sixty percent of the unclassified exams lead to a change in management.

Although brains MRIs done at Temple University Hospital were considered "usually appropriate" in more than half of the cases there was still a significant percentage of brain MRIs that could've been avoided if the ACR criteria were applied. Of note, about a quarter of brain MRIs lay outside the scope of the ACR criteria and often lead to a change in management.

The Impact of Alemtuzumab and Basiliximab Induction on Graft and Recipient Survival in Orthotopic Lung Transplantation

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To assess the impact of Alemtuzumab, Basiliximab, and No Induction agents on patient survival and chronic rejection in orthotopic lung transplantation (OLT), 6343 patients were identified in the UNOS database 2006-2013, of which 764 (12%) received Alemtuzumab induction, 2890 (45.6%) received Basiliximab induction, and 2690 (42.4%) received no induction. Alemtuzumab recipients were older and more likely to be white; p<.001. Alemtuzumab recipients had donors who were less likely to be male and more likely to be white; p<.01. The groups were evenly matched in terms of recipient gender and donor age.

Alemtuzumab recipients had higher LAS, as compared to Basiliximab and No Induction, (41.8 vs. 38.0 vs. 41.0; p<.001), were less frequently race mismatched (31.4% vs. 43.6% vs. 42.4%; p<.001), and were more likely to require mechanical ventilation as a bridge to transplantation (21.7% vs. 7.1% vs. 7.1%; p<.001). Median survival time was longer for Alemtuzumab and Basiliximab recipients compared to patients that did not receive induction therapy (2301 vs. 2319 vs. 1900 days; p<0.001). The use of Alemtuzumab (HR: 0.79; p=0.003) and Basiliximab (HR: 0.83; p<0.001) were independently associated with survival on multivariate analysis. Variables associated with mortality included race mismatch, ischemic time, recipient creatinine and the use of ventilator pre-transplantation. The Alemtuzumab group had longer median time to BOS (2451 vs. 1476 vs. 1461 days; p<.0001).

While both induction therapies were associated with improved survival, patients that received induction therapy with Alemtuzumab had a longer median time to BOS.

Quantitative CT Patterns in Smokers Without Airflow Obstruction and Their Effect on Severe Respiratory Exacerbations

Jason S. Krahnke, Victor Kim, Huaqing Zhao, Nathaniel Marchetti, A. James Mamary, Gerard Criner, Michael Jacobs

Rationale: High-resolution CT (HRCT) has been used in recent years to quantify emphysema and airway disease in COPD. We hypothesized that patients with a significant history of smoking but who lack airflow obstruction on spirometry (FEV₁/FVC ≥0.7) will have a greater risk of respiratory exacerbations that rises with increasing percent emphysema and airway wall thickness.

Methods: Subjects included were smokers who had a FEV₁/FVC ratio ≥0.7 on spirometry from the COPDGene database. Subjects were divided into two groups based on a history of severe exacerbation within the past year prior to enrollment. Emphysema was assessed on HRCT by quantifying the low attenuation area (LAA) lower than -950 HU. Airway thickness was assessed by the square root wall area of Pi10 and Pi15 measures.

Results: 528 subjects were evaluated (264 subjects with a history of severe exacerbation and 264 matched controls without an exacerbation). Between the two groups there were no differences in baseline demographics, past medical history, smoking history, home O_2 use, or spirometry (Table 1). The severe exacerbation group had greater airway wall thickness as assessed by the Pi10 SRWA (3.75±0.15mm versus 3.72±0.12mm, P=0.04). Total percent LAA-950 and percent LAA-950 in the upper and lower lung thirds did not statistically differ between groups.

Conclusion: There are patients with a significant smoking history who suffer from severe respiratory exacerbations but do not have airflow obstruction. In this cohort, subjects with a history of severe respiratory exacerbation in the prior year had greater 10mm airway wall thickness, but similar measures of emphysema.

Post-Traumatic Stress Disorder is Strongly Associated with IBS in African Americans

Natalya Iorio MD, Kian Makipour MD, Amiya Palit MD, Frank Friedenberg MD

<u>Background</u>: Psychosocial stressors play a role in irritable bowel syndrome (IBS). IBS is more common in females and associated with emotional and physical abuse. Our aim was to explore the relationship between PTSD and IBS in an urban African American (AA) population.

<u>Methods</u>: A registry of AA in North Philadelphia was used for geographical mapping and complex sampling. Rome III criteria for IBS and Primary Care Post-Traumatic Stress Disorder screener (PC-PTSD) were administered. Norm-based physical (PCS) and mental (MCS) component summary scores from SF-36 v2 were calculated.

Results: 419 subjects corresponding to a weighted population of 21,264 were included (56.9% female; mean age 44.2 \pm 2.1 yrs). The weighted prevalence of IBS was 8.2 % and considerably higher in females (11.8 vs. 3.5%; P <0.001) and PTSD (19.5 vs. 5.0%; P <0.001). In regression analysis, female gender (OR=3.10; 2.70-3.57), age > 40 (OR=2.44; 2.14-2.79), college education (OR=4.47; 3.55-5.62), divorce (OR=1.35; 1.16-1.60), and PTSD (OR=2.03; 1.79-2.32) were independently associated with IBS. PTSD was independently associated with depression, anxiety, harmful drinking, substance abuse, and lower mean PCS (42.9 \pm 10.2 vs. 47.6 \pm 10.2) and MCS (39.2 \pm 11.1 vs. 54.6 \pm 9.9) QOL scores.

<u>Conclusions</u>: The prevalence of IBS in our sample of urban AA was 8.2%. After adjusting for confounders, the risk of IBS was 2-fold higher in those suffering from PTSD. PTSD was associated with adverse lifestyle choices and poor impact on QOL. Screening for PTSD in AA patients under evaluation for IBS may be beneficial.

Comparative Outcomes of Catheter Directed Thrombolysis Plus Anticoagulation Versus Anticoagulation Alone in the Treatment of Proximal Deep Vein Thrombosis in Patients with Chronic Kidney Disease

Yevgeniy Brailovsky, Harish Jarrett, Chad Zack, Huaging Zhao, Riyaz Bashir

Background: The nationwide safety outcomes and the role of catheter-directed thrombolysis (CDT) in the treatment of deep vein thrombosis (DVT) in patients with chronic kidney disease (CKD) are unknown.

Methods: We used the Nationwide Inpatient Sample (NIS) database from 2005 to 2011 to identify all patients admitted with a principal discharge diagnosis of proximal lower extremity and caval DVT in patients with chronic kidney disease. In these patients, we evaluated the inhospital outcomes and trends in the utilization rates of CDT. We compared in-hospital outcomes between the matched groups treated with CDT plus anticoagulation (Group A – 306 patients) vs. anticoagulation alone (Group B - 306). We used propensity scores and Elixhauser comorbidity index to match the two treatment groups.

Results: Among a total of 11,613 CKD patients admitted with principal discharge diagnosis of proximal lower extremity or caval DVT, 2.7% (309) underwent CDT. The national CDT utilization rates in these patients gradually increased from 1.4% in 2005 to 3.4% in 2011. Females were less likely to be treated with thrombolysis (2.1% versus 3.3%; p <0.001). In-hospital mortality was not significantly different between the CDT group and the anticoagulation alone group (2.9% versus 1.3%; p= 0.262). The rates of blood transfusion, pulmonary embolism, intracranial bleeding, vena caval filter placement, and acute renal failure were significantly higher in the CDT group. The CDT group also had significantly increased length of stay (9.97±9.1 vs. 6.83 ± 5.5 days; p<0.001) and hospital charges (\$104334 \pm 80789 vs. \$42141 \pm 59031; p<0.001) than the anticoagulation alone group.

Conclusions: In this nationwide observational study of CKD patients, we found that in-hospital morbidity with CDT remains higher than anticoagulation alone, however the in-hospital mortality was not significantly different between the two groups.

An Unusual Cause of Acute Coronary Syndrome

Harish Jarrett, Dharmini Shah, Daniel Edmundowicz

Introduction: Contemporary management of symptomatic coronary artery disease often involves the use of coronary stents. Coronary stent fracture is an increasingly reported, under-recognized complication following drug-eluting stent (DES) implantation; however, bare metal stent (BMS) fracture is extremely rare. We describe a case of a BMS fracture resulting in an acute coronary syndrome.

Case description: An 82-year old man presented with resting anginal chest pain and was diagnosed with an acute coronary syndrome. He had previously required four coronary artery bypass grafts for similar symptoms in 1998 and had symptom recurrence in 2006 needing implantation of two BMS to his native first diagonal branch. Angiography revealed significant instent re-stenosis with stent fracture at the site of the proximal BMS. Percutaneous coronary intervention with a DES at the site of the stent fracture resulted in complete resolution of his symptoms.

Discussion: Stent fracture is an uncommon complication of coronary stent implantation. It increases risk of in-stent re-stenosis with need for target lesion revascularization and sudden cardiac death. Reported incidence rates vary between 0.84% - 8.4%. Predictors of stent fracture relate to shear and hinge stress. These include right coronary artery location, overlapping stent placement, stent length and high vessel tortuosity. Optimal management of this problem is unclear. Repeat stent placement, as in our case, provides symptom relief; however, the new stent will be subject to the same stresses in an at-risk area for re-stenosis. Further research and technological advancement is needed to prevent an increasingly recognized complication of a common intervention.

Contemporary National Trends and Outcomes of Catheter Directed Thrombolysis in Patients with Proximal Lower Extremity Deep Vein Thrombosis

Harish Jarrett, Michael Lashner, Chad Zack, Huaqing Zhao, Eric Choi, Grayson Wheatley, Riyaz Bashir

Background: The role of catheter-directed thrombolysis (CDT) in patients with proximal lower extremity deep venous thrombosis (DVT) is controversial. However, the contemporary national trends in CDT utilization rates and outcomes are unknown.

Methods: We used the Nationwide Inpatient Sample (NIS) database from 2005 to 2011 to identify all patients admitted with a principal discharge diagnosis of proximal lower extremity or caval DVT (ICD-9-CM 453.41, 453.2). Among a total of 108,243 patients, 4.5% (4826) underwent CDT. We evaluated the national trends in CDT utilization rates and in-hospital outcomes in these patients.

Results: The national rate of CDT utilization in the overall group increased from 2.3% in 2005 to 6.7% in 2011 (p<0.01). CDT rates for caval DVT increased from 16% in 2005 to 34.7 % in 2011 (p<0.01). The in-hospital mortality rate in patients undergoing CDT decreased from 1.4% in 2005 to 1.0% in 2011. The rates of blood transfusion, pulmonary embolism, and IVC filter placement remained steady in both groups during the study period. From 2005 to 2011 a significant increase in hospital charges of \$69,065 to \$104,925 (p<0.001) and a decrease in length of stay of 7.8 days to 6.9 days (p=0.003) associated with CDT was also noted.

Conclusion: In this nationwide observational study, we found that CDT utilization rates are increasing significantly in the United States in patients with proximal lower extremity and caval DVT. We also found that CDT utilization was associated with increased costs and healthcare resource utilization.

Atherosclerotic Cardiovascular Disease in African-Americans: More than LDL Lowering

Harish Jarrett MD, Estefania Oliveros MD, Sara Sirna MD, Alfred Bove MD

BACKGROUND: African Americans (AA) have a high ASCVD burden and are less likely to achieve target LDL levels compared with Hispanics (H) and Caucasians (C). We conducted a retrospective cohort study to determine relationships between race, LDL goal attainment and ASCVD.

METHODS: Electronic medical records were studied from 2009 to 2013. Patients with fasting lipid panel with therapy initiation and repeat testing between 3-12 months were included. Goal attainment was recorded for LDL. We analyzed the effect of age, gender, tobacco use, BMI, hypertension and Charlson co-morbidity index on achieving LDL targets using analysis of variance and multivariate logistic regression.

RESULTS: We identified 364 patients (58.8% AA, 23.1% H and 15.7% C). Mean LDL levels (mg/dl) were similar between AA (106.5±42.4), C (110.4±47.2) and H (109.17±45.1). There was a high prevalence of tobacco use (68.4%), hypertension (90.7%), ASCVD (66.5%) and diabetes (41.8%). AA constituted 61.6% of patients with ASCVD, they were more likely to have hypertension (P=<0.001), diabetes (P=<0.001) and had higher HDL levels (P=0.003). No significant race effect was noted with LDL goal attainment following statin therapy (P=0.59). The presence of peptic ulcer disease (P=0.04) and chronic kidney disease (P=0.05) correlated with not reaching LDL goal.

CONCLUSION: No relationship between race and LDL goal attainment was demonstrated. Baseline LDL levels described here in a highly co-morbid population are much lower than previously reported in the literature. Higher prevalence of ASCVD in AA population suggests that optimal hypertension and diabetes management may be of equal importance to LDL goal attainment.

A Paradox of Anticoagulation: Warfarin Induced Skin Necrosis

Asad Javed MD, Gina M. Simoncini

A paradox of Anticoagulation: Warfarin Induced Skin Necrosis

A 63 year old woman with a history of gastric adenocarcinoma and a newly diagnosed DVT presented with a tender 'rash' on her left breast. She was on bridging anticoagulation with warfarin and Low Molecular weight heparin (LMWH). She reported not administering the LMWH and taking the warfarin, four days later she noticed the painful rash. A diagnosis was Warfarin skin necrosis was made; she was treated with FFP, Vitamin K and switched to Fondapurinox for anticoagulation. Her skin lesions resolved over the next 3 days. Skin necrosis is a rare but dangerous complication of warfarin therapy, often necessitating surgical intervention if therapy is delayed. Its prompt recognition and treatment can be life-saving.

Contemporary National Trends and Outcomes of Inferior Vena Cava Filter Placement in High Bleeding Risk Patients with Proximal Lower Extremity Deep Vein Thrombosis

Michael Lashner DO, Chad J. Zack MD, Huaqing Zhao Ph.D, Eric Choi MD, Grayson Wheatley MD, Riyaz Bashir MD

The role of inferior vena cava (IVC) filter placement in patients with proximal lower extremity deep vein thrombosis (DVT) is controversial but mainly indicated for those patients at high risk of bleeding during anticoagulation. The nationwide outcomes and utilization rates are unknown.

We used the Nationwide Inpatient Sample database from 2005 to 2011 to identify all patients admitted with a principal discharge diagnosis of proximal lower extremity or caval DVT (ICD-9-CM 453.41, 453.2). Among a total of 5,796 patients at high risk for bleeding, 43% (2506) underwent IVC filter placement. We evaluated the national trends in the utilization rates of IVC filter placement using unmatched patients. Patients who underwent IVC filter (Group A) were compared with those who did not (Group B). We used propensity score matching with 48 variables including the Elixhauser comorbidity index, patient demographics and hospital characteristics for match comparison between the two groups. After 1:1 matching, we compared outcomes in 2,093 patients in each group.

The national IVC filter placement rates have ranged between 42% to 46% (p=0.147) during the seven-year study period. The comparative outcomes analysis of the matched groups showed that in-hospital mortality was not significantly different between the two groups (Group A - 3.0% versus group B 3.1%; p= 0.856). The rates of blood transfusion, pulmonary embolism, and acute renal failure were significantly higher in Group A. The filter group also had increased length of stay (Group A 9.3 \pm 8.3 versus Group B 8.1 \pm 7.9 days; P < 0.001) and hospital charges (Group A \$ 68426 \pm 77977 versus Group B \$49651 \pm 74637; p<0.001).

In this nationwide observational study, we found that in-hospital morbidity with IVC filters remains higher even in high bleeding risk patients; however, the in-hospital mortality was not significantly different between the two groups. We also found that IVC filter placement was associated with increased costs and healthcare resource utilization.

The Effect of Thyroid Function on the Acute Heart Failure Exacerbation: A Retrospective Study

Meredith A McFarland, MD, Qalb Khan, MD, Rene J Alvarez, MD, Ajay D Rao, MD, MMSc

Background: Studies examining the association between thyroid function and all-cause mortality have yielded conflicting results, mostly because of heterogeneity of baseline cardiovascular risk. A direct link between TSH and cardiac function has been lacking. A functional thyrotropin receptor has been found to be expressed in ventricular myocytes and has been implicated in TSH-induced brain natriuretic peptide (BNP) secretion, suggesting direct functional effect of TSH on the heart(1). In a recent NHANES study, hypothyroidism was associated with greater mortality as compared to euthyroidism in those participants with congestive heart failure (CHF)(2). Hypothyroidism was also associated with greater mortality in Blacks with CHF(2). We hypothesized that thyroid function status would be a predictor of morbidity in patients admitted with acute heart failure exacerbations as measured by BNP, ejection fraction (EF), and hospitalizations in a predominantly non-white population.

<u>Methods</u>: We conducted a retrospective study at Temple University Hospital (TUH, Philadelphia, USA). We identified admissions for heart failure to the TUH Heart Failure Service during the calendar year 2012 with TSH values drawn during the inpatient admission. Data extracted included race, age, gender, thyroid function, any prior history of hypothyroidism, EF, amiodarone use, creatinine level, brain natriuretic peptide level, and history of drug or alcohol abuse. We also measured the total number of hospitalizations these patients had for an acute heart failure exacerbation from January 2012 to December 2013.

Results: 344 admissions for heart failure were examined during the calendar year 2012. The population was predominantly male (62% male) with mean age of 59 ± 14 years and mostly Black (66% Black, 9% Hispanic, 15% White). Median ejection fraction was 25% (interquartile range (IQR) 15-45%) and median BNP was 1134 pg/mL (IQR 361-1930 pg/mL). Median TSH was 1.88 mIU/L (IQR 0.983-3.44 mIU/L) and TSH was above the upper limit of normal of the hospital assay (>5.10 mIU/L) in 15% of the admissions. Both TSH (r=0.15, p=0.01) and EF (r=0.34, p<0.01) significantly correlated with BNP. In those admissions where TSH > 5.10, BNP was significantly higher (1923 ±185 pg/mL vs 1245 ±76 pg/mL, p=0.0008). TSH did not correlate with hospitalizations during the calendar years 2012-2013. Having a TSH > 5.10 was a significant predictor of BNP (p=0.04), even after accounting for age, gender, ethnicity, # of hospitalizations, and EF.

<u>Conclusions</u>: This retrospective study demonstrates an association between thyroid status and cardiac function in mostly non-white individuals admitted for CHF. Potential cross-talk between TSH and natriuretic peptides may be a further line of inquiry within these racial/ethnic groups. Definitive studies examining the role of thyroid supplementation and their effect on BNP in this population is needed.

- (1) Huang et al., Endocrine 2013 Sep 26 Epub ahead of print.
- (2) Rhee et al., JCEM 2013 Jun;98(6):2326-36.

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A Case of Coronary Vasospasm Caused by Undiagnosed Hyperthyroidism

Meredith McFarland, MD, Matthew Gordon, MD, Kristian Holmes, MD, Sara Sirna, MD

Coronary vasospasm is a transient constriction of the coronary arteries, diagnosed by angiographic evidence of reversible constriction. Untreated, this vasospasm may result in anginal symptoms, and ultimately, myocardial ischemia and necrosis. Adding to the growing body of literature identifying hyperthyroidisms as a causal agent in coronary vasospasm is the case of a 53 year old male with four weeks of unstable angina associated with a 20lb unintentional weight loss.

On arrival, an NSTEMI and persistent sinus tachycardia was noted. Given the age and risk factors, the patient was treated for acute coronary syndrome (ACS) without significant improvement in symptoms. A left heart catheterization was performed, where coronary vasospasm of the mid left anterior descending artery (LAD) was identified on angiography, with subsequent reversal during administration of nitrates. Concurrent evaluation of unintentional weight loss revealed thyrotoxicosis. Subsequent administration of calcium channel blockers, long acting nitrates, and methimazole resulted in complete resolution of angina symptoms.

Coronary vasospasm is a debilitating condition with significant morbidity and mortality. If left untreated, patients can develop significant cardiac ischemia and subsequent cardiovascular failure. Our case adds to the growing body of evidence supporting hyperthyroidism as a causal and more importantly reversible agent in coronary vasospasm.

Spontaneous Tumor Lysis Syndrome in Renal Cell Carcinoma - A Case Report

Scott Michael Norberg, D.O.; Michelle Oros, D.O.; Mark Birkenbach, M.D.; Marijo Bilusic, M.D., PhD

Spontaneous tumor lysis syndrome (STLS) is a rare oncologic emergency caused by acute and massive death of tumor cells prior to the initiation of any anti-cancer therapy. It is commonly associated with aggressive hematological malignancies; however, it has been more frequently recognized in multiple solid tumors. Our literature search of STLS in solid tumors revealed these common characteristics: large primary tumor with metastatic disease involving the liver and bones and elevated levels of uric acid and lactate dehydrogenase (LDH). In this report, we describe, to our knowledge, the first case of STLS caused by an aggressive, poorly differentiated renal cell carcinoma and discuss the utility of using LDH and uric acid as screening tests in patients with extensive metastatic disease.

Severe Thrombocytopenia Due to Macrophage Activation Syndrome Borne from Adult Onset Still's Disease

Anand Patel, MD and Michael Bromberg, MD, PhD

Macrophage Activation Syndrome (MAS) is an uncommon syndrome in which cytokine storm and disregulation of macrophages can rapidly progress to lethal cytopenias.

A 61 year old woman developed profound thrombocytopenia after suffering polyarthritis of small and medium joints, salmon colored truncal rash, subjective fever and malaise for 4 months. Systemic steroids given at an outside hospital resolved the rash, but she developed ferritin of >30,000 and platelet count of 17,000.

Adult onset Stills (AOS) Disease was suspected, as she fulfilled 4 major criteria (polyarthritis, truncal rash, persistent fever and leukocytosis) and 2 minor criteria (elevated ferritin and splenomegaly).

Ferritin remained elevated, and hypocomplementemia, elevated ESR and CRP were noted. Thrombocytopenia worsened to a platelet nadir of 10,000.

Empiric treatment for MAS with intravenous immunoglobulin (IVIG) was ineffective, so serum levels for the soluble IL-2 receptor, CD-25, and a bone marrow biopsy were checked, and the CD-25 was markedly elevated at 2442, and bone marrow showed a rare hemophagocytic histiocyte amidst increased megakaryocytes; both the hemophagocytic macrophage and the elevated CD-25 were consistent with MAS.

Anakinra, an IL-1 receptor antagonist with reported success treating some known precipitants of MAS, including Still's disease and Juvenile Rheumatoid Arthritis, was given along with steroids. Over one week, her arthralgias, fever, and thrombocytopenia resolved.

This case demonstrates the potential cytopenic crises due to MAS, which require tailored hematologic therapy. Recognizing symptoms of Still's disease and identifying its association with MAS aides in prompt diagnosis and treatment for rapidly progressive and life threatening hematologic emergencies.

A Case of Unrecognized May-Thurner Syndrome Leading to Recurrent Pulmonary Embolism

Jeydith Gutierrez Perez, Eugene Brailovsky, Estefania Oliveros, Vladimir Lakhter, Riyaz Bashir

May-Thurner syndrome or iliac compression syndrome occurs as the result of repetitive compression of the left common iliac vein by the overlying right common iliac artery against the lumbar spine. Besides the physical compression this also results on a thickening or "spur" within the vessel, likely due to inflammation. May-Thurner syndrome usually affects young women and presents with leg symptoms including deep venous thrombosis (DVT), chronic venous stasis, pain or swelling of the left leg. Less commonly this can lead to further complications including pulmonary embolism. We present an unusual case of a 45 year old female with recurrent pulmonary embolisms despite anticoagulation and no findings of peripheral DVTs. She was treated with anticoagulation and placement of an inferior vena cava (IVC) filter. Months after, she presented with abdominal pain and was found to have complete IVC thrombosis associated with the IVC filter. After thrombolysis was performed, a venogram confirmed the diagnosis of May-Thurner syndrome, possibly associated with the recurrent pulmonary embolisms. The patient was successfully treated with endovascular stent and anticoagulation. May-Thurner or lliac compression syndrome is generally underdiagnosed and should be considered when pulmonary embolism presents without an obvious cause.

Behavioral Locus of Control and Reduction of Cardiovascular Risk

Val Rakita, Carol Homko, Abul Kashem, Alfred A. Bove

Background: Cardiovascular disease (CVD) is not only the most widespread chronic illness in the United States, but is also the leading cause of morbidity and mortality. Risk modification may be the function of differences in multidimensional health locus of control (MDHLC), which can influence decision making about healthy behaviors.

Methods: Secondary analysis of a prospective, randomized trial among an underserved innercity 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 asked to fill out a Behavioral Locus of Control Questionnaire to assess their beliefs with regards to health-related issues and determine their MDHLC (Internal, Powerful Others, or Chance).

Results: The average patient age was 61.3 ± 10.1 years, average A1C was $6.7 \pm 1.6\%$, average total cholesterol was 201 ± 44 mg/dl. The average BMI was 31.8 ± 6.4 kg/m², and the average blood pressure was $146 \pm 18/82 \pm 11$ mm/Hg. In a multivariate regression analysis controlling for age, gender, ethnicity, and health knowledge, those with the Internal Locus of Control showed a statistically significant (p=0.047) reduction in CVD risk, compared to those with an external locus of control (Powerful Others or Chance), with Powerful Others trending toward significance.

Conclusion: Traditional views of risk factor modification have not shown to be as promising as once thought. Targeting patients' locus of control and focusing on behavioral modification, specifically taking advantage of their internal motivations and possibly their response to external influence by healthcare professionals, can lead to more significant CVD risk reduction.

Gastroesophageal Reflux and Dysmotility in End Stage Lung Disease Patients

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Background: Gastroesophageal Reflux (GER) has been implicated in the development of idiopathic pulmonary fibrosis (IPF) and worsened prognosis following lung transplantation. Our aim was to assess the prevalence of esophageal dysmotility and GER in patients with IPF and symptomatic chronic obstructive pulmonary disease (COPD) patients undergoing evaluation for lung transplantation, and to evaluate whether the presence of GER-associated symptoms could predict abnormal test results.

Methods: All patients with IPF and GER-symptomatic COPD evaluated for lung transplantation at our institution between January 2009 and July 2013 were included and underwent esophagram, manometry (HREM), and/or pH testing with quantitative reflux testing.

Results: 265 patients underwent transplant evaluation during this time period, of which 136 had COPD and 100 had IPF. HREM was performed in 16 symptomatic COPD and 40 IPF patients. Esophageal dysmotility was defined as less than 80% peristaltic swallows or a reduced mean distal amplitude of contraction (<43 mmHg). 31% of symptomatic COPD patients had esophageal dysmotility on HREM, compared to 50% of IPF patients (p=0.24). Increased reflux was seen in 29% of symptomatic COPD patients, compared to 55% of IPF patients (p=0.09). Overall, 80% of IPF patients had abnormal HREM and/or quantitative reflux testing, with only 56% reporting GER symptoms.

Conclusion: There is high prevalence of esophageal dysmotility and GER in patients with IPF being evaluated for lung transplant. Around half of the IPF patients with abnormal testing were asymptomatic, underscoring the need to consider esophageal testing for "silent" GER in all IPF patients being evaluated for lung transplant.

COPD Patients with Greater Rate of Change in Daily Peak Expiratory Flow Have More Disease Instability

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Rationale: COPD is a major cause of morbidity, mortality and cost to the US healthcare system. Peak expiratory flow rate (PEFR) monitoring could provide a daily objective measurement of lung function in COPD patients at home. We hypothesized that subjects with greater variability in daily PEFR would signal an unstable patient population with worse outcomes.

Methods: We conducted a retrospective analysis of prospectively collected data in COPD patients using an electronic diary to record daily PEFR dyspnea, sputum quantity, color, thickness, cough, wheezing, sore throat, nasal congestion, and temperature. Patients with GOLD grades \geq 3 with >14 days of data were analyzed. Rates of PEFR change were used to characterize patients into stable (absolute slope \leq ±0.3) and unstable (absolute slope \geq ±0.3) groups. Exacerbation-free days, hospitalization days, 6MWD, time to first exacerbation and all-cause mortality were assessed.

Results: 58 COPD patients were observed for 20,958 patient-days. The absolute slope of PEFR change was $> \pm 0.3$ in 35 [*unstable*] and $\leq \pm 0.3$ in 23 [*stable*] patients. There were no significant differences in symptoms, demographics, baseline FEV₁, FVC, TLC, or comorbidities between groups. The RV was smaller (164.8 vs. 193.8% predicted, p=0.04) and more patients were on oral steroids (68.6 vs. 39.1%, p=0.03) and inhaled steroids (97.1 vs. 78.3%, p= 0.02) in the unstable group compared to the stable group (Table 1). The unstable group had significantly fewer exacerbation-free days (160 vs. 280 days, p=0.003), shorter time to first hospitalization (137.1 vs. 288.6 days, p=0.01), and shorter 6MWD (216.4 vs. 276m, p=0.03). There were also more deaths (5 vs. 2) in the unstable vs. stable group.

Conclusion: Patients with moderate to severe COPD with greater changes in PEFR (unstable group) have less exacerbation free days, shorter 6MWD, and reduced time to first hospitalization despite similar demographic, spirometric and comorbid parameters. Daily home peak flow monitoring can be a useful tool in identifying less stable COPD patients prone to more frequent and severe exacerbations.

Strongyloides Hyperinfection Mimicking Endocarditis

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A 59-year-old Puerto Rican male with a history of polysubstance abuse, pulmonary embolism, non-ischemic cardiomyopathy, and hepatic abscess six months ago presented to the emergency department with abdominal pain and right knee pain for one week. On admission, he was febrile, tachycardic and jaundiced. Exam was notable for right upper quadrant tenderness and right knee warmth and tenderness with effusion and decreased range of motion.

CT scan of the abdomen demonstrated new irregularly shaped hypodensities throughout the liver concerning for micro abscesses and splenic infarct. Blood cultures, urine cultures, and synovial fluid grew *Escherichia coli*. Despite antibiotics he remained bacteremic for 9 days. Subsequent synovial fluid cultures grew *E. coli* despite multiple washouts of the right knee joint. The persistent gram-negative bacteremia and his tropical origins prompted us to evaluate for *Strongyloides* hyperinfection. His course was complicated by osteomyelitis of right sternoclavicular joint with septic arthritis requiring resection a rib, clavicle and part of manubrium after treatment for 6 weeks. Bone cultures were negative, presumably due to antibiotics, but pathology showed subacute osteomyelitis.

Repeat CT scan after two weeks of treatment showed a decrease in the number and size of the liver hypodensities.

Our patient presented with symptoms mimicking endocarditis. The fact that his bacteremia cleared after ivermectin suggests SHS. SHS classically presents as fever, nausea, vomiting, diarrhea, dyspnea and wheezing. Mortality from untreated *SHS* approaches 100% and exceeds 25% with treatment.

Strongyloides hyperinfection should be considered in patients from endemic areas with unexplained gram-negative bacteremia, even if immune competent.

Medical Students Learning Global Health through Service: Temple Emergency Action Corps Service Trip – Managua, Nicaragua, 2014

Katherine Selman, Daniel Zarif, Paul Navo, Emily Kirchner, Corbin Muetterties, Manish Garg, Ellen Tedaldi, Eileen Farnon, on behalf of the 2014 Temple Emergency Action Corps Nicaragua team

Background: The Temple Emergency Action Corps (TEAC) was established in 2005 by a group of medical students responding to Hurricane Katrina. Its mission is to provide students with education and practical opportunities in disaster relief. Funded by the Greenfield Foundation, TEAC activities include domestic and international medical service projects.

Methods: During March 31—April 4, 2014, TEAC established a temporary clinic in Barrio Grenada, a community in Managua, Nicaragua affected by poverty and annual flooding where TEAC had worked during 2012. The team included 14 medical students, one resident and two attending physicians from Temple, partnered with logisticians and translators from Compañeros, Inc., a private organization facilitating service projects in Nicaragua. First-year and upper-year students were paired and rotated daily among six teams. One team performed triage and five teams interviewed and examined patients before presenting to the physicians. Two first-year students managed the pharmacy, which included medications packaged in standardized treatment courses for common conditions.

Results: During five days, we saw a total of 356 patients. Of these, 163 (45.8%) were aged ≤12 years. Common diagnoses included respiratory infections, musculoskeletal strains, and headaches. We also dispensed deworming medications to children, vitamins, and toothbrushes.

Conclusions: For future trips, we recommend preparing for a large proportion of pediatric patients, and increasing connections with the local medical system to inform counseling and management of chronic conditions in a temporary clinic. The TEAC team was well received by the community and provided a valuable experience for students interested in Global Health.

Spontaneous MAVS Aggregation May Contribute to Excessive Type I Interferon in SLE Patients

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Increased levels of IFN-I and increased transcription of IFN-I inducible genes are characteristic of systemic lupus erythematosus (SLE). Because IFN-I has a key role in immune responses. heightened levels of this cytokine and the many genes it activates may underlie the immune hyperreactivity and autoimmunity of SLE. The RIG-I anti-viral pathway is an important regulator of IFN-I production and could explain its increase in SLE. In response to viral nucleic acid, RIG-I activates the mitochondrial adaptor protein MAVS, leading to subsequent IFN production. Activated MAVS forms large prion-like aggregates, which might reflect RIG-I activation and which could be detectable ex vivo in SLE patients. To investigate the role of MAVS in SLE, Mitochondria lysates were prepared from SLE patients and control blood, and MAVS aggregation was identified with semidenaturing gel and confocal immunofluorescence microscopy. Twenty-two of 61 SLE patients showed clear MAVS aggregation, yet none of the RA patients and only three of 33 healthy controls had abnormal MAVS. 82.4% MAVS-aggregate positive SLE patients had anti-SSA antibodies, compared to 40% MAVS-aggregate negative patients, p<0.01 by Chi-square. 64.7% aggregation-positive patients had active SLE disease (skin rash, arthritis, increased ESR, low C4, and active renal disease), compared to 10% of the aggregation-negative patients. Our findings are consistent with the notion that activation of the RIG-I pathway through inappropriate or persistent MAVS aggregation may lead to increased IFN-I production, immune stimulation, and systemic autoimmunity in SLE.