Eastern Regional Meeting
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Scientific Session I
Cardiovascular, Endocrinology/Metabolism
8.30AM – 10.30AM

1 VITAMIN D REPLETION REDUCES ADIPOSE TISSUE FIBROSIS AND IMPROVES INSULIN SENSITIVITY

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Purpose of Study Adipose tissue fibrosis has been implicated as a contributing factor to insulin resistance and adipose inflammation in obesity. Vitamin D (vit D) has been shown to reduce fibrosis in other tissue types by inhibiting pro-fibrotic processes and collagen synthesis. Thus we hypothesized that vit D repletion could reduce adipose tissue fibrosis and improve insulin sensitivity.

Methods Used In a randomized, double-blind, placebo-controlled trial, stepped euglycemic, hyperinsulinemic (30 and 80 mU/m^2/min) clamp studies were performed in 19 obese and insulin resistant human subjects with vit D deficiency (~13 ng/ml) to quantify endogenous glucose production (EGP) and glucose uptake (GU) before and after placebo or sufficient vit D therapy to normalize vit D levels (>30 ng/ml).

Summary of Results After vit D repletion, we observed that expression of the pro-fibrotic genes TGF-β1, HiF1α, Collagen I, V, VI and MMP7 in whole fat decreased by 0.81, 0.72, 0.56, 0.56, 0.43, and 0.62-fold, respectively (all $p<0.05$). Collagen I immunofluorescence decreased by 61% ($p=0.04$). In addition, adipose tissue inflammation also decreased significantly with 0.67, 0.61, 0.71 and 0.70-fold decreases of expression of the following pro-inflammatory factors: TNF-α, IL-6, iNOS and PAI-1 (all $p<0.05$). The expression of the same pro-inflammatory factors in adipose tissue macrophages also decreased by 0.44, 0.32, 0.53 and 0.70-fold, respectively (all $p<0.05$). Importantly, these findings were associated with a 24% greater ability of insulin to suppress EGP ($p=0.04$). GU, however, did not show significant change. In the placebo group, there were no significant changes in expression of pro-fibrotic or pro-inflammatory genes (all $p>0.05$), although there was an intriguing trend toward worsening fibrosis and inflammation as well as hepatic insulin resistance when followed for 6 months.

Conclusions Vit D repletion elicited three beneficial effects in obese, insulin-resistant humans: reduced adipose tissue fibrosis, improved hepatic insulin sensitivity, and decreased adipose tissue inflammation. Thus, correcting vit D deficiency in obese, insulin resistant individuals may have favorable metabolic effects, and might therefore have public health benefits in light of the obesity epide2mic.

2 LIPID RICH PLAQUE BY CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY ASSOCIATES WITH CHOLESTEROL EFFLUX CAPACITY INDEPENDENT OF TRADITIONAL CARDIOVASCULAR RISK FACTORS IN THOSE AT RISK FOR MYOCARDIAL INFARCTION

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Purpose of Study Cholesterol efflux capacity (CEC), a measure of high density lipoprotein (HDL) function, has been shown to be associated with future cardiovascular (CV) events. Lipid rich plaque is associated with higher plaque rupture and future CV events, and can be readily phenotyped by coronary CT angiography (CCTA). Whether CEC associates with lipid rich plaque is not known and can inform preventive strategies for reducing future MI.

Methods Used Consecutively recruited patients (N=94) underwent CCTA (Toshiba 320 slice) to assess plaque burden within the coronary arteries by QAngio CT (Medis, The Netherlands). CEC was measured using an ex vivo validated assay.

Table 1: Demographic and clinical characteristics of the study groups.

Variable	N=94
Demographic and clinical characteristics	
Age, years	60.88 ± 8.50
Males, N (%)	50 (53.19%)
Statin Treatment, N (%)	50 (53.19%)
Body Mass Index, kg/m^2	29.37 ± 6.48
Race Distribution	
Caucasian	66 (70.21%)
African American	15 (15.96%)
Asian	12 (12.77%)
Unknown	1 (1.06%)
Clinical and Lab values	
SBP, mm Hg	115.17 ± 14.56
DBP, mm Hg	61.01 ± 10.61
Total Cholesterol, mg/dL	178.35 ± 32.52
HDL Cholesterol, mg/dL	58.53 ±17.04
LDL Cholesterol, mg/dL	92.73 ± 30.03
TG, mg/dL (Median [IQR])	112.25 (77-160)
Cholesterol Efflux Capacity	1.03 ± 0.17
Coronary Plaque Burden	
Total Plaque (x100), mm^2 (Median [IQR])	1.05 (0.79-1.37)
Lipid Rich Plaque (x100), mm^2 (Median [IQR])	1.00 (0.77-1.33)
Calcified Plaque (x100), mm^2 (Median [IQR])	0.005 (0.002-0.027)

Values reported in the table as Mean±SD or median (IQR) for continuous variables and as N (%) for categorical variables.

Abstract 2 Figure 1

*denotes Eastern Scholar Awardee. Bold denotes presenting author.

Summary of Results The study population mean age was 61 and had normal cholesterol, HDL, low density lipoprotein (LDL), and triglyceride levels (Table 1). CEC was 1.03 ±0.17 while total plaque and lipid rich plaque were 1.05 (0.79–1.37) mm^2 and 1.00 (0.77–1.33) mm^2, respectively. Lipid rich plaque inversely associated with CEC beyond adjustment for age, gender, systolic blood pressure, statin treatment, total cholesterol, LDL, and HDL (β= –0.18, p=0.002).

Conclusions CEC associated with lipid rich plaque independent of CV risk factors. These findings suggest early atherogenesis may be tightly related to HDL function and that strategies to improve HDL function may mitigate future MI. Longer prospective studies are needed to confirm these findings.

3 IMPACT OF OPIOID AND ADRENERGIC RECEPTOR ACTIVATION ON HYPOGLYCEMIA-ASSOCIATED AUTONOMIC FAILURE (HAAF)

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Purpose of Study Attainment of tight glycemic goals in type 1 diabetes is limited by iatrogenic hypoglycemia. Antecedent hypoglycemia and exercise lead to blunting of counter-regulatory responses and Hypoglycemia-Associated Autonomic Failure (HAAF). Since hypoglycemia and exercise are associated with a rise in both endorphins and epinephrine, it is vital to establish whether activation of opioid and/or adrenergic receptors contribute to HAAF.

Methods Used Twenty three healthy, non-diabetic subjects (13 M, 7 F, age 30.5±7.3 years, BMI 24.5±2.9 kg/m^2, HbA1c 5.4±0.3%) underwent paired, saline-controlled 2 day study protocols. On Day 1 the subjects received infusions of epinephrine (EPI, 0.03 μg/kg/min, n=11) or morphine (MOR, 0.1 μg/kg/min, n=12) from t=0–2 h and t=4–6 h. On Day 2 all subjects underwent 200 min stepped hypoglycemic clamps (nadir 60 mg/dL) with evaluation of epinephrine responses, endogenous glucose production (EGP, using 6,6-D2-glucose), and hypoglycemic symptoms. All subjects also underwent a normal saline (SAL, n=20) study with hypoglycemic clamp, in random order at least 3 weeks apart from the EPI or MOR studies.

Summary of Results Compared with saline, morphine induced a 30% reduction in epinephrine response to hypoglycemia (at 60 mg/dL glucose step SAL=419.4±20.4 pg/mL vs MOR 292.5±15.7 pg/mL, p=0.02), a small reduction in EGP that reached significance at the 80 mg/dL glucose step (P=0.04), with significantly fewer hypoglycemic symptoms (p=0.03). Conversely, while there was a trend toward lower plasma epinephrine responses in the studies in which EPI was infused on day 1 (274.8±65.1 pg/mL) compared to saline studies (356.3±37.7 pg/mL), this was not significant (p=0.2). Additionally, the number of hypoglycemic symptoms decreased following EPI infusion (Figure 1).

Conclusions Thus, comparing the effect of opioid vs. adrenergic receptor activation on subsequent responses to hypoglycemia, our findings suggest that while opioid receptor activation induces HAAF, the antecedent hypoglycemia-associated rise in plasma epinephrine impacts hypoglycemia awareness.

4 NOVEL INSIGHT INTO IMPAIRED CHOLESTEROL TRANSPORT IN CHRONIC KIDNEY DISEASE: DEMONSTRATION OF REVERSIBILITY WITH VITAMIN D AND ACE-INHIBITOR

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Purpose of Study Atherosclerotic cardiovascular disease (CVD) is the primary cause of death in dialysis/chronic kidney disease (CKD) patients. Initiation of statins are ineffectual in dialysis patients and efficacy is diminished in advanced CKD, yet improved CVD mortality with ACE-inhibitors (ACEi) and Vitamin D (Vit D) has been shown. We examined ACEi and Vit D effects on cholesterol transport gene expression in the CKD setting because these crucial genes in atherosclerosis are statin-insensitive.

Methods Used Following THP-1 human macrophage (10^6/ml) incubation (24 h) in plasma from 10 CKD or 10 healthy control (HC) subjects, mRNA was quantified by RT-PCR using specific primers for ATP binding cassette transporter (ABC)A1/G1, CD36 and ScRA1. Foam cell formation was assayed using Dil-acetylated-LDL on 5 samples per group. THP-1 exposed to plasma from 5 CKD and 5 HC was studied ±Vit D (calcitriol, 10^{-8} M) or ±ACEi (enalapril, 50 μM).

Summary of Results With CKD vs. HC plasma exposure, ABCA1 was reduced to 87% (p<0.01), ABCG1 was reduced to 50% (p<0.01), CD36 was reduced to 90% (p<0.05), while ScRA1 increased by 83% (p<0.01); foam cells increased by 36±11% (p<0.01) by total fluorescence per cell corrected for total nuclei in frame. ACEi improved ABCA1 to 105%(p<0.05), ABCG1 to 108%(p<0.01), reduced CD36 further to 80% (p<0.05) and decreased foam cells by 28±16% (p<0.01). Vit D improved ABCA1 to 111% (p<0.05), ABCG1 to 63% (p<0.05), further lowered CD36 to 68% (p<0.05) and decreased foam cells by 64±22% (p<0.01).

Conclusions CKD based pro-atherogenic impairment of efflux genes ABCA1 and ABCG1, along with enhanced scavenger receptor mediated influx through ScRA1, while CD36 is suppressed, differs from our prior finding in rheumatoid arthritis where, in addition to lowering of ABCA1, augmentation of CD36 influx was observed. Suppression of ABC transporters and promotion of ScRA1 may be pivotal to elevated CVD risk. ACEi and Vit D reduced foam cell accumulation through amelioration of efflux genes. Further defining of lipid handling changes in CKD could lead to novel, targeted CVD treatments in the CKD population.

5 ASTHMATIC BRONCHIAL AIRWAY EPITHELIAL EXOSOMES DO NOT PROMOTE MESENCHYMAL FIBROSIS DESPITE EXOSOMAL MICRORNA PREDICTED TARGETS

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Purpose of Study Upon establishing a xenograft model of asthma, we sought to determine the role of exosomal intercellular communication between the epithelium and mesenchyme. We hypothesize that exosomal intercellular communication occurs between the airway epithelium and the underlying mesenchyme, contributing to airway fibrosis.

Methods Used Non-asthmatic and asthmatic human primary bronchial airway epithelia were grown in exosome-depleted media. Media secretions were collected and exosomes were isolated. For miRNA expression experiments, exosomal miRNA was isolated and hybridized to Affymetrix miRNA arrays. Xenografts were constructed from plastic cassettes and acellular rat tracheas and implanted into Nu/Nu mice. Beginning 48 hours post-surgery, grafts were injected daily with isolated exosomes for 12 days, after which time the grafts were harvested. Tissue sections were analyzed for collagen using Masson's Trichrome immunohistochemistry.

Summary of Results Statistical analyses of miRNA array expression revealed 41 mature miRNAs present at significantly different levels in exosomes from asthmatics compared with non-asthmatics. These differentially expressed mature miRNAs putatively target 5,630 mRNAs, with TGFβ signaling among the top ranked canonical pathways ($p=.01$). miR-let7a-5p ($FC=-1.25$, $p=0.05$) and miR-486-5p ($FC=-1.19$, $p=0.01$) were down-regulated, which has been shown to contribute to excessive expression of collagen and promotion of fibrosis. Unexpectedly, xenografts exposed to non-asthmatic airway epithelial exosomes showed abundant Masson's Trichrome staining while xenografts exposed to asthmatic airway epithelial exosomes were thinner with less Masson's Trichrome staining.

Conclusions Our miRNA profiling data suggest that xenografts exposed to asthmatic airway epithelial exosomes would result in an increase in TGFβ signaling, thereby promoting fibrosis. Instead, we found more abundant Masson's Trichrome staining in grafts exposed to non-asthmatic exosomes, suggesting exosomes play a role in proper matrix formation. Further investigation is necessary to elucidate the role exosomes play in the epithelial-mesenchyme trophic unit.

6 ADIPOCYTE-DERIVED EXOSOMAL MICRORNAS FROM VISCERAL ADIPOSE TISSUE AND URINE CORRELATE TO GLYCATED HEMOGLOBIN

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Purpose of Study We have previously identified dysregulated adipocyte-derived exosomal microRNAs in obese individuals in comparison to lean. Furthermore, we have established beneficial modification of microRNAs one year following bariatric surgery from adipocyte-derived exosomes in the serum. To further develop exosomal microRNAs as biomarkers for cardiometabolic health, a better understanding of the relationship between adipocyte-derived exosomal microRNA profiles from different biofluids (e.g. urine) and phenotype is needed. In this study, we tested the hypothesis that adipocyte-derived exosomal miRNAs from visceral adipose tissue (VAT) and urine correlated to indices of blood glucose homeostasis.

Methods Used VAT and urine were collected from adolescent African-American females with obesity ($N=10$; $Age=17.3\pm2.3$; $BMI=52.5\pm9.2$; Hemoglobin A1c (HbA_{1c})$=5.7\pm1.1$). Pearson product-moment correlation coefficient determined relationship between HbA_{1c}, a clinical measure of blood glucose homeostastis, and adipocyte-derived exosomal miRNAs from VAT and urine.

Summary of Results Correlation analysis identified 147 exosomal miRNAs from VAT and 206 from urine to be significantly ($p<0.05$) related to HbA_{1c}; 7 were found to be significant in both sample types. Among miRNAs identified to be significant fromt both sources were miR-27b (VAT: $r=0.66$, $p=0.04$; Urine: $r=0.78$, $p<0.01$) and miR-593 ($r=0.76$, $p<0.01$; $r=0.75$, $p=0.01$). MiR-27b has previously been linked to impairments in adipocyte differentiation through peroxisome proliferator-activated receptor gamma while miR-593 was found to be associated with obesity and type-2 diabetes mellitus.

Conclusions These data indicate adipocyte-derived exosomal miRNAs isolated from urine share similar relationships to HbA_{1c} as those isolated directly from VAT, and thus urine may be a viable biofluid in pursuing diagnostics related to obesity.

7 VISCERAL BUT NOT SUBCUTANEOUS ADIPOSE TISSUE ASSOCIATES WITH VASCULAR INFLAMMATION BY 18-FDG PET/CT IN HUMAN INFLAMMATION

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Purpose of Study Visceral adiposity (VAT) has been shown to be associated with increased CV events, however, the association of vascular inflammation (VI) by 18-FDG PET/CT with VAT compared to subcutaneous adiposity (SAT) is not known. Therefore, we sought to compare the association of VAT and SAT with VI by 18-FDG PET/CT.

Methods Used Consecutively recruited PSO patients (N=77) underwent 18-FDG PET/CT scans to measure VI and abdominal adiposity represented as target-to-background ratio (TBR) and cm^3 respectively. VAT/SAT volume was quantified from vertebral level T10 to the pubic symphysis. The relationship of VAT and SAT with VI was analyzed using multivariable regression models.

Summary of Results The cohort had a low Framingham Risk Score [Median (IQR); 4 (2–7)] and and mostly mild skin disease [Median (IQR); 5.2 (3.0–8.5)]. VAT remained significantly associated with TBR (β=0.45, p=0.002) while SAT did not retain significance (β=−0.04, p=0.84) following adjustment for BMI (Table).

Conclusions VAT significantly associated with TBR, while SAT attenuated significance after adjustment for BMI. This supports the concept that VAT may modulate vascular inflammation directly, whereas SAT operates via BMI. Larger studies are needed to confirm these findings.

Visceral Adipose Tissue, but not Subcutaneous Adipose Tissue Associates with Vascular Inflammation of the Entire Aorta in Models Adjusted for Body Mass Index

VAT Models	β (p-value)
Model 1	0.70 (<0.001)
Model 2	0.74 (<0.001)
Model 3	0.68 (<0.001)
Model 4	0.45 (0.002)
SAT Models	
Model 1	0.37 (0.001)
Model 2	0.51 (<0.001)
Model 3	0.43 (<0.001)
Model 4	−0.04 (0.83)

Model 1: Unadjusted.
Model 2: Adjusted for age and sex.
Model 3: Adjusted for Model 2 plus Framingham Risk Score, systemic/biologic treatment, hypertension hyperlipidemia, and lipid treatment.
Model 4: Adjusted for Model 3 plus body mass index.

8 ADIPOCYTE-DERIVED EXOSOMES FROM OBESE SUBJECTS HAVE ATHEROGENIC EFFECTS ON CHOLESTEROL EFFLUX IN THP-1 HUMAN MACROPHAGES

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Purpose of Study Obesity is a chronic inflammatory state that increases risk for atherosclerotic cardiovascular disease (CVD). Inflammation within adipose tissue is thought to contribute to atherosclerosis, but the mechanism through which adipocytes affect monocytes and macrophages in atherosclerotic plaques is unclear. This study tests the hypothesis that, compared to exosomes of normal BMI subjects, exosomes derived from adipose tissue of high BMI subjects will exhibit atheroma-promoting properties that influence macrophage cholesterol handling.

Methods Used THP-1 human macrophages (10^6/ml) were exposed to exosomes from adipose tissue of 10 obese subjects (BMI=39.1±6) and 10 normal subjects (BMI=23.2±1) in RPMI1640. THP-1 macrophages were also transfected with mimics for miR33 and miR374. After incubation, total protein and RNA were isolated. Message level of the ATP-binding cassette transporters (ABC)A1 and ABCG1, 27-hydroxylase (27OH), and nuclear receptor proteins PPARγ and LXRα were evaluated by real-time PCR and confirmed by immunoblot. Cholesterol efflux was measured by fluorometric assay. Foam cell formation was analyzed with dil-acetylated LDL.

Summary of Results Exosomes of high BMI subjects suppressed THP-1 macrophage expression of ABCA1 and 27OH, 45% (95%CI −17,+54%, p<0.01) and 36% (95% CI −20,+38%, p=0.01), respectively, vs. normal BMI. PPARγ, ABCG1 and LXRα did not differ significantly. Exosomes from high BMI subjects decreased cholesterol efflux to medium by 10%±6% (p<0.01) and increased LDL accumulation by 48%±18% (p<0.05). Exposure to miR33 and miR374 decreased expression of ABCA1, 27OH, and PPARγ, with no significant effect on foam cell formation.

Conclusions Exosomes from adipose tissue mediate communication between adipose tissue and cells of atherosclerotic plaque, including monocytes and macrophages. Exosomes from adipose tissue of high BMI subjects decrease expression of cholesterol efflux genes, decrease efflux, and increase LDL accumulation in macrophages. It is likely that some of these effects are mediated through microRNA cargo of adipocyte-derived exosomes.

9 IMPROVEMENT IN VASCULAR INFLAMMATION BY 18-FDG PET/CT IS ASSOCIATED WITH REDUCTION IN GLYCA LEVELS AT 1-YEAR IN PSORIASIS

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Purpose of Study Psoriasis (PSO), a chronic inflammatory disease associated with increased cardiovascular (CV) risk, provides a human model to study inflammatory atherogenesis. GlycA, a complex nuclear magnetic resonance (NMR) signal, is a novel composite biomarker of systemic inflammation that was associated with vascular inflammation (VI) in PSO. We hypothesize that a longitudinal reduction in GlycA would associate with an improvement in VI by 18-FDG PET/CT.

Methods Used Consecutively recruited 123 PSO patients underwent 18-FDG PET/CT scans to measure VI as target-to-background ratio (TBR), at baseline and 1 year. GlycA levels were measured by NMR spectroscopy (LabCorp). The change in VI was analyzed by multivariable regression modeling.

Summary of Results The cohort had low CV risk by FRS and mild to moderate PSO (Table 1). GlycA decreased significantly from baseline to 1 year ($p<0.001$) (baseline: mean±sd – 407.92±67.52 vs. 1 year: 379.34±63.83). TBR improved by a mean of 5% ($p<0.001$). Improvement in aortic VI associated with a reduction in GlycA independent of traditional CV risk, change in hsCRP, change in SBP, change in HDL, statins use and systemic/biologic therapy ($\beta=0.24$, $p=0.04$).

Conclusions Improvement in VI by 18-FDG PET/CT was associated with a reduction in GlycA, suggesting that GlycA may provide a stable, modifiable biomarker for the longitudinal assessment of vascular disease. Larger prospective studies are needed to confirm our results.

Table 1: Demographic and clinical characteristics of the study groups.

Variable	Psoriasis Patients at baseline (N=123)	Psoriasis Patients at one year follow up (N=123)	p
Demographic and Clinical Characteristics			
Age, years	49.64±12.89	50.75±12.87	<0.001
Males, N (%)	73 (59.35%)	73 (59.35%)	1.00
Hypertension, N (%)	31 (25.20%)	27 (22.31%)	0.21
Hyperlipidemia, N (%)	63 (51.22%)	61 (50.41%)	0.64
Type-2 Diabetes, N (%)	10 (8.13%)	9 (7.44%)	0.56
Body Mass Index, Kg/m^2	28.89±5.57	28.87±5.50	0.46
Current Smoker, N (%)	16 (13.01%)	13 (10.74%)	0.18
Clinical and Lab Values			
Systolic BP, mm Hg	124.04±14.46	117.30±13.99	<0.001
Diastolic BP, mm Hg	72.52±9.84	68.88±8.85	<0.001
Total Cholesterol, mg/dL	183.24±37.73	184.40±42.13	0.36
High Density Lipoprotein, mg/dL	56.07±18.36	59.03±21.78	0.004
Low Density Lipoprotein, mg/dL	102.03±31.96	100.45±36.37	0.29
Triglycerides, mg/dl (Median [IQR])	99.0 (78.0-136.0)	115.0 (79.0-156.0)	0.10
High-sensitivity C-reactive protein (Median [IQR])	1.6 [0.6-3.8]	1.2 [0.6-3.2]	0.02
Framingham Risk Score (Median [IQR])	3.0 [1.0-6.0]	2.0 [1.0-5]	0.10
Erythrocyte Sedimentation Rate (Median [IQR])	8.0 [5.0-13.0]	7.0 [5.0-12.0]	0.02
GlycA, µmol/L	407.92±67.52	379.34±63.83	<0.001
Psoriasis Severity			
Psoriasis Area Severity Index Score (Median [IQR])	5.2 [3.0-8.9]	3.3 [2.0-5.7]	<0.001
Systemic or Biologic Treatment, N (%)	45 (36.59%)	70 (57.85%)	<0.001
Lipid Treatment, N (%)	40 (32.52%)	39 (32.23%)	0.74
Vascular Inflammation			
TBR at Ascending Aorta	1.82±0.25	1.73±0.20	<0.001

All values are expressed as Mean ± S.D, unless specified otherwise. P values were calculated by comparing baseline and one year follow-up values using paired t-test or Wilcoxon signed-rank test for continuous variables and Pearson's chi-squared test for categorical variables. TBR-Target-to-background ratio.

Abstract 9 Figure 1

10 AORTIC VASCULAR INFLAMMATION BY 18-FDG PET/CT ASSOCIATES WITH HIGH-RISK CORONARY PLAQUES IN YOUNG PSORIASIS PATIENTS

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Purpose of Study Psoriasis, a chronic inflammatory skin disease, is associated with vascular inflammation (VI) by FDG PET/CT and an elevated risk for myocardial infarction, especially in younger patients. Coronary computed tomography angiography (CCTA) identifies rupture prone, high-risk coronary plaques (HRP) that are predictive of cardiovascular (CV) events. We hypothesize that increased aortic VI would associate with HRP in young psoriasis patients.

Methods Used Consecutive psoriasis patients (N=105) underwent FDG PET/CT scans to assess VI as target-to-background ratio (TBR), and CCTA (Toshiba) to identify HRP, defined as remodeling index≥1.1, low attenuation (< 30 HU), or spotty calcification. The relationship

Table 1: Characteristics of different groups based on median target-to-background ratio (TBR) in psoriasis patients.

Parameter	TBR < Median (N=52)	TBR > Median (N=53)	P
Demographics and medical history			
Age, years	47.7±1.8	52.6±1.6	**0.02**
Male sex, n (%)	24(46)	41(77)	**0.001**
Body mass index, kg/m^2	27.1±0.5	32.6±0.9	**<0.0001**
Hypertension, n (%)	13(25)	19(36)	0.23
Hyperlipidemia, n (%)	18(35)	34(64)	**0.002**
Type 2 diabetes mellitus, n (%)	5(10)	7(13)	0.56
Current tobacco use, n (%)	2(4)	611)	0.15
Lipid therapy, n (%)	10(19)	25(47)	**0.002**
Clinical and laboratory values			
Systolic blood pressure, mmHg	122.8±1.9	126.6±2.2	0.09
Total cholesterol, mg/dl	185.1±5.9	177.8±4.8	0.17
Triglycerides, mg/dl	99.9±5.6	148.4±14.1	**0.001**
HDL cholesterol, mg/dl	62.4±2.8	49.1±1.9	**0.0001**
LDL cholesterol, mg/dl	101.1±5.1	100.4±3.9	0.46
Framingham Risk Score (IQR)	2(1-4)	4(3-7)	**<0.0001**
ESR, mg/L (IQR)	8.5(5.0-13.0)	8(5.0-13.0)	0.77
High-sensitivity CRP, mm/hour (IQR)	1.9(0.6-3.8)	1.8(0.8-4.2)	0.38
Cholesterol efflux capacity	0.99±0.02	0.92±0.02	**<0.0001**
Insulin, IU/ml	9.4(6.9-13.1)	16.7(10.4-26.1)	**<0.0001**
HOMAIR	2.2(1.6-3.2)	4.1(2.7-7.2)	**<0.0001**
Psoriasis Severity and Treatment			
Disease duration, years	18.1±1.8	20.2±1.7	0.21
PASI score (IQR)	4.5(2.7-8.3)	6.2(3.0-10.1)	0.32
Total Body Surface Area (IQR)	4.2(2.0-10.0)	4.0(1.2-12.4)	0.21
Systemic/Biologic therapy, n (%)	19(37)	19(36)	0.94
Vascular inflammation (FDG PET/CT)			
Average Aortic Inflammation, TBR	1.55±0.01	1.92±0.03	**<0.0001**
High Risk Plaques			
High-risk plaque, n (%)	13 (25)	23 (43)	**0.047**

*Median=1.68. Continuous variables are expressed as Mean±SEM or Median (IQR) and Categorical as n (%). P values were calculated using Student's t-test or Mann-Whitney U test for continuous variables based on normality, and by Pearson's Chi-square test for categorical variables. HOMAIR: Homeostasis Model Assessment of Insulin Resistance, PASI: Psoriasis Area Severity Index, IQR: Interquartile Range.

Abstract 10 Figure 1

between VI and HRP was analyzed using multivariable regressions (STATA 12).
Summary of Results The cohort had low Framingham risk [Med (IQR): 4 (1-6)] but high TBR [Med (IQR): 1.68 (1.59-1.83)]. Patients with greater TBR (>Median TBR: 1.68) were found to have higher HRP (Table 1). Finally, on stratification based on median age (51 years), VI associated with HRP beyond traditional CV risk factors, psoriasis severity and systemic/biologic therapy (β=0.42; p=0.02) in younger patients. However, similar association was not seen in older patients (β= -0.04; p=0.85).
Conclusions Aortic VI by FDG PET/CT associated with HRP in young psoriasis patients, suggesting that extra-coronary VI may provide a valid surrogate for HRP in the coronaries. However, larger studies are needed to confirm these findings.

11 TGF-β GENES IN OBESE ASTHMATICS HAVE ALTERED EXPRESSION PROFILES COMPARED TO LEAN ASTHMATICS

Samuel B. Epstein, Shomik Ghose, Brennan Harmon, Evan Nadler, Matthew D. Barberio, Madeleine Goldberg, Lisa Maltz, Robert J. Freishtat. Children's National Medical Center, Washington, DC

10.1136/jim-2017-000429.11

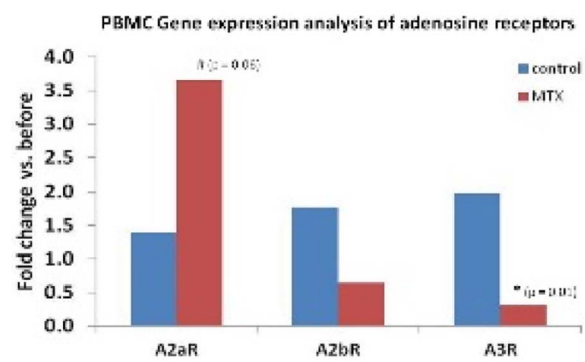
Purpose of Study Pediatric obesity is a major risk factor for intractable asthma, a condition characterized by reduced lung function and poor corticosteroid response, resulting in worse clinical outcomes and quality of life. Previous publications by our group reported that obese visceral adipose-derived exosomes contain miRNAs capable of impairing the TGF-β signaling cascade. Therefore, we hypothesized that genes in the TGF-β pathway would be significantly dysregulated in obese asthmatics. We looked to identify changes in the expression of TGF-β signaling relevant genes in a similar cohort.
Methods Used Subjects in the AsthMaP-2 cohort (youth with physician-diagnosed asthma) were selected at the extremes, populating obese (n=10) and lean (n=10) subgroups. We isolated peripheral blood mononuclear cells (PBMCs) from whole blood and extracted RNA and DNA content with the Norgen RNA/DNA Purification Kit (cat # 48700). A Nanostring custom gene expression panel targeting TGF-β pathway genes was used to count relevant mRNA transcripts.
Summary of Results Selected obese subjects had a BMI≥95th percentile and lean subjects had a BMI≤25th percentile for age and sex. Normality of gene expression data was assessed with a Shapiro-Wilk test and log-transformed as needed. Differences in gene expression between lean and obese were assessed using two-sample t-tests and relationships of gene expression to body-mass index (BMI) were determined via Pearson product correlation coefficient. Significant differences were detected in ACVR1B (fold change=1.5, p=0.04), BMP2 (FC=2.2, p=0.02), and SERPINE1 (FC=−1.44, p=0.03).
Conclusions PBMCs from obese asthmatics contain dysregulated mRNAs relevant to the TGF-β signaling pathway as compared to lean asthmatics, and the gene expression correlated with BMI. These differences in gene expression may help explain why obese asthmatics have poorer asthma control than their lean counterparts. This is consistent with previously published miRNA data that indicates TGF-β signaling as a potential target for obese adipocyte-derived exosomal miRNAs.

12 PERIPHERAL BLOOD MONONUCLEAR CELLS OF CIRT PATIENTS MAINTAIN THEIR ADENOSINE A2A RECEPTORS IN THE PRESENCE OF LOW DOSE METHOTREXATE

Isaac Teboul,[2] Allison B. Reiss,[1] Nicolle Seigart,[1] Lora J. Kasselman,[1] Steven E. Carsons,[1] Joshua De Leon[1]. [1]Medicine, Winthrop University Hospital, Mineola, NY; [2]SUNY Upstate Medical University, Syracuse, NY

10.1136/jim-2017-000429.12

Purpose of Study The Cardiovascular Inflammation Reduction Trial (CIRT) is designed to assess whether reduction of inflammation with Low Dose Methotrexate (LD-MTX) will reduce future cardiac events in high risk metabolic syndrome or type 2 diabetes (T2DM) patients who are post-myocardial infarction or have multi-vessel disease. Our previous work indicates that MTX confers atheroprotection via adenosine A2A receptor (A2AR) activation. In order for A2AR ligation to reduce cardiovascular events, A2AR levels would need to be preserved in the presence of MTX.
Methods Used 20 post-MI T2DM patients enlisted in CIRT were randomized to either 6 weeks LD-MTX (n=10) or 6 weeks placebo (n=10). Blood samples were drawn from all patients at enrollment and after 6 weeks. Peripheral blood mononuclear cells (PBMC) were isolated and evaluated for expression of adenosine receptors by real time PCR. Average fold change between time points was calculated and compared using factorial ANOVAs.
Summary of Results Compared to placebo, the LD-MTX group exhibited a trend toward an increase in A2AR (p=0.06), while A3R expression was significantly decreased (p=0.01) after 6 weeks (Figure). PBMC did not lose A2AR which is an indication that resisatance to atheroprotective effects of MTX did not develop with continued use.
Conclusions Here we report a nearly significant increase in A2AR expression and a significant decrease in the A3R



Abstract 12 Figure 1

expression in LD-MTX treated patient PBMC as compared to placebo patient PBMC. Taken together, this may reflect an anti-inflammatory profile of these cells, since the A2AR is implicated in the anti-inflammatory response and the A3R is considered pro-inflammatory. Thus, if CIRT reveals anti-atherogenic effects of LD-MTX, adenosine receptors may be critical to the efficacy of this drug and A2AR levels may be predictive of a response in precision medicine evaluation of patients.

Moderated Posters
11.45AM – 12.45PM

MP1 THE EFFECT OF HYDROXYCHLOROQUINE ON REVERSE CHOLESTEROL TRANSPORT IN THP1 MACROPHAGES

Justin Konig,[1,2] Heather A. Renna,[2] Joshua De Leon,[2] Steven E. Carsons,[2] Hirra A. Arain,[2,3] Neal Shah,[2,4] Allison B. Reiss,[2] Lora J. Kasselman[2]. [1]Stony Brook University, Flushing, NY; [2]Medicine, Winthrop University Hospital, Mineola, NY; [3]Hofstra University, Long Island, NY; [4]New York College of Osteopathic Medicine, Long Island, NY

10.1136/jim-2017-000429.13

Purpose of Study The risk of cardiovascular (CV) disease is elevated in patients with rheumatoid arthritis (RA) and other inflammatory diseases. We have shown that plasma from RA patients causes pro-atherogenic derangements in cholesterol transport leading to macrophage foam cell transformation, a hallmark of atherosclerosis. The TARGET Trial is a randomized clinical trial of 2 RA drug regimens aimed at determining which has superior CV benefits. Comparison is between methotrexate (MTX)+sulfasalazine (SSZ)+hydoxychloroquine (HCQ) versus MTX +an anti-TNF antibody. This study examines HCQ effects on lipid transport to deepen understanding of mechanisms underlying TARGET outcomes.

Methods Used THP1 differentiated macrophages were exposed to the following conditions: media, IFN-γ (pro-atherogenic cytokine, 100 U/ml), HCQ (100, 1000, and 10,000 ng/ml), or IFN-γ+HCQ (100, 1000, and 10,000 ng/ml) for 24 hrs. Gene expression was measured using RT-qPCR. Foam cell formation was measured using Oil-Red-O and fluorescent- oxidized LDL. Cell viability was assessed with trypan blue. Intracellular cholesterol and efflux were quantified using the Amplex Red cholesterol assay, and cytoplasmic pH was measured with the pHrodo Green AM intracellular pH indicator.

Summary of Results We observed a dose-response effect (trends) on gene expression with higher concentrations of HCQ increasing expression of all genes, both those related to efflux (ABCA1, ABCG1, and 27-hydroxylase) and influx (SCRA1 and CD36). However, the effect was balanced between influx and efflux. HCQ did not alter intracellular cholesterol, cholesterol efflux, foam cell formation, cell viability, or cytoplasmic pH.

Study Limitations This study was done using cultured macrophages and not patient-derived macrophages, so must be repeated in peripheral blood mononuclear-derived cells.

Conclusions HCQ does not appear to have any effect on reverse cholesterol transport in THP-1 macrophages at physiologically relevant doses. This is consistent with the hypothesis of TARGET which postulates a superior effect of anti-TNF antibody over SSZ+HCQ. Next step will be to examine SSZ alone.

MP2 ADMIT OR DISCHARGE? A COST ANALYSIS OF MANAGING INFANTS 29-60 DAYS OLD WITH PRESUMED PYELONEPHRITIS AT LOW RISK FOR BACTEREMIA

Astrid Sarvis, David Mathison. Pediatric Emergency, Childrens National Medical Center, Washington, DC

10.1136/jim-2017-000429.14

Purpose of Study Emergency room physicians typically admit infants less than 2 months old with presumed pyelonephritis due to a concern for concomitant bacteremia, even if the risk of bacteremia and subsequent complications are low. The objective of this study is to perform a comparative cost analysis for admitting and discharging infants 29-60 days old presenting to the emergency department with presumed pyelonephritis meeting low risk criteria for bacteremia and adverse events.

Methods Used This study uses a decision analysis approach to estimate and compare costs for admitting versus discharging infants with presumed pyelonephritis at low risk of bacteremia and adverse events. A probability of bacteremia and adverse events of 3.2% and 0%, respectively, was obtained from a 20-center retrospective study of 1895 infants 29-60 days old with fever and UTI that established criteria for identifying low-risk infants. To derive cost structure, we performed a retrospective chart review of infants diagnosed with febrile UTI in the emergency department at a tertiary, academic, urban, pediatric hafmospital who also met low risk criteria. We determined costs, charges and reimbursements using a combination of two methods: itemized billing charges of infants at our hospital, and billing records from a national pediatric inpatient database. Our primary outcome is the difference in total cost, charges, and reimbursements, per bacteremic patient, between admitting and discharging.

Summary of Results The relative cost savings for discharging infants would be $80,333 per bacteremic patient ($19,126 discharge vs. $99,459 admit). The charge savings for discharging infants would be $304,949 per bacteremic patient ($70,437 vs. $375,386). The reimbursement savings for discharging would be $148,924 per bacteremic patient ($73,279 vs. $222,203).

Conclusions The relative cost savings for discharging low-risk infants with presumed pyelonephritis will be significant without reciprocal increase in adverse events. Similar outcomes were demonstrated for hospital charges and reimbursements, which further strengthens these results. This study emphasizes how risk stratification in clinical decision-making can lead to substantial cost savings without sacrificing patient outcomes.

MP3 DISTINGUISHING CHARACTERISTICS OF SEVERE OBSTRUCTIVE SLEEP APNEA IN INNER-CITY CHILDREN AND ADOLESCENTS

Sasikumar Kilaikode, Miriam Weiss, Rosema Megalaa, Princi Kovacs, Rupa Koothirezhi, Lana Mukharesh, Seth Wolf, Daniel Lewin, Geovanny Perez, Gustavo Nino. Pediatric Pulmonology, Childrens National Health System, Washington, DC

10.1136/jim-2017-000429.15

Purpose of Study Obstructive sleep apnea (OSA) is a common condition affecting 3% of the pediatric population in the United States.There is lack of data describing the characteristics of severe OSA in inner-city minority children. We examined the clinical, polysomnographic and socioeconomic features of severe pediatric OSA in Washington D.C area. Specifically, we hypothesized that inner city minority children will have higher prevalence of severe OSA and will be more likely to have a delayed severe OSA diagnosis (>1 year after the onset of symptoms)

Methods Used Retrospective review was done including cases of severe OSA followed in our Pediatric Sleep Center. Severe OSA was defined as an obstructive apnea hypopnea index (OAHI) of more than 10 events per hour based on initial overnight polysomonogram (PSG). We used electronic medical record review PSG variables to characterize individuals with severe OSA and stratified results based on racial/ethnic background as well as geographic/socioeconomic status

Summary of Results 150 eligible children (mean age 7 years, ±SD 5.3) were enrolled during the study period (Sept 2015-2016). We identified that the vast majority of children in our inner city cohort were African American (AA)/Black (n=91, 61%). Importantly, AA/black children had a median duration of symptoms prior to diagnosis of 24 months (IQR 12-43 months), which was double of that in Caucasian/White. Moreover, severe hypoxemia due to OSA (SaO2 nadir <75%) was significantly more common in AA/black (n=39, 64%) than in other ethnic groups. We also observed that the county with the largest proportion of minorities and low income families in D.C. metropolitan area accounted for most severe OSA cases (Prince George county, MD, 44%). In addition, we observed the highest prevalence of severe OSA in DC wards with the highest poverty levels

Conclusions Inner city AA/black children had the highest prevalence of severe OSA and were more likely to have a delayed diagnosis. Geographical distribution of severe OSA corresponded to low economic status. Our study indicates that there is a critical need to focus care, resources and education to identify and treat pediatric OSA in minority communities of inner city areas

MP4 EFFECTS OF ADDING SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS TO STANDARD CARE IN PATIENTS WITH TYPE 2 DIABETES

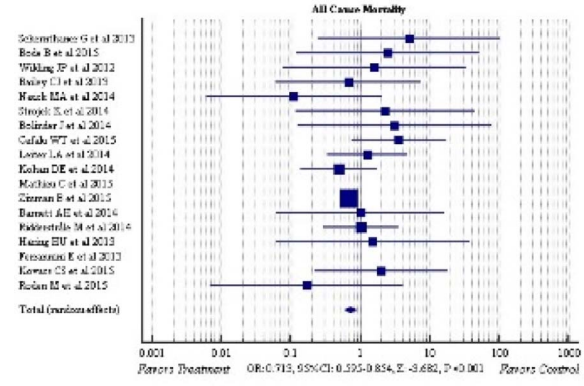
Abhishek Sharma,[1,2] Haroon Kamran,[1] Sunny Goel,[3] Debabrata Mukherjee[4]. [1]Division of Cardiovascular Medicine, State University of New York, Downstate Medical Center, Brooklyn, NY; [2]Institute of Cardiovascular Research and Technology, Brooklyn, NY; [3]Maimonides Medical Center, Brooklyn, NY; [4]Texas Tech University, El Paso, TX

10.1136/jim-2017-000429.16

Purpose of Study To evaluate the effects of sodium-glucose cotransporter 2 inhibitors (SGLT-2 inhibitor), in addition to standard care, in patients with type 2 diabetes.

Methods Used We searched Medline, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) to identify randomized controlled trials (RCTs) assessing the incremental effect of SGLT-2 inhibitor to standard care, in patients with type 2 diabetes. Endpoints were all-cause mortality, cardiovascular (CV) mortality, myocardial infarction (MI), heart failure (HF), stroke, and renal failure. Event rates were compared using a Forest plot of odds ratio (OR) using a random effects model.

Summary of Results We included 18 RCTs with 17,966 patients for final analysis. There was significant reduction in all cause mortality [OR 0.71 (95% CI 0.59 to 0.85)]; and CV mortality [OR 0.64 (95% CI 0.51 to 0.80)] with addition of SGLT-2 inhibitor to standard of care in patients with type 2 diabetes. However, there was no statistically significant difference in MI [OR 0.86 (95% CI 0.70 to 1.07)]; HF [OR 1.656 (95% CI 0.347 to 7.893)]; Stroke [OR 1.109 (95% CI 0.867 to 1.418)] and renal failure [OR 1.332 (95% CI 0.817 to 2.172)] with addition of SGLT-2 inhibitor. There was no significant heterogeneity among the studies included in the analysis for various end points.



Abstract MP4 Figure 1 Effect of SGLT-2 inhibitor on all cause mortality

Conclusions In patients with type 2 diabetes, addition of SGLT-2 inhibitor to standard care, results in a reduction in all cause and CV mortality. Additional studies are indicated to better understand the mechanism of mortality reduction with SGLT-2 inhibitors.

MP5 PEDIATRIC CONCUSSION RECOGNITION AND MANAGEMENT BY RESIDENTS IN THE EMERGENCY ROOM

Zachary Traino,[1] Sean Gillen,[1] Daniel Schoenherr,[1] Robert Grell,[2] Rana Alghamdi,[1] Vanessa Grant,[1] Jasmine Harris,[1] Shireen M. Atabaki[1,2]. [1]Children's National Health System, Washington, DC; [2]George Washington University School of Medicine and Health Sciences, Washington, DC

10.1136/jim-2017-000429.17

Purpose of Study Acute recognition and management of concussion is essential to optimize outcomes. Validated concussion evaluation tools for the emergency department (Acute Concussion Evaluation—Emergency Department (ACE-ED)) and ACE-ED Care Plan have been shown to improve concussion recognition and management. These tools are integrated into the electronic health record (EHR) in the pediatric ED (PED) of a tertiary care children's hospital. The ACE-ED decision support tool uses conditional logic to generate an ICD-9 code and recommendation, indicating the patient has been diagnosed with a concussion and should receive the ACE-ED Care Plan on discharge. Validated prediction rules to avoid unnecessary radiation by identifying children at low risk of clinically important TBI are also built into the EHR. An Evaluation of Stage 3 Meaningful Use Objectives project demonstrated that the ACE-ED was used only 17% of the time it was indicated, and the CDS tool to determine CT scan eligibility for patients with head injury was utilized 30% of the time indicated. Knowledge gaps exist among physicians regarding concussion recognition and management, leading to underutilization of concussion evaluation tools and underrecognition of concussions.

Methods Used We will implement a resident lecture series for concussion education. We distribute and analyze a survey/post-test to assess effectiveness of the curriculum, as well as familiarity with and barriers to use of clinical decision support (CDS) tools in the EHR. We will also compare rates of use of CDS interventions before and after implementing the resident lectures. We aim to improve CDS workflow based on resident survey/post-test results.

Summary of Results In 2015, 2,326 patients presented to the PED with a chief complaint of head injury and 18.1% were diagnosed with concussion.

Conclusions The actual incidence of concussion in patients presenting with head injury is known to be significantly larger than previous studies have shown. We plan to improve recognition and management of concussion in the PED through resident education and subsequent increased use of concussion-related CDS tools.

MP6 NATION-WIDE ANALYSIS OF DISPOSITION IN GERIATRIC (≥ 65 YEARS) CANCER PATIENTS RECEIVING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Achuta K. Guddati, Iuliana shapira. Hematology/Oncology, SUNY Downstate Medical Center, Brooklyn, NY

10.1136/jim-2017-000429.18

Purpose of Study The disposition and complications of hematopoietic stem cell transplant (HSCT) in the geriatric population has not been extensively studied and compared with younger patients. Given the difference in the burden of medical comorbidity in the geriatric population, this study sought to study the differences in complications and disposition after autologous and allogeneic transplantations.

Methods Used Data regarding patients who underwent HSCT was extracted from the Nationwide Inpatient Sample (NIS) from 2000 to 2011 using ICD-9-CM codes. HSCT hospitalizations were classified into allogeneic transplantation, autologous transplantation, subsequent hospitalization (s/p transplant) with graft versus host disease (GVHD) and subsequent hospitalization (s/p transplant) with other complications.

Summary of Results The proportion of geriatric patients being discharged to nursing homes has increased over the past decade. The trends from 2000 to 2011 are shown in Table 1. The rate of major complications: mechanical ventilation, tracheostomy and requirement of new dialysis are similar in both the patient populations and have not significantly changed over the studied 12 year time period. However, the proportion of geriatric patients with GVHD being discharged to nursing homes has increased ~380% compared to a 45% increase in non-geriatric patients over the same time period.

Conclusions Although the rate of transplant associated complications are similar in geriatric and non-geriatric populations, a higher percentage of geriatric cancer patients who receive HSCT are being discharged to nursing homes.

	50 to 64 years			
	Autologous transplantation	Allogeneic transplantation	s/p transplant with GVHD	s/p transplant with other complications
Nursing Home	3.2% to 2.1%	4% to 1.4%	9.5% to 13.8%	8% to 11%
Mechanical Ventilation	2% to 0.9%	5.7% to 4.1%	9.2% to 8.9%	4.1% to 4.8%
Tracheostomy	0.3% to 0.13%	0.8% to 1%	0.9% to 1.4%	0.2% to 0.5%
New Dialysis	1.3% to 0.8%	3% to 1.4%	3.4% to 2.1%	1% to 1.5%
	≥ 65 years			
	Autologous transplantation	Allogeneic transplantation	s/p transplant with GVHD	s/p transplant with other complications
Nursing Home	3% to 4%	7.4% to 1.8%	6.3% to 24%	11% to 18%
Mechanical Ventilation	4% to 2.6%	4.2% to 3.3%	9.4% to 9.5%	2.7% to 4.8%
Tracheostomy	2.1% to 0.8%	1.7% to 1.7%	2.3% to 1.5%	0.4% to 0.1%
New Dialysis	0.9% to 0.7%	4.2% to 0.9%	7.5% to 3.9%	1.1% to 1.8%

Abstract MP6 Figure 1

This proportion is even higher for those who develop GVHD. More medical services and resources will be required to support the growing elderly population undergoing HSCT.

MP7 ABSENCE OF GENDER SENSITIVITY TO SINGLE DOSE STREPTOZOTOCIN IN OUTBRED MICE

John S. Pixley. *Internal Medicine, Texas Tech University HSC, Lubbock, TX*

10.1136/jim-2017-000429.19

Purpose of Study Streptozotocin (STZ) has been used in laboratory animals to induce diabetes because of its relatively selective destruction of endogenous pancreatic β-cells. Protocols have been developed in a variety of laboratory animals yet "despite widespread use, the data available concerning drug preparation, dosing and administration, time to onset and severity of DM, and any resulting moribundity and mortality are often limited and inconsistent" (*Lab Anim*. doi:10.1258/la.2010.010090). This includes differential gender sensitivity to STZ. We are interested in assaying human stem cell differentiation capacity following fetal tolerance induction in normal mice. As a preliminary step to determine endocrine differentiation, we evaluated the effectiveness of diabetes induction using the single high dose technique to avoid insulitis.

Methods Used 4 week old male and female Swiss-Webster mice were injected with varying doses of STZ 150 - 400 mg/kg in acetate buffer (pH 4.5) via intraperitoneal injection.

Summary of Results Preliminary studies in 10 mice demonstrated rapid toxicity and loss at doses above 300 mg/kg in either sex. We then evaluated 150-300 mg/kg doses for 14 days. At 150 mg/kg, 5 females developed glucose elevations day 9-14 and required 3 doses of 1 unit protamine zinc insulin (glucose>300 mg/dl). In 2 males, overt diabetes was present by day 10 but neither mouse required insulin. For doses 200 to 300 mg/kg, all mice developed overt diabetes one day after injection and required insulin at varying intervals. At 300 mg/kg, all females died 4 days after STZ administration while all males survived to day 14 with overt diabates requiring insulin. A summary of average blood glucose readings after 200 and 250 mg/kg STZ administrations are outlined in Table 1 and reveal no differential gender sensitivty to STZ. Water intake in all 200-250 mg/kg cohorts increased significantly ($p<0.05$) while only @ 150 mg/kg administrations in either sex did body weight increase significantly.

Conclusions We conclude that there is no gender difference in β-cell sensitivity to STZ in Swiss-Webster mice using the single high dose protocol.

MP8 STATINS WERE NOT EFFECTIVE IN PROMOTING CHOLESTEROL BALANCE IN HUMAN MACROPHAGES TREATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS PLASMA: A GENE EXPRESSION ANALYSIS AND IMPLICATIONS FOR STATIN USE

Hirra A. Arain,[1] Michelle Petri,[2] Lora J. Kasselman,[1] Nicolle M. Siegart,[1] Heather A. Renna,[1] Steven E. Carsons,[3] Joshua De Leon,[3] Allison B. Reiss[1,3]. [1]Biomedical Research, Winthrop University Hospital, Mineola, NY; [2]Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD; [3]Medicine, Winthrop University Hospital, Mineola, NY

10.1136/jim-2017-000429.20

Purpose of Study Atherosclerotic cardiovascular disease (CVD) remains a major cause of mortality for patients with Systemic lupus erythematosus (SLE). Due to the need for CVD treatment in SLE, the Lupus Atherosclerosis Prevention Study (LAPS) investigated the efficacy of statins, a primary CVD treatment known for its lipid lowering and anti-inflammatory properties, against CVD in SLE patients. LAPS demonstrated that a 2 year administration of statins did not reduce atherosclerotic progression in lupus patients. In this substudy, we further investigated the impact statins had on the cholesterol gene profile in a subset of human macrophages, key players in plaque formation, using plasma from SLE subjects in the LAPS trial to observe how statins may affect plaque progression induced by the SLE environment.

Methods Used Plasma from SLE patients enrolled in the LAPS was isolated pre- and post-atorvastatin therapy. THP-1 differentiated macrophages were treated for 18 hours in RPMI 1640+10% SLE patient plasma obtained pre- and post-statin therapy. Gene expression of the following cholesterol transport genes was measured using qRT-PCR: Efflux- ATP-binding cassette transporters (ABC) A1 and G1, 27-hydroxylase (27-OH), Peroxisome proliferator-activated receptor (PPAR)γ and Liver X receptor (LXR)α; Influx- CD36 and scavenger receptor (ScR)A1.

Summary of Results In the presence of lupus plasma with statins, we observed a 0.47 and 0.45 fold suppression of ABCA1 and ABCG1 respectively ($P<0.001$ and $P<0.001$ respectively; $n=46$). We further observed a 1.72 fold increase in 27-OH mRNA ($P<0.0001$; $n=31$), though no change in influx receptors ScRA1 and CD36, nor nuclear receptors LXRα and PPARγ were observed.

Conclusions This study provides mechanistic insight into LAPS by demonstrating that statins were overall ineffective in altering the balance of cholesterol transport expression of human macrophages in the SLE environment. We further provide evidence that statins as CVD treatment for SLE patients may not be useful as statin could not attenuate lipid overload.

MP9 THE PREDICTIVE POTENTIAL OF PROTHROMBIN TIME (PT) AND D-DIMER FOR TPA-RELATED HEMORRHAGE

Wenjun Deng, Bo Song, Sherry Chou, Lindsay Fisher, Maxwell Oyer, IY Richard Chou, Thomas Wickham, Kathleen F. Heizelmann, David McMullin, Elizabeth Van Cott, Eng H. Lo, Ferdinando S. Buonanno, MingMing Ning. Neurology, Massachusetts General Hospital, Boston, MA

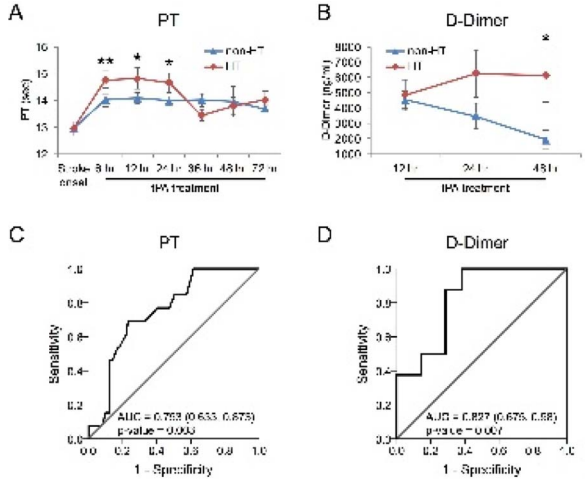
10.1136/jim-2017-000429.21

Purpose of Study Tissue plasminogen activator (tPA) is an efficacious treatment of acute ischemic stroke. However, its utilization has been deterred by hemorrhagic complications. Our previous exploratory study found that following tPA administration, ischemic stroke patients with hemorrhagic transformation (HT) had a significantly longer prothrombin time (PT) than those without HT. Here we aim to study the effect of post-tPA parenchymal hemorrhage on a wide range of coagulation labs in a lager cohort of patients.

Methods Used 308 tPA-treated stroke patients were recruited in accordance with IRB approval. Coagulation labs were analyzed at 6, 12, 24, 36, 48 and 72 hr post tPA. Patients on anticoagulants or with other conditions (e.g. liver, kidney dysfunctions) that may affect these labs were excluded.

Summary of Results As determined by head CT scan, 16 patients (5.19%) developed post-tPA HT. Compared to patients without HT, those with HT had higher levels of PT within the first 24 hr post tPA (Figure 1A), and PT levels at 6 hr have the potential to predict subsequent HT (Figure 1C, AUC=0.753, p=0.003). Moreover, D-Dimer remained at high levels even after 48 hr (Figure 1B), suggesting sustained fibrinolysis abnormality or possibly indicating active bleeding. D-Dimer levels at 24 and 48 hr were also predictive of tPA-induced HT (Figure 1D, AUC=0.827, p=0.007).

Conclusions Our results suggest PT and D-Dimer as early markers of tPA-related HT in ischemic stroke patients. Their differential predictive ability at different time points may offer the possibility to monitor the clinical efficacy of tPA over a longer time window to guide adjunct treatment. Studies in additional coagulation factors in an expanded patient cohort are ongoing.



Abstract MP9 Figure 1

MP10 HIGH WHITE BLOOD CELL (WBC) COUNT IS PREDICTIVE OF TPA-RELATED HEMORRHAGE

Wenjun Deng, Bo Song, Lindsay Fisher, IY Richard Chou, Maxwell Oyer, Thomas Wickham, David McMullin, Ferdinando S. Buonanno, Eng H. Lo, MingMing Ning. Neurology, Massachusetts General Hospital, Boston, MA

10.1136/jim-2017-000429.22

Purpose of Study Infection is a major complication of ischemic stroke and contributes to the morbidity and mortality of stroke patients. Although growing evidence highlights the close relationship between inflammation and coagulation/fibrinolysis cascades, little has been reported regarding the influence of tPA on human immune system. Here, we explore changes in white blood cell (WBC) counts pre/post IV tPA and their association with tPA-related hemorrhagic transformation (HT).

Methods Used 308 tPA-treated ischemic stroke patients were recruited with IRB approval, of which 16 developed HT within 24 hr post tPA. Routine WBC was analyzed at 1 month pre stroke, during stroke onset and during the first 48 hr post tPA.

Summary of Results We found that WBC was significantly increased within 12 hr post IV tPA and gradually reduced after 24 hr (Figure 1A). However, compared with patients without HT, HT patients had much higher levels of WBC throughout tPA treatment, and their WBC remained above normal even after 48 hr (Figure 1B). More importantly, we also found that HT patients had already developed elevated WBC as early as 1 month before their stroke onset (Figure 1B), which was predictive of tPA-related HT (Figure 1C, ROC AUC=0.889, p=0.001). Furthermore, the early elevation in WBC post-tPA was not associated with clinical evidence of infection.

Conclusions Our results provide early clinical evidence that in addition to activating fibrinolytic pathway, tPA may also modulate immune system during stroke treatment. In addition, elevated WBC pre-stroke maybe a predictive marker of tPA-related hemorrhage. While elevated WBC early in ischemic stroke was reported to correlate with poorer clinical outcome, the transient peak in WBC post tPA in this patient cohort ultimately had better clinical outcome, and is of interest. Further studies are needed and ongoing to evaluate differential WBC, stroke severity and long term clinical outcome, and to understand the molecular basis of tPA in immune cell modulation.

MP11 PLASMA LEVELS OF OXIDATIVE STRESS MARKER ASYMMETRIC DIMETHYLARGININE IS REDUCED BY SUCCESSFUL PFO CLOSURE

Wenjun Deng, Thomas Wickham, Lindsay Fisher, Maxwell Oyer, IY Richard Chou, Bo Song, Scott Silverman, David McMullin, Ignacio Inglessis, Igor Palacios, Ferdinando S. Buonanno, Eng H. Lo, MingMing Ning. Neurology, Massachusetts General Hospital, Boston, MA

10.1136/jim-2017-000429.23

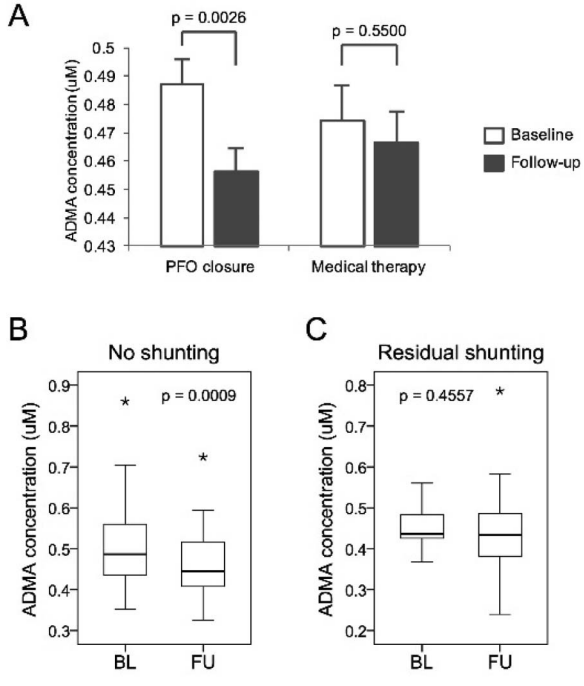
Purpose of Study Patent foramen ovale (PFO) is an independent risk factor of ischemic stroke. It enables venous clots and vasoactive factors to enter arterial circulation and

contribute to a prothrombotic status. Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, contributes to vascular disease and has been linked with increased levels of homocysteine, which creates additional oxidative stress by inhibiting ADMA clearance. We previously identified a reduction of homocysteine by PFO closure. Here we study the influence of PFO on ADMA levels, a marker of oxidative stress.

Methods Used 97 PFO-stroke patients were recruited in accordance with IRB, of which 61 received PFO closure and 36 underwent medical therapy alone. Peripheral venous blood was collected at baseline (BL) and 1 year follow-up (FU) post treatments. Plasma ADMA was quantified by mass spectrometry.

Summary of Results Compared to BL, plasma ADMA levels were significantly reduced post PFO closure (p=0.0026), while no changes were observed for patients treated with medications alone (p=0.5500) (Figure 1A). Moreover, among the PFO-closed patients, ADMA reduction was only pronounced for those without residual shunting (p=0.0009) but not for those with residual shunting (p=0.4557) (Figure 1B, C).

Conclusions Successful PFO closure without residual shunting reduced oxidative stress marker ADMA in circulation. Our results support the hypothesis that PFO-related interatrial blood shunting may causally contribute to the high level of vasoactive factors in circulation. Further studies on expanded patient cohort are ongoing.



Abstract MP11 Figure 1

MP12 **THE EFFECT OF BLOOD TRANSFUSION ON HOSPITAL LENGTH OF STAY IN PEDIATRIC SICKLE CELL PATIENTS WITH ACUTE CHEST SYNDROME**

Adelle N. Singh, Oluwakemi Badaki-Makun. Pediatric Emergency Medicine, Johns Hopkins Children's Center, Baltimore, MD

10.1136/jim-2017-000429.24

Purpose of Study Acute chest syndrome (ACS) is a major complication of sickle cell disease (SCD) associated with significant morbidity and mortality. While acute blood transfusions have commonly been incorporated in the treatment of ACS, there are few studies that evaluate the effect of packed red blood cell (PRBC) transfusion on outcomes in patients with ACS. The objective of this study was to determine the association between PRBC transfusion and hospital length of stay (LOS) in SCD patients admitted with the diagnosis of ACS.

Methods Used In this cross-sectional study, pediatric (age ≤21 years) patients admitted to hospitals within the Pediatric Health Information System (PHIS) network from January 1st 2008 to December 31st 2012 with International Classification of Diseases – 9 (ICD-9) diagnoses of SCD and ACS were included. Data were analyzed using descriptive statistics and t-tests. The primary outcome was hospital LOS.

Summary of Results Mean age at time of admission was 10.1±5.6 years. Males accounted for 56% of visits and in 73% of visits, patients possessed the hemoglobin SS genotype. Of the 8361 participants, 827 received PRBC transfusions and were found to have a mean LOS of 6.1 days (95% confidence interval (CI) 5.7 to 6.5 days) as compared to the non-transfused group, which had a mean LOS of 5.0 days (95% CI 4.9 to 5.1 days), p <0.001.

Conclusions The administration of PRBC in the acute management of ACS in this pediatric population is associated with an increased LOS. Future studies should aim to determine factors contributing to this increase in hospital LOS.

Scientific Session II
12.45PM – 2.45PM

13 **AN INTRONIC VARIANT IN DCHS2 IS ASSOCIATED WITH BONE MINERAL DENSITY IN CHILDREN AND YOUNG ADULTS**

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10.1136/jim-2017-000429.25

Purpose of Study Fragility fractures lead to significant morbidity and mortality in seniors. Recently, Compressive

Strength Index (CSI) has been validated as a predictor of hip fracture risk. Han et al. have identified 3 genes that may play a role in determining CSI in Caucasians and Asians: FADS1, FADS2 and DCHS2 containing SNPs (FADS1/rs174549; rs174583, FADS2/rs174577, DCHS2/rs7672337). This study sought to examine whether these polymorphisms also influence other measures of bone quality in children and young adults.

Methods Used *Cohorts:* The Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY) cohort included Caucasian males: N=55 (avg 24 yrs) and females: N=54 (avg 22 yrs). Total body and lumbar bone mineral density (BMD) were analyzed. The Bone Health Cohort included African American children (age 5-9): 46 males and 41 females. Phenotypes were total body minus head BMD and lumbar BMD. *Genotyping:* Three SNPs were genotyped using the Illumina Multi-Ethnic Genotyping Array. Rs7672337 was genotyped utilizing a Taqman assay. The relationship between genotype and phenotype was tested using ANCOVA models where phenotype was the independent variable, genotype was the dependent variable, and age was a co-variant.

Summary of Results In the AIMMY cohort, lumbar BMD was found to be significantly associated with rs7672337 (DCHS2) in Caucasian females (p=0.047). No other significant associations were seen within the AIMMY or Bone Health cohorts.

Conclusions A significant association was found between DCHS2 and lumbar BMD in Caucasian females in the AIMMY cohort. No other significant associations were uncovered. In African Americans, other genes may have a more prominent impact on bone health phenotypes. Future research may demonstrate that DCHS2, FADS1 and FADS2 have a stronger association with the parameters that determine CSI, such as femoral neck area and hip BMD.

14 UNABLE TO BE PUBLISHED

15 UNABLE TO BE PUBLISHED

16 COGNITIVE DEFICITS IN ATHEROSCLEROSIS-PRONE LUPUS MICE ATTENUATED BY RESVERATROL VIA THE ADENOSINE A2A RECEPTOR

Lora J. Kasselman, Heather A. Renna, Nicolle M. Siegart, Hirra A. Arain, Melissa Fazzari, Steven E. Carsons, Allison B. Reiss. Biomedical Research, Winthrop University Hospital, Mineola, NY

10.1136/jim-2017-000429.28

Purpose of Study Neuropsychiatric lupus (NPSLE), a complication of systemic lupus erythematosus (SLE), presents with diverse deficits such as cerebrovascular disease, cognitive dysfunction, movement and mood disorders. NPSLE is extremely difficult to treat. SLE is also associated with high risk of cardiovascular complications such as accelerated atherosclerosis, stroke, and heart attack, all of which compromise vascular health that is key to maintaining cognitive function. Acute neurologic symptoms resulting from NPSLE do not always respond to typical anti-inflammatory SLE medications such as steroids and hydroxychloroquine. This indicates that cognitive changes in NPSLE are not due to inflammation alone, but may be attributed to the interaction between vascular disease and chronic inflammation. *Our goals here are to determine if atherosclerosis in lupus contributes to cognitive complications and if resveratrol, a dietary supplement with anti-atherogenic and neuroprotective properties, can reverse or delay onset of lupus-related cognitive sequelae.*

Methods Used Atherosclerosis-prone lupus mice (ApoE/Fas double knockout) were treated with either resveratrol (10 mg/kg/day) or resveratrol+istradefylline (adenosine A2A receptor antagonist, 5 mg/day) for 10 wks. Pre- and post- treatment, behavioral testing was done. Bone marrow derived macrophages and brain tissue were evaluated for changes in gene and protein profiles. Foam cell formation was measured.

Summary of Results Atherosclerosis-prone lupus mice were unable to distinguish novel objects and showed impaired motor coordination. Resveratrol improved both cognitive deficits, but these improvements were abolished upon exposure to istradefylline. Resveratrol increased brain expression of macrophage markers and fractalkine, and decreased expression of angiogenic factors; these changes were also attenuated by exposure to istradefylline.

Conclusions Resveratrol, a polyphenolic compound found in red wine and grapes, may be beneficial in reversing or slowing progression of cognitive changes in lupus via adenosine A2a receptor activation. The favorable safety profile of this nutraceutical and lack of other effective NPSLE treatments encourage further exploration of resveratrol in human NPSLE clinical trials.

17 CONCUSSION RECOGNITION AND MANAGEMENT IN THE PEDIATRIC URGENT CARE SETTING

Deena Berkowitz,[2,1] Gia Badolato,[1] **Sean M. Gillen,[1]** Rob Grell,[2] Rhana Alghamdi,[2] Shireen Atabaki[2,1]. [1]Emergency Medical Trauma Center, Children's National Medical Center, Washington, DC; [2]The George Washington University School of Medicine and Health Sciences, Washington, DC

10.1136/jim-2017-000429.29

Purpose of Study Concussion often goes unrecognized in urgent care. The Acute Concussion Evaluation- ED (ACE-ED) and ACE–ED Care plan, a psychometrically validated concussion diagnostic tool and management plan, were integrated into the electronic health record (EHR) at a level 1 urban pediatric emergency department (PED) and onsite urgent care. Our objective is to assess the effect of integration of these diagnostic and management tools into the EHR.

Methods Used Patients <21 years old with a chief complaint of head injury were enrolled. Patients triaged to urgent care had the ACE-ED completed by their clinician.

This electronic decision support tool uses conditional logic to generate a diagnosis and recommendation. For patients meeting criteria for a concussion, the tool launches an icon on the tracking board informing staff that the patient has a concussion and should receive the ACE-ED Care Plan upon discharge.

Summary of Results In 2015, 2,236 patients presented with chief complaint related to head injury and 18.1% were diagnosed with concussion. Of the 2,326, 443 (19%) were seen in the urgent care and subsequently 13.4% were diagnosed with a concussion. We were more likely to diagnose concussion in the PED. (OR 1.5 (95%CI: 1.1-2.1) A quality improvement (QI) intervention to facilitate workflow decision support to improve the diagnosis and management of concussions in the pediatric urgent care patients is warranted.

Conclusions Clinical decision support tool for concussion diagnosis is feasibly integrated into the electronic health record for urgent care. This clinical decision support results in fewer concussion diagnoses in the urgent care setting when compared to the emergency department. A quality improvement intervention for urgent care provider education and workflow integration may increase the number of patients correctly diagnosed with a concussion, decrease practice pattern variation, and improve patient education for concussion management after discharge.

18 LONG-TERM RESPONSE AND PROBABLE CURE OF PATIENTS WITH B-CELL MALIGNANCIES WITH DOSE-ESCALATED RITUXIMAB

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10.1136/jim-2017-000429.30

Purpose of Study Rituximab (R), a chimeric monoclonal antibody targeting CD20 antigen on B-cells, has become standard in B-cell malignancies, most often in conjunction with cytotoxic chemotherapy. Dose escalation of R as a single agent has demonstrated improved activity in previously treated/poor prognosis chronic lymphocytic leukemia (CLL) (O'Brien 2001, Wiernik 2011).

Methods Used We initiated dose-escalated R treatment (Rx) as a single agent in 4 patients (pts), who declined cytotoxic chemotherapy, 3 with no prior Rx (2 – peripheral blood/marrow only disease – CLL variant, 2 clones; mantle cell lymphoma (MCL) variant; 1- follicular lymphoma (FL) with bulky nodes and open, draining biopsy wound; 1 – Waldenstrom's (WM) with severe anemia requiring transfusion and Karnofsky performance status of 50%). All received (wkly) induction doses x 4 wks, starting at 375-500 mg/m2, followed by wkly or monthly dose escalation to 1500 mg/m2.

Summary of Results Table shows biologic characteristics of pts and Rx courses. 3 achieved complete responses (CR) after R alone, durable now for 6.5+ – 15+ years. The pt with WM has been clinically stable with no anemia or transfusion for 13+ years; her serum protein electrophoresis (SPEP) continues to show stable abnormal immunoglobulin (Ig) levels. All tolerated R escalation with no complications except initial infusion reaction. The pt with FL demonstrated healing of her wound as the LN reduced in size from treatment.

Conclusions Dose-escalated R may be curative for some pts with B-cell malignancies, unlike the empiric dose of 375 mg/m2, and deserves further study.

19 AN ANALYSIS OF COMPUTED TOMOGRAPHY-RELATED RADIATION EXPOSURE IN PEDIATRIC TRAUMA PATIENTS

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10.1136/jim-2017-000429.31

Purpose of Study Traumatic injury is a leading cause of pediatric death and morbidity. Although computed tomography (CT) scans may be necessary to evaluate injury, there is concern that exposure to radiation increases lifetime risk of developing cancer. Recent evidence suggests that pediatric trauma patients imaged at referring facilities (RF) may be exposed to higher CT radiation doses than patients imaged at a pediatric trauma center (PTC). To define the problem in our region, we compared the radiation doses used for pediatric CTs obtained at RFs to those obtained at our PTC to assess the consistency of the radiation exposure between sites.

Methods Used In this retrospective case-control study, patients 0-18 years of age with CT imaging performed either at a RF prior to transfer or at the PTC within an academic children's hospital from 1/1/2015 to 1/5/2016 were

Pt/age dx/Rx w R	Diagnosis (dx)	Verifying Lab	Dosing Rituximab	Response/duration
41/M – Rx age 42	CLL/Marginal Zone PB/marrow only	t(2;7); CD5+ CD23-, CD 20 ++	375-1500 mg/m2 Intermittent, 3 yrs	CR x 10+ years
52/F – Rx age 52	MCL variant PB/marrow only	t(11;14); CD5+ CD23-, CD20++	500– 1500 mg/m2 6 total doses	CR x 15+ years
60/F – Rx age 60	FL; bulky left inguinal/iliac LNs	Kappa, BCL6, BCL2– 65% of B cells; Ki67 -20%	375– 1500 mg/m2 Induction/maint x 8 mo	CR x 6.5+ years
58/F - (prior RX) RX w R age 64	WM – marrow/bone/severe anemia	IgM>400; IgG 173; IgA <7	375-1500 mg/m2 1 year	PR/SD – no anemia, no clinical findings; SPEP stable x 13+ years

identified from the institutional trauma registry. Demographic and clinical data were obtained from the trauma registry. CT scan data were obtained from review of CT images and compared using descriptive statistics.
Summary of Results We identified 483 patients (179 RF, 304 PTC) with a total of 589 CT scans (225 RF, 364 PTC). Of these, 288 head CTs (81 RF, 207 PTC) and 86 abdominal/pelvic CTs (28 RF, 58 PTC) had identifiable doses. The mean radiation dose [measured in dose-length product (DLP)] was significantly higher for RF scans in comparison to PTC scans [head: mean RF DLP= 541±333 vs PTC 451±214 ($p < 0.01$); abdomen/pelvis: mean RF DLP= 279±160 vs PTC 181±201($p<0.05$)]. The RF and PTC groups did not differ significantly by age, weight, or gender. The RF and PTC groups with abdominal/pelvic CTs differed significantly by race [white: RF=71%, PTC=43%; African American: RF=14%, PTC=44% ($p<0.01$)].
Conclusions Our data suggest that pediatric trauma patients in our region with CT scans performed at RFs are exposed to significantly higher doses of radiation when compared to similar patients with CT scans performed at the PTC. These data support further study to identify factors associated with increased radiation exposure as well as outreach to RFs to promote reduction of radiation exposure.

20 PEAK COUGH FLOW MEASUREMENTS IN CHILDREN WITH NEUROMUSCULAR DISORDERS, 5 YEARS OF EXPERIENCE AT A TERTIARY CHILDREN'S HOSPITAL

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10.1136/jim-2017-000429.32

Purpose of Study Pulmonary function testing (PFT), more specifically, forced vital capacity(FVC), maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP) and peak cough flow (PCF) are recommended at regular intervals to guide medical interventions in patients with neuromuscular disease (NMD). In particular PCF measurements are used to recommend the initiation of assisted cough. However, the vast majority of PCF data derives from subjects with DMD and small sample sizes which could limit their application to other populations. The goal of this study was to characterize PCF values among different NMDs
Methods Used Retrospective cross sectional study of patients seen in the Multidisciplinary Pediatric Muscular dystrophy clinic from 2010–2016. Clinical and demographic variables were obtained by review of Electronic Medical record at Children's National Medical Center and included age, gender, ambulation status, FVC, MEP, MIP and PCF
Summary of Results 339 patients(mean age 14.2 years,± SD 6.26) were included in this study. The most common diagnosis included Duchene's muscular dystrophy (DMD) (n=102, 30%), congenital muscular dystrophy (CMD) (n=39, 11.5%), Charcot Marie Tooth disease (CMT) (n=39, 11.5%) and Becker's muscular dystrophy (BMD) (n=24, 7%). A sub-analysis of PFTs among the four major diagnoses showed lower mean FVC and PCF values in DMD and CMD compared to BMD and CMT. PCF values had a poor correlation with FVC among DMD, BMD and CMT (R2 adjusted 1.1%, 14% and 3.6% respectively) independently of ambulation status, however it had a better correlation in subjects with CMT (R2 adjusted 49%). PCFs were not statistically different among diagnosis when adjusted by ambulatory status (mean 269±97.7 vs 286.8±99.4 lt./min). Interestingly young children (under 10 years of age) had lower PCF relative to older subjects (mean 190.3 ± SD 50.9 vs 322.9 ± SD 96.7 lt./min)
Conclusions PCF values had a poor correlation with FVC, except for CMT disease. PCF values in young children were under 270 lt./min; the cutoff value suggested for starting cough assisted techniques. These results raise the question of using specific adult derived cutoff values to guide therapies in the pediatric population and highlight the importance of conducting longitudinal trials to identify PFTs natural history among different types of NMD

21 EVALUATION OF A SPINAL PROTECTION PROTOCOL CHANGE BY THE MARYLAND EMERGENCY MEDICAL SYSTEM

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10.1136/jim-2017-000429.33

Purpose of Study Spinal immobilization has been the standard of care for trauma patients since the 1960s, despite limited supporting evidence. Recent studies show that immobilized children report more pain, receive more radiographs, and are more frequently admitted compared to controls. The Maryland Emergency Medical System (MD EMS) instituted a new spinal protection protocol in 2015 with more restrictive criteria for which children should be immobilized. The Pediatric Emergency Care Applied Research Network & EMS have identified the development and validation of spinal immobilization guidelines for children as a priority area for pre-hospital research.
Methods Used We conducted a retrospective chart review of trauma patients transported by MD EMS to our Pediatric Trauma Center from July 2014 to June 2016. We examined rates of radiographs, spinal imaging, admission and length of stay (LOS) pre and post protocol change using bivariate analysis. Analysis of patients transported by a neighboring jurisdiction (DC) with no change in spinal immobilization protocol were analyzed for comparison. Subset analysis was performed on patients with higher acuity triage levels.
Summary of Results 3,621 encounters met inclusion criteria (1660 from MD, 1961 from DC). Post protocol, MD trauma patients had a reduction in rates of plain radiographs that did not reach statistical significance (20 vs 17%; $p=0.15$) and a significant decrease in admission rates (25 vs 18%; $p=0.0004$). Median LOS was 262 vs 250 minutes ($p=0.08$). DC patients did not show any significant changes in imaging rates, admission or LOS. Subset analysis of higher acuity patients showed similar results

except the median LOS increased from 305 to 330 minutes (p=0.02).

Conclusions After the MD EMS protocol change we observed a reduction in imaging rates that did not reach statistical significance, and a significant reduction in admission rates. A nearby jurisdiction did not show comparable changes in imaging or admission rates. Further research with larger cohorts, including patients transported to community hospitals, and linking of EMS and hospital data is needed to further describe whether such protocol changes can reduce rates of immobilization, radiography and admission for pediatric trauma patients.

22 THE TEMPORAL DYNAMICS OF THE TRACHEAL MICROBIOME IN TRACHEOSTOMISED PATIENTS WITH AND WITHOUT LOWER RESPIRATORY INFECTIONS

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10.1136/jim-2017-000429.34

Purpose of Study Airway microbiota dynamics are still poorly understood due, in part, to insufficient longitudinal studies and lack of uncontaminated lower airways samples. Furthermore, upper airway microbiomes are frequently used as a proxy for lower airway microbiomes, but their similarity is still under debate. Here we address these issues by comparing the diversity and temporal dynamics of tracheal microbiotas in tracheostomised patients with (YLRI) and without (NLRI) lower respiratory infections (LRIs) sampled over one calendar year. Tracheal microbiotas sampled via tracheostomy are free of upper airway microbes since they are directly aspirated from the trachea.

Methods Used We prospectively collected 127 tracheal aspirates during four consecutive quarters (seasons) from 40 patients, of whom, 20 developed LRIs and 20 remained healthy. All aspirates were collected when patients had no LRI. We generated 16S rRNA-based microbial profiles and analyzed them using Mothur and the SILVAv123 database.

Summary of Results Tracheal microbial profiles differed from those previously reported for the nose and oral cavity. Alpha- and beta-diversity varied significantly ($P<0.05$) between NLRI and YLRI patients and seasons. *Pseudomonas aeruginosa* was detected in all patients, but no symptoms of nosocomial infections were observed. *Haemophilus* was significantly ($P<0.05$) more abundant in YLRI patients (9.3%) than in NLRI patients (4.9%), while *Corynebacterium* showed the inverse relationship (4.7% in YLRI and in 6.6% NLRI). Fusobacteria, *Fusobacterium*, *Stenotrophomonas* and *Pseudomonas* also changed significantly ($P<0.05$) between seasons in the NLRI patients, while Proteobacteria, *Haemophilus*, *Stenotrophomonas* and *Streptococcus* changed in YLRI patients.

Conclusions Upper and lower airway microbiotas differ in the proportions of their most abundant bacteria. The taxonomic composition and diversity of tracheal microbiotas vary significantly according to whether or not individuals developed LRIs and the time (season) of sampling. Future studies aiming to investigate or manipulate the airway microbiota need to be cognizant of their temporal instability.

23 OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE PLACEMENT IN HOSPITALIZED CANCER PATIENTS IN THE UNITED STATES

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10.1136/jim-2017-000429.35

Purpose of Study The decision to provide enteral feeding in cancer patients is based on several factors including the scope of reversibility, nutritional requirements, overall morbidity, involvement of the gastrointestinal tract and palliative care considerations. Outcomes of PEG tube placement in cancer patients have not been studied and compared with non-cancer patients over an extended period on a national basis. This is an analysis of a database with nationwide representation for outcomes over a 13 year period.

Methods Used Data regarding cancer and non-cancer patients who underwent PEG tube placement was extracted from the Nationwide Inpatient Sample (NIS) from 2000 to 2012 using ICD-9-CM codes. NIS variables were used to identify in-hospital mortality, discharge dispositions. We also examined the admissions related to complications from PEG tube placement. Chi square test and Wilcoxon rank test were used to compare categorical and continuous variables respectively.

Summary of Results 2,325,603 hospitalized patients underwent PEG tube placement from 2000 to 2012. Of these, 465,049 (20%) were cancer patients. Of all cancer related admissions, 0.86% received PEG tube placement. The rate of PEG tube placement in cancer patients has gradually increased from 2000 to 2012 ($p=0.007$). The number of hospital admissions with PEG tube-related complications have increased from 6696 in 2000 to 9640 in 2012. The in-hospital mortality in non-cancer patients who received PEG tube was higher than in those who did not get PEG tube (9.85% vs. 8.05%, $p=0.0000$). Cancer patients who underwent PEG tube placement were discharged to nursing homes less often than non-cancer patients (47% vs. 80%, $p<0.001$).

Conclusions The rates of PEG tube placement in cancer patients and related complications have increased in the last decade. The in-hospital mortality of non-cancer patients who received PEG tube placement was higher and these patients were discharged to nursing homes more often than cancer patients who received PEG tube placement. The decision to place a PEG tube in cancer patients should be individualized taking into consideration the effect of possible PEG tube-related complications, availability of support systems, prognosis of the underlying malignancy and the desired quality of life.

24 BLOCKADE OF THE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS IS NOT SUFFICIENT TO PREVENT ATHEROGENIC DISRUPTION OF LIPID METABOLISM BY PLASMA FROM TYPE 1 DIABETES PATIENTS: A CLUE IN THE SEARCH FOR IMPROVED CARDIOVASCULAR HEALTH IN DIABETES

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10.1136/jim-2017-000429.36

Purpose of Study Advanced glycation end products (AGE) are glycated proteins prevalent in diabetes mellitus (DM) that promote atherosclerosis. We have demonstrated that plasma from type 1 DM (T1DM) patients is atherogenic, decreasing cholesterol efflux proteins in cultured THP-1 macrophages compared to healthy control (HC) plasma. Here we explore the impact of the receptor for AGE (RAGE) on macrophage lipid handling, a key factor in atherosclerosis.

Methods Used THP-1 macrophages (10^6/ml) were incubated for 18 h in RPMI media in the presence of 10% plasma from each enrolled patient in triplicate±anti-RAGE antibody. Cholesterol influx and efflux proteins were quantified by real-time RT-PCR. Intracellular cholesterol composition and cholesterol efflux were measured. Uptake of oxidized (ox)LDL and foam cell formation were quantified.

Summary of Results Expression of the cholesterol efflux protein ABCA1 was significantly higher in macrophages exposed to anti-RAGE antibody in both T1DM and HC plasma conditions ($p<0.001$). Similarly, 27-hydroxylase (27-OHase) message was increased with anti-RAGE antibody and was highest in HC plasma+anti-RAGE ($p<0.001$). Anti-RAGE antibody downregulated scavenger receptor LOX-1 mRNA in both HC and T1DM plasma-treated cells ($p<0.001$). Macrophages exposed to T1DM plasma had increased intracellular cholesterol ester levels that were not corrected by pre-treatment with anti-RAGE ($p=0.05$). T1DM treated cells had increased oxLDL uptake not mitigated by anti-RAGE ($p=0.75$).

Conclusions We demonstrate that elevated AGE in T1DM patient plasma inhibits cholesterol efflux genes and suppresses intracellular cholesterol processing via 27-OHase and ABCA1 in naïve macrophages. RAGE inactivation restores mRNA for the ABCA1 transporter and 27-OHase enzyme, but increased intracellular cholesterol ester levels and oxLDL uptake are not prevented by blocking RAGE. These findings suggest that factors other than AGE that compromise cholesterol transport in T1DM may be targets for future prevention and treatment of atherosclerosis.

Display Posters

DP1 APPROACH TO PATIENTS WITH LABELLED PENICILLIN ALLERGY

Josie Joy Go, Marianne Frieri. Nassau University Medical Center, East Meadow, NY

10.1136/jim-2017-000429.37

Purpose of Study True penicillin allergy accounts for less than 20% of the patients with self-reported penicillin allergy. This paper aims to provide insights to clinicians on the effect of penicillin allergy mislabeling on antibiotic stewardship and the appropriate measures that could be done.

Methods Used A comprehensive search of medical literature was conducted using PubMed database. Only literatures written in English language from year 2000 to 2016 were included. The database was searched using the keywords penicillin allergy guidelines and antibiotic stewardship.

Summary of Results Misclassification based on a self-reported history of penicillin allergy (PA) is common. Clinicians are now using broader spectrum antibiotics, like fluoroquinolones and vancomycin, due to a self-reported history of PA. This leads to increases in economic cost, medication side effects (clostridium difficile colitis) and multidrug resistant pathogens (methicillin resistant staphylococcus aureus, vancomycin resistant enterococcus).

A thorough history taking including the chronology of symptom onset after penicillin exposure is very helpful in differentiating between a true PA from other adverse reactions. All patients with history inconsistent with a true PA should undergo further allergic testing. Allergic skin testing against the major and minor determinants of penicillin is the best initial diagnostic test in determining a real penicillin allergy. Penicillin challenge test can also be done and is useful in excluding patients with low probability of PA resensitization. Patients with history consistent with anaphylaxis should not undergo a challenge test as the risk for recurrent anaphylaxis is high. Both penicillin skin test and challenge test are done in a controlled setting by an allergist or a trained personnel.

Conclusions Only few patients labelled with PA have a true PA. These patients should be referred to and evaluated by an allergist or trained personnel to determine if the patient has a true PA or not. This is important because mislabeling patients as PA places a great burden on economic cost, antibiotic stewardship, morbidity and mortality.

DP2 DIRECT TO CONSUMER TELEMEDICINE: PROVIDER AND PATIENT PERCEPTIONS

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Purpose of Study Lack of access to pediatric subspecialty care is a major barrier to pediatric health for underserved populations in the Washington DC, Virginia and Maryland area. Lack of transportation, long wait times, missed work and school, prevent sub-specialty care. Direct to consumer (DTC) telemedicine provides subspecialized care in patient's homes through computers, tablets and smart phones.

Methods Used Structured interviews of parents and providers were performed pre-implementation of a subspecialty DTC telemedicine progam for underserved children in

Washington DC, Virginia and Maryland. Participating subspecialties included providers in neuropsychology, neurology, diabetes, and gastroenterology.

Summary of Results Pre-implementation, structured interviews demonstrated a need for a more time-effective, convenient solution to the current model for subspecialty care. Parents reported telemedicine could save them time and cost while eliminating driving, parking and waiting for an in-person appointment. Parents stated that for conditions such as feeding disorders the benefits of observing the child in their home environment would reduce stress/anxiety. Providers reported two most positive aspects of telemedicine to be for follow-up education in the families' homes and coordination of multiple specialities/personnel in a single visit.

Conclusions Parents desire expansion of DTC telemedicine subspecialty services. Providing subspecialty care directly into a patient's home may improve parent satisfaction and eliminate barriers.

DP3 EARLY ONSET OF PEMPHIGUS VULGARIS IN A PUERTO RICAN PATIENT

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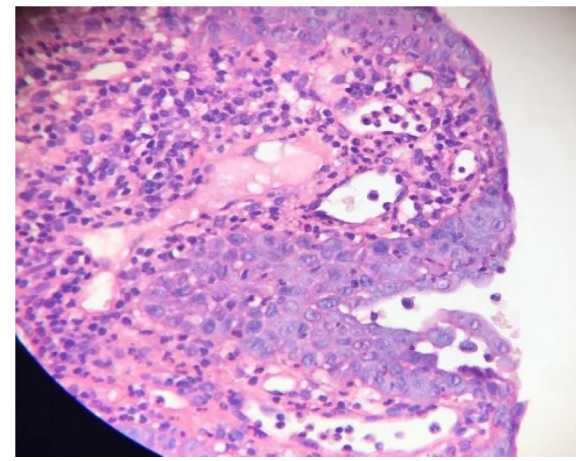
Purpose of Study Pemphigus Vulgaris is a life-threatening blistering disorder characterized by acantholysis that results in the formation of intraepithelial blisters in mucous membranes and skin. There are 0.5 to 3.2 cases reported each year per 100,000 population, with the highest incidence in the 5th and 6th decade of life. Diagnosing this disease early is very important to prevent complications and avoid unnecessary treatments.

Methods Used Observational study.

Summary of Results A 31 year-old homeless man presents to HURRA complaining of mouth pain, dysphagia and odynophagia for both solids and liquids, white oral plaques and many ulcers, which began 6 months back and has been unable to eat for the last 5 days due to pain. He was treated for oral candida but lesions did not improved. On physical exam, his vital signs were stable. He had visible ulcerated lesions in his lips with severe swelling and in the inner oral mucosa. Nikolsky sign showed a positive reaction, there were white plaques within oropharynx. On labs HIV 1 and 2 were non-reactive, CD4 and CD8 count and IgG, IgM, IgE, IgA were normal .On the other hand desmoglein type 3 was positive and type 1 was negative, punch biopsy was performed and revealed intraepidermal vesicles with acantholysis, Immunofluorescence study IgG and C3 were positive; the findings were consistent with pemphigus vulgaris. Patient was treated with prednisone and markedly improvement of signs and symptoms were reported.

Conclusions Diagnosis of Pemphigus Vulgaris can be challenging when the suspected disease presents with symptoms that mimics other diseases, causing a delay in establishing an early definitive diagnosis. This case involved a young man who went multiple times to ER- hospitals settings due to symptoms mentioned without finding improvement. Recognizing the signs and symptoms allows for early detection and treatment to prevent complications.



Abstract DP3 Figure 1 Acantholysis

DP4 WHEN REFRACTORY HPERKALEMIA IS NOT A REBOUND

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Purpose of Study Highlight the effect of heparin as a cause of refractory hyperkalemia and to raise awareness about the effect of heparin as a cause of refractory hyperkalemia more than 48 hours post-hemodialys

Methods Used: Clinical course of illness On admission date 08/18/2014 showed a serum potassium level of 7.4 mEq/L (normal range 3.3–5.1) from non-hemolyzed sample, confirmed with a second sample with a potassium level of 7.2 mEq/L, each blood sample was taken 16 hours after hemodialysis was done.Urgent hemodialysis was started. The patient was scheduled for hemodialysis every 2 days with the following parameters: On 1st day of post-hemodialysis the K +: 7.2 mEq/l, 2nd Post-HD, K+ levels were 6.1 and on 3rd HD K+ levels were 6.9 mEq/ LHeparin was identified as a possible cause of refractory hyperkalemia to hemodialysis. Heparin was discontinued and after the 3rd round of hemodialysis, the potassium level was 3.4 mEq/l.

Summary of Results Potassium is the most abundant intracellular cation (100-150 mmol/L) and is critical in many physiological functions. Hyperkalemia is a life-threatening condition in which serum potassium exceeds 5.5 mmol/L During hemodialysis, serum potassium may decrease as much as 1.2 to 1.5 mEq/h. In our case, potassium persisted at elevated levels even with a low potassium intake and three hemodialysis sessions. Heparin sodium is routinely used in the prophylaxis against deep venous thrombosis in medical and surgical patients. While most physicians are aware of heparin induced thrombocytopenia and skin necrosis, the association of heparin and hyperkalemia is not well-recognized.

Conclusions A rebound hyperkalemic effect is expected within the 6 hours post hemodialysis, in our case the samples were taken 16 hours post hemodialysis from non-hemolized blood. During the course of illness, no change on hemodialysis parameters were made. The use of heparin was detected as the cause of hyperkalemia refractory to hemodialysis.The aim of this case report is to highlight the effect of heparin as a cause of refractory hyperkalemia and to raise awareness about the effect of heparin as a cause of refractory hyperkalemia more than 48 hours post-hemodialysis.

DP5 HELICOBACTER PYLORI ASSOCIATED IMMUNE THROMBOCYTOPENIA

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Purpose of Study Idiopathic thrombocytopenic purpura (ITP) is a common hematologic disorder characterized by platelet autoantibodies, low platelet counts, and bleeding. The development of Helicobacter pylori associated Idiopathic thrombocytopenic purpura appears to depend on multiple factors. Approximately 25 million Americans suffer from Helicobacter Pylori disease at some point in their lifetime. Each year there are 500,000 to 850,000 new cases and the incidence of immune thrombocytopenia among adults in the USA is estimated to be 3.3 per 100,000 adults/year. Eradication therapy is simple and inexpensive, the advantage of avoiding long-term immunosuppressive treatment for those who respond.
Methods Used Case report
Summary of Results Idiopathic thrombocytopenic purpura is a diagnosis of exclusion that needs to be considered in patients with low platelets count and with association of helicobacter pylori, this association has been increasing in importance with more cases found in medical literature showing that with proper treatment there is improvement of symptoms and platelet levels.
Conclusions This case represent the importance of keeping in mind the association between thrombocytopenia and Helicobacter Pylori infection. New cases-reports and research can provide more information about how to recognize this pathologies, their interaction and development of adequate treatment.

DP6 EXTRANODAL DIFFUSE LARGE B-CELL LYMPHOMA PRESENTING EXCLUSIVELY IN THE TESTICLE

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Purpose of Study We aim to contribute to the body of scientific literature on and enhance understanding of the pathology and therapeutics of diffuse large B-cell lymphoma as it unusually presents in the testicle.
Methods Used A review of the literature as well as case reports of extranodal diffuse large B cell lymphoma as it presents in primarily in the testicle.
Summary of Results We present the case of a 90 year old man who was diagnosed with left-sided testicular diffuse large B cell lymphoma (DLBCL) at the age of 89 years. He initially presented with left testicular pain and palpable mass prior to the diagnosis. He noticed this mass over one year before diagnoses, but did not seek medical attention when it first manifested. He was found to have a malignant mass on sonographic imaging and subsequently underwent a left orchiectomy one month after diagnosis and pathology of this neoplasm returned positive for DLBCL. A bone marrow biopsy was performed and found to show normal findings. Subsequent CT imaging of the patient revealed iguninal adenopathy and no other evidence of disease. He is currently in standard treatment for DLBCL with a combination chemotherapeutic regimen of rituxan, cyclophosphamide, doxorubicin, vincristine and prednisone and is tolerating therapy well.
Conclusions Primary testicular lymphoma is an aggressive and rare form of extra-nodal non-Hodgkin lymphoma (NHL) which only accounts for <5% of all testicular malignancies and fewer than 2% of all cases of NHL. Most cases of this malignancy are histologically found to be diffuse large B-cell lymphoma. In this case study and review, we discuss the epidemiology, clinical manifestations and factors of prognosis of testicular DLBCL. We present a summary of the recent advances in our understanding of this disease as well as the standard therapy and advancements in the scope of therapy involving promising improvements in survival with combination chemotherapy, radiation therapy and prophylaxis of described relapse in the central nervous system. We review findings of the large retrospective series as well as prospective clinical trials and therapeutic philosophies in the field for current practitioners.