2ND ANNUAL

RESEARCH RETREAT 2023

Saturday, September 30th
7:30 am to 1:20 pm

Fourth Floor Auditorium
New Academic Building

UPSTATE
MEDICAL UNIVERSITY

Department of Medicine

WELCOME TO THE 2ND ANNUAL DEPARTMENT OF MEDICINE **RESEARCH RETREAT**

Today's event features research projects by junior faculty, fellows, residents, and medical students affiliated with the Upstate Medical University Department of Medicine.

Each abstract will be presented in poster form to allow for project-related discussion between the authors and any attendee. This is a unique opportunity for clinical investigators and trainees to meet and discuss collaborative efforts leading to new discoveries on the causes, diagnosis, and treatment of the broadest range of disorders managed by the Department of Medicine.

Selected podium speakers will have eight minutes to present followed by two minutes to discuss their research abstracts. Further discussions can take place during the poster session.

We hope you enjoy this interactive and informative event. Feedback on the format and future retreats will be sought from all attendees.

UPSTATE
MEDICAL UNIVERSITY

Department of Medicine

Welcome to the 2nd Department of Medicine
Research Retreat, September 30th, 2023.

The event features research projects by junior faculty, fellows, residents, and medical students affiliated with the Department of Medicine. Each abstract will be presented in poster form to allow for project-related discussion between the authors and any attendee. This is a unique opportunity for clinical investigators and trainees to meet and discuss collaborative efforts leading to new discoveries on the causes, diagnosis, and treatment of the broadest range of disorders managed by the Department of Medicine. Selected podium speakers will have 8-minutes to present followed by a 2-minutes to discuss their research abstracts. Further discussions can take place during the poster session.

We hope you enjoy this interactive and informative event.

Feedback on the format and future Retreats will be sought from all attendees.

Table of Content

Program:

Pulmonary/Critical Care - Moderator: Markus Gutsche, MD

8:50-9:00AM Clinical Features of Genetic Resilience in COPD

Authors: *Auyon J. Ghosh*, Matthew Moll, Brian D. Hobbs, Jonathan Hess, Liam Coyne, Michael H. Cho, Frank A. Middleton, Andras Perl, Edwin K. Silverman, Craig P. Hersh, Stephen J. Glatt

Internal Medicine – Hospitalist Medicine; Moderator: Sri Narsipur, MD

9:00-9:10AM Severity and impact of glucose-6 phosphate dehydrogenase deficiency in living right lobe liver donors undergoing right lobe hepatectomy

Authors: *Azhar Hussain*, Abdul Wahab Dogar, Kaleem Ullah, Abdul Ghaffar, Shams-ud-din, Subhash Gupta

9:10-9:20AM The baking of quality into Internal Medicine Residency Program: A Transformation

Author: *Harvir Gambhir*

9:20-9:35AM BREAK

9:35-9:45AM High-Dose STATIN given as loading dose prior to PCI reduces NO-Reflow Phenomenon in acute coronary syndrome: A Meta-Analysis of 4829 Procedures

Authors: *Jenish Bhandari*, Sonali Sachdeva, Udita Gupta, Avilash Mondal, Abdulrahman Hashem, Mahnoor Sukaina, Harshwardhan Khandait, Farah Yasmin, Rupak Desai, Akhil Jain, Hasnan M. Ijaz, Ankit Vyas

9:45-9:55AM Prevalence and long-term outcomes of intravenous iron sucrose THERAPY in heart failure with reduced ejection fraction: A single institution retrospective cohort study.

Authors: *Anuforo Anderson*, Shweta Paulraj, Prashanth Ashok Kumar, Ayo Soipe, Toluwalase Awoyemi, Michael Sandhu, Ashwini Ashwath, Eloho Olojakpoke, Ravi Singh, Alexander Somerville, Sherna Menezes, Joshua Harrison, Andrew Weinberg

Rheumatology & Clinical Immunology- Moderator: Andras Perl, MD, PhD

10:00 -10:10AM An unorthodox HLA-DRhi 'Hybrid' population in Rheumatoid Arthritis characterized using Spectral Cytometry – Supported by a DOM grant

Authors: *Christian Geier*, Haani Qudsi, Jihad Ben Gabr, Robert Winchester, Andras Perl

10:10-10:20AM Associations between antiphospholipid antibodies and thromboembolic events in COVID-19 infected and COVID-19 vaccinated patients: a single-center retrospective analysis.

Authors: *Sandy Nasr*, Andras Perl

Hematology Oncology- Moderator: Stephen Graziano, MD

10:20-10:30AM Bladder Primary Sarcomas (BSar): A Genomic Landscape and Clinical Outcomes Study – Supported by a DOM grant

Authors: *A Basnet*, J Jacob, R Lemma, R Wong, H Goldberg, D Pavlick, R Huang, D Lin, PE Spiess, R Li, AM Kamat, P Grivas, A Necchi, J Ross, G Bratslavsky

Nephrology- Moderator: Michael Lioudis, MD

10:30-10:40AM Renal transplant failure by COVID-19 associated collapsing glomerulopathy

Authors: *Sara Hashemi*, Asim Ali, Irshad Hussein, Brian Gallay

10:40-10:55AM- Dr. George Holz, Professor of Medicine and Pharmacology

Discovery of a New Class of Incretin Hormone-Based Designer Peptides for Treatment of Obesity and Diabetes

11AM- 11:45AM - Keynote Speaker: Gyongyi Szabo, MD, PhD, FAASLD, AGAF, FACP; Mitchell T. Rabkin, M.D. Chair; Professor of Medicine and Faculty Dean for Academic Affairs - Harvard Medical School; Chief Academic Officer - Beth Israel Lahey Health and Beth Israel Deaconess Medical Center

Inflammation in Steatotic Liver Disease: From Bench to Bedside

12:00PM – 1:00PM Poster Session During Lunch

1:00-1:20PM Closing Remarks – Cynthia Taub, MD, MBA,
Chair, Department of Medicine

Department of Medicine Research Mission Statement

The Department of Medicine conducts cutting edge research in 12 academic divisions. Our faculty has made paradigm-shifting discoveries during the last decade which are described in the research pages of each division. The Department is home to basic and translational research laboratories and investigator-initiated clinical trials supported by the National Institutes of Health, Research Foundations, and Pharmaceutical Organizations.

DOM VC Research Activity Report

Research Metrics in September of 2023:

Annual Research Grant expenditures:

RF accounting, kindly shared by Matt Hutz:

Endocrinology	1,518,113.11
Gastroenterology	7,011.01
Hematology/Oncology	1,042,400.42
Infectious Disease	940,497.06
Nephrology	6,721.50
Pulmonary/Critical Care	128,658.79
Rheumatology/Clinical Immunology	2,125,436.65
Total:	**5,768,838.54**

DOM VC Research Outline from 2022 forward

1. Training – Research Residency
    a. Scholarship model for 3rd IM year, seek UH allocation for years 1-2
    b. Grant writing –
    c. Statistics: open to all residents, fellows, and faculty; needed for QI projects
    d. Administrative support needs to be worked out jointly with VC for Education.
    e. Track may be attractive the applicants to conventional residency position.
2. Mentoring – Promotion incentive
    a. Resident
    b. Fellow
    c. Junior Faculty
3. Research –Financial support
    a. Pilot grants to secure extramural funding
    b. Collaborative Projects support
    c. COVID19 RFAs on mechanism of pathogenesis, characterization of clinical impact, effect of comorbidities, e.g., CVD/aPL/NAC/cytokine blockade
4. Career Development – Academic track/tenure track
    a. Salary protection for 3 years for new recruits,
    b. Salary protection for 5 years with candidates having NIH grants that includes salary support
    c. Salary protection with continued extramural support, productivity and support package to be reviewed every 5 years.
    d. State line support is to be provided for academic research track faculty.
    e. DDF should be used to support incentive packages.
5. Career Track Changes
    a. Tenure-track faculty will be offered transition to Clinical Tracks: Clinical-Educator track or Clinical Investigator track.
    b. Clinical Investigators are expected to have research grants to secure protected time
6. Grant Review
    a. DOM grants are reviewed by the Research Council
    b. Reviewers cannot review grants from the same DOM Division
    c. Grant Review Form has been developed
    d. Annual Commitment of ≤ $100,000 is awarded
    e. Review criteria have been developed, primarily aimed at promoting career development via extramural support
    f. Collaboration between Faculty and Trainees is encouraged

7. Research Council – Representatives from each division
    a. Mentoring.

    b. Review and help adjudicate pilot projects.
    c. Create salary and support incentive package for physician-scientists in academic/research/tenure-track position.
    d. Address financial transparency
8. Development of Centers and Institutes focused on Interdisciplinary Research and Clinical Care
    a. Centers should be supported by a percentage of indirect cost
    b. Centers should be reviewed every 5 years for productivity and support
    c. Centers should be a hub for research training, joint mentorship, and creations of clinical centers of excellence
9. DOM Research Webpage
    a. DOM Research News
    b. DOM Research Centers and Core – Links to Divisional Research Webpages
    c. DOM Research Training (joint with Educational Webpage)
    d. DOM Publications

Department of Medicine Grant Program

The Department of Medicine support research projects that are based on collaboration of the Faculty and Trainees, including medical and graduate students, residents, clinical and research fellows.

Grant Application Guide and Forms for Funding period 7/1/2022-6/30/2023.

1. The DOM grant application form provides detailed instructions on preparation and submission of the application. The application form follows the template of the Upstate Intramural Grant Program and it anticipates that all applicable regulatory policies will be satisfied. Deadline for submission: May 1, 2023.
2. Important items to consider:
    1. The Principal Investigator is expected to be a full-time faculty member of the Department of Medicine.
    2. Submission or active grant by a Principal Investigator is limited to one per year.
    3. The grant applications will be scored on the basis of significance, impact, feasibility, qualifications of the PI and collaborators, potential to secure extramural support, and inclusion of trainees.
    4. Trainees need to be involved and listed on the face page of the application.
    5. Progress report would be expected upon completion of the project.
    6. Applications will be reviewed by the DOM Research Council with representatives sought from each Division. Members of the council will be excluded from scoring grants of a PI from the same division.
    7. Applications and inquiries can be sent to Ms. Rosa Trpcevski at TrpcevsR@upstate.edu

Grant Applications Funded for the period 7/1/2021-6/30/2022

1. Alina Basnet, MD : Association of Molecular Profiles and Mutational Status with Distinct Histological Lung Adenocarcinoma Subtypes. An Analysis of the LACE Bio I and II Data.

2. Christina Geier, MD: Potential pathogenic functions and metabolic signatures of HLA-DR+CD45RA+ myeloid cells

3. Hiroshi Kato, MD: SLE Treg cells Expand Pathogenic CD8+ Memory T cells

4. Abirami Sivapiragasam, MD: Neurocognitive changes in breast cancer patients on hormonal therapy. Is there a difference between objective and perceived neurocognition?

Grant Applications Funded for the period 7/1/2022-6/30/2023

1. Auyon Ghosh, MD, MPH: Optimizing the Lung Gene Expression and Network Imputation Engine

2. Christian Geier, MD: Transcriptomic characterization of HLA-DR+ myeloid cells for potential pro-inflammatory pathways

Grant Applications Funded for the period 7/1/2023-6/30/2024

1. Auyon Ghosh, MD, MPH: Transcriptomic Predictors and Biomarkers of Sepsis-Induced Cardiomyopathy

2. Christian Geier, MD: Functional Studies of HLA-DR positive Myeloid Subsets in Rheumatoid Arthritis

3. Jivan Lamichhane: Evaluation of Large Language Models for Risk Prediction in the Heart Failure Population

4. Katja Reuter: Understanding gaps and barriers to care and support services among adolescents and young adults (AYAs) with thyroid cancer to inform an intervention and improve survivorship.

5. Koh-Eun Narm: Retrospective analysis of hospitalized patients with acute pulmonary embolism at SUNY Upstate Medical University

Congratulations to Auyon J. Ghosh, M.D., M.P.H.
Recipient of the 1st K08 Training Grant from the NIH by a member of the DOM:

Grant Title: “Genetic and Transcriptomic Resilience in COPD”

Research Abstracts

Internal Medicine

RESIDENT ABSTRACTS

Anderson Anuforo:

PREVALENCE AND LONG-TERM OUTCOMES OF INTRAVENOUS IRON SUCROSE THERAPY IN HEART FAILURE WITH REDUCED EJECTION FRACTION: A SINGLE INSTITUTION RETROSPECTIVE COHORT STUDY

Anuforo Anderson, Shweta Paulraj, Prashanth Ashok Kumar, Ayo Soipe, Toluwalase Awoyemi, Michael Sandhu, Ashwini Ashwath, Eloho Olojakpoke, Ravi Singh, Alexander Somerville, Sherna Menezes, Joshua Harrison, Andrew Weinberg

ABSTRACT

Background

Iron deficiency (ID) is prevalent in heart failure with reduced ejection fraction (HFrEF) defined as left ventricular ejection fraction (LVEF) ≤ 40%. Most trials used in the 2022 AHA/ACC guidelines studied iron carboxymaltose; most had a short follow-up and evaluated heart failure readmissions. We explored the prevalence of iron use, long-term therapeutic benefit and impact on all-cause readmission for patients with HFrEF.

Methods

We analyzed electronic medical record data from a university hospital from 2016 to 2021 with an ICD-10 code of systolic heart failure (LVEF < 50%) and ID, or iron deficiency anemia (IDA) (n=619). Intravenous (IV) iron sucrose group was matched to a control group (n = 43) by propensity score matching for age and sex. Conditional logistic regression was utilized to estimate unadjusted odds ratios (uOR) with 95% confidence interval (CI), while Mann-Whitney test was utilized to compare median values of nonparametric estimates.

Results

66.7% of the studied population were male and 61.1% were ≥ 65 years. The common comorbid conditions were ischemic cardiomyopathy (39.6%), chronic kidney disease (CKD) (26.2%), and gastrointestinal (GI) bleeding (12.3%). ID was present in 115 (18.6%); IDA in 95 (15.4%) while 43 (6.9%) received IV iron sucrose. IV iron administration was significantly associated with LVEF 41-49% (uOR = 2.65, 95% CI: 1.10 - 6.43), GI bleeding (uOR = 16.00, 95% CI: 2.12 - 120.65), chronic kidney disease (uOR = 3.67, 95% CI: 1.49 – 9.04), iron deficiency (uOR = 26.00, 95% CI: 3.53 - 191.60]) and iron deficiency anemia (uOR = 24.00, 95% CI: 3.23 - 177.41). LVEF ≤40% was non-significantly associated with all-cause mortality (uOR = 1.50, 95% CI: 0.61 – 3.67). The IV iron group had a higher median rate of 6-year readmissions (8 [IQR:8] vs.1 [2]; p<0.001), and blood transfusions (11 [24] vs. 3.5 [2]; p=0.05).

Conclusions

Patients with HFrEF were less likely to receive IV iron sucrose and more likely to die. Those with frequent blood transfusions, GI hemorrhage and CKD were more likely to receive IV iron. The study indicates the impact of disease severity and comorbidities on management. Larger studies are needed to investigate this postulation.

Anderson Anuforo:

Evaluating Utilization of Home BP Monitoring Over a 1-year Period, to Guide Hypertension Management and Minimize Complications in High-risk Hypertensive Patients.

Anuforo, Anderson MBBS[1]; Melfi, Michelle BA[1]; Soipe, Ayorinde MBBS[1]; Akhter, Mohammad MD[1]; Ashwath, Ashwini MBBS[1]; Murphy, Meaghan PharmD, BCACP[2]; Singh, Ravi MBBS[1]; Toomey, Caitlin MD[1].

Abstract:

Background

Blood pressure has well-established direct positive effects on age-related mortality rates from vascular disease.[1] Currently, not all patients with hypertension are recommended home blood pressure monitors (HBPMs) by their physicians. Those that do receive such recommendations typically have better insurance coverage, more education, and an existing antihypertensive drug regimen,[2] and long-term adherence to HBPM use has been observed in patients residing in wealthier areas.[3]

Methodology

We performed a retrospective study of hypertensive patients with HBPMs and hypertensive controls without HBPMs matched for age, sex, and comorbidities. A total of 1,415 patients between the ages of 18 and 89 seen at the Upstate Health Care Clinic from July 2019 to July 2020 were included. Data was obtained from EPIC Chart review.

Results

Of the 1,415 patients sampled, only about 3.7% have HBPMs. These patients were significantly more likely to be under 61 years old ($p = 0.03$) and prescribed standard antihypertensive medications, including calcium channel blockers ($p = 0.04$), aldosterone receptor blockers ($p = 0.03$), and thiazide diuretics ($p = 0.03$). Notably, the HBPM group was also significantly more likely to have resistant hypertension, defined as treatment with 3 or more antihypertensives ($p = 0.02$). The most common comorbidities across the sample included obesity (56.8%), diabetes mellitus (54.2%), and obstructive sleep apnea (33.3%). Patients with diabetes were more likely to have HBPMs ($p < 0.001$).

Discussion

This study suggests that HBPMs are an underutilized tool that are often reserved for patients with more advanced disease courses (i.e. younger hypertensive patients who are likely to have resistant hypertension.) HBPMs may help mitigate comorbidities and complications seen in a large proportion of hypertensive patients, such as strokes, heart failure and progression of kidney disease.

Conclusion

By further establishing the importance of HBPMs in achieving target blood pressure and reducing the risk of complications from hypertension, we hope to bring awareness to an intervention that should be increasingly implemented as a standard of care for all hypertensive patients.

References:

1. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360(9349):1903-1913. DOI: 10.1016/S0140-6736(02)11911-8.

2. Tang O, Foti K, Miller ER, Appel LJ, Juraschek SP. Factors Associated With Physician Recommendation of Home Blood Pressure Monitoring and Blood Pressure in the US Population. Am J Hypertens. 2020;33(9):852-859. DOI: 10.1093/ajh/hpaa093.

3. Vickneson L, Rogers A, Anbarasan T, Rorie DA, MacDonald TM, Mackenzie IS. Factors influencing participation and long-term commitment to self-monitoring of blood pressure in a large remote clinical trial: The treatment in morning versus evening (TIME) study. J Hum Hypertens. 2021;36:1099-1105. DOI: 10.1038/s41371-021-00621-5.

Anuj Raj Kadel:

Case report on Heterozygous mutation in PRF1 gene linked to risk of HLH in Adulthood

Authors: Bhavya Poudyal[1], Anuj Raj Kadel[1], Jihad BenGabr[2],

Abstract: Familial hemophagocytic lymphohistiocytosis (FHL) is a rare but potentially life-threatening disease which makes early detection important. Heterozygous mutations in the PRF1 gene may be associated with a later age of onset of hemophagocytic lymphohistiocytosis (HLH). We present a case of a 34-year-old patient with a heterozygous mutation of the PRF1 gene with markedly reduced perforin expression who presented with delayed onset of HLH symptoms.
Infective and autoimmune workups were largely unremarkable. However, given hyperinflammatory labs, high ferritin and significantly elevated soluble IL2R, elevated LFTs, low fibrinogen, and borderline elevated triglycerides with splenomegaly, the clinical picture was concerning for HLH. He was treated with high-dose steroids, IVIG, and Anakinra with adequate response. He is currently maintained on anakinra and IVIG. He had undergone genetic testing for HLH and a primary immunodeficiency panel that showed a heterozygous mutation of the PRF1 gene which likely explains his markedly low perforin levels.

INTRODUCTION:

Familial hemophagocytic lymphohistiocytosis (FHL) is a rare but potentially life-threatening disease which makes early detection important. Homozygous mutation in PRF1 is the most common gene defect in FHL, associated with a severe perforin deficiency that commonly presents with severe clinical manifestations within the first year of life. Heterozygous mutations in the PRF1 gene may be associated with a later age of onset of HLH. We present a case of a patient with a heterozygous mutation of the PRF1 gene with markedly reduced perforin expression who presented with delayed onset of hemophagocytic lymphohistiocytosis (HLH) symptoms.

CASE PRESENTATION:

Here we present the case of a 34-year-old male who initially presented with a 4-week history of progressive lower extremity weakness, fevers, fatigue, and shortness of breath.

On examination, he was febrile at 38.3 ^{o}C, heart rate was 102 beats per minute (BPM), respiratory rate of 32 BPM, blood pressure was 106/73 mmHg, and he was saturating 95% on room air. He was alert and oriented and appeared to be uncomfortable. His lung exam was normal without wheezing or rhonchi. On cardiac exam, he was tachycardic without murmur or pericardial friction rubs. His lower extremity motor strength was reduced bilaterally, however difficult to fully assess due to anasarca. He had normal strength in bilateral upper extremities. There was no joint tenderness or obvious joint swelling or synovitis. The remainder of the physical and neurologic examination was unremarkable.

He had no known drug allergies. His family history was not remarkable for any autoimmune disease. He was not on any prescribed medications.

He underwent extensive workup during his hospital course. Complete blood count with differential showed normocytic anemia (H/H: 9.3 g/dl/27.9%), normal WBC count (12.8 10^3/uL) with 96% neutrophils, low platelet count (144 10^3/uL), lactic acid was elevated (8.5 mmol/L), procalcitonin was elevated (1.46 mg/mL). CMP showed normal renal function (BUN/Creatinine: 23 mg/dL /057 mg/dL), Potassium was low at 2.9 mmol/L, and liver function tests (AST/ALT 484/223 U/L), alkaline phosphatase was within normal limits (114 U/L), albumin was low (2.6 g/dL), calcium was low (8.4 mg/dL), total and direct bilirubin was within normal limits, he had high LDH (1140 U/l) very low Haptoglobin (<10 mg/dL), direct Coombs test was negative. Creatine kinase (CK) was elevated at 2440, U/L, and aldolase was elevated (46.2 U/L). Autoimmune panel including ANA, ANA specificity, antiphospholipid panel, ANCA, myositis panel, hydroxymethylglutaryl-coenzyme A reductase (HMG-CoA), myositis panel was negative.

Ferritin was elevated (10,931 ng/ml), triglycerides were slightly elevated (286 mg/dl), D-dimer was elevated (3.12 ug/mL), fibrinogen was low (181 mg/dl), interleukin 2 receptor soluble (CD25) was very high 37309.9 pg/mL. His sedimentation rate (2 mm/hr) and C-reactive protein (<3 mg/L) were decreased. Natural killer cell function was very low, perforin/granzyme B assay showed markedly decreased perforin expression in cytotoxic cells.

Extensive infectious workup including Epstein-Barr virus (EBV), cytomegalovirus (CMV), full respiratory panel, urine studies, blood cultures, hepatitis screen, HIV, Lyme screen, toxoplasma, syphilis screen, human T-cell lymphotropic virus type 1 and 2 screens were all negative aside from positive coronavirus OC 43.

His autoimmune work-up including HMG-CoA reductase, IgG subclasses, myomarker panel, ANA, and aPLA panel were unremarkable. Right quadriceps muscle biopsy showed myopathy with necrotic fibers with CD4 T cell infiltrates and widespread expression of MHC class.

Imaging done included magnetic resonance imaging (MRI) of the lower extremity that revealed extensive musculature edema involving most of the right hip and thigh. Computed tomography (CT) thorax and abdomen/pelvis with contrast showed multifocal solid bilateral pulmonary nodules, slight splenomegaly, and mildly enlarged retroperitoneal lymph nodes.

He underwent a transbronchial biopsy that showed necrotic tissue and rare large B cells concerning for lymphoproliferative process. A left upper lobe lung biopsy showed lymphomatoid granulomatosis with necrosis. Flow cytometry was negative for leukemia/lymphoma and molecular diagnostics were negative for a T-cell clone consistent with a reactive process. Right quadriceps muscle biopsy was consistent with extensive necrosis in the setting of rhabdomyolysis, however, there was CD4 T-cell infiltrates with MHC class 1 upregulation seen. Bone marrow biopsy reported lymphomatoid granulomatosis grade 1. His

flow cytometry did not detect a monoclonal B-cell population, and PCR was positive for IgH gene rearrangement.

PET CT demonstrated multiple FDG avid pulmonary nodules consistent with known pulmonary lymphomatoid granulomatosis, and multifocal regions of increased metabolic uptake within the musculature, related to his myopathy

Given hyperinflammatory labs, high ferritin and significantly elevated soluble IL2R, elevated LFTs, normal ESR, low fibrinogen, and borderline elevated triglycerides with splenomegaly, the clinical picture was concerning for HLH. He was treated with high-dose steroids with Intravenous (IV) methylprednisolone 1000mg for 5 days then transitioned to oral prednisone 60mg daily with marked improvement, he was eventually tapered off of steroids after 6 weeks. Although his bilateral lower extremity weakness improved and CK trended down, he continued to have mild weakness in his lower extremities.

There was also a concern for possible lymphoma, and he continues to be monitored by oncology closely. There was no morphologic evidence of lymphoma, his PCR did detect IgH gene rearrangement, the same clone as that in the lymph node involved by lymphomatoid granulomatosis. He was monitored closely with repeat PET scans.

Eight months after his initial hospitalization, he has had 3 episodes with similar complaints of lower extremity weakness, SOB, and once with a morbilliform rash. 1 episode was managed inpatient with steroids and IVIG and the other 2 episodes were managed as an outpatient with steroids, IVIG, and the addition of Anakinra. He is currently maintained on Anakinra 100mg daily subcutaneous injections and IVIG 2gm/kg every 4 weeks with dramatic improvement in his labs and symptoms. He had undergone genetic testing for HLH and a primary immunodeficiency panel that showed a heterozygous mutation of the PRF1 gene which likely explains his markedly low perforin levels. To date the patient is currently stable on his current regimen however, his lymphomatoid granulomatosis will need close monitoring by oncology should it convert to high grade.

DISCUSSION:

HLH has been known to be a rare and potentially life-threatening disease, which makes an early diagnosis and treatment very important. Primary HLH usually manifests in childhood, whereas secondary can occur later in life. The most common triggers were noted to be malignancy, infection, autoimmune and hereditary disorders [1,2,3, 4]. Several studies have found that males are affected more than females sometimes by a 2:1 ratio [1,2,3]. Genetic composition was noted to play a role in the manifestation of the disease. When comparing PRF1(a gene not involved in degranulation) and genes involved in degranulation “deg” (MUNC13-4, STXBP2, STX11, and RAB27A), one study showed that the majority of deg/deg patients had an earlier age of onset when compared to PRF1/deg patients. Age of onset similar to deg/deg patients was also seen with biallelic mutations in any of the homozygous or compound heterozygous genes mentioned above. The same study showed that a single heterozygous patient had a later age on onset [5]. One north American study demonstrated that PRF1 mutation was

present in at least 50% of patients with primary HLH and that those patients with a residual perforin activity, as opposed to absence, had a later age of onset. Fever was a universal finding in patients with HLH in a study along with hyperferritinemia and a bi- or trilineage cytopenia with hepatomegaly and splenomegaly in 55% of patients, elevated liver enzymes and hyperfibrinogenemia in 50% and hypertriglyceridemia in 40% of patients [3]. According to a 2017 study however, hyperferritinemia is not specific to either pediatric or adult HLH[6] Currently, the diagnosis of HLH can be done using the HLH-2004 guideline [7], however, the criteria have not been studied extensively in adults with secondary HLH [8]. An established protocol for the management of HLH for pediatric populations like the HLH-2004 is well established however a definite treatment for adults is not defined [9]. A case at UT MD Anderson Cancer Center was treated with alemtuzumab, etoposide, and dexamethasone in addition to intrathecal methotrexate and hydrocortisone [4] whereas treatment initially with dexamethasone and later with cyclosporine was used for a case in Switzerland. In some reports, it was reported that complete treatment of underlying etiology resulted in the resolution of HLH[10].

Our case further shines a light on the need for clinicians to maintain a high index of suspicion for HLH in adults given the high morbidity and mortality of this rare but life-threatening disease without early diagnosis and management. It's important to recognize that patients with heterozygous mutation of the PRF1 gene may be at risk of primary HLH in adulthood. Further studies must be undertaken to fully understand the disease process and specific management regimens.

REFERENCES:

1. Parikh SA, Kapoor P, Letendre L, Kumar S, Wolanskyj AP. Prognostic factors and outcomes of adults with hemophagocytic lymphohistiocytosis. Mayo Clin Proc. 2014 Apr;89(4):484-92. doi: 10.1016/j.mayocp.2013.12.012. Epub 2014 Feb 26. PMID: 24581757.

2. Otrock ZK, Eby CS. Clinical characteristics, prognostic factors, and outcomes of adult patients with hemophagocytic lymphohistiocytosis. Am J Hematol. 2015 Mar;90(3):220-4. doi: 10.1002/ajh.23911. Epub 2015 Jan 16. PMID: 25469675.

3. Shabbir M, Lucas J, Lazarchick J, Shirai K. Secondary hemophagocytic syndrome in adults: a case series of 18 patients in a single institution and a review of literature. Hematol Oncol. 2011 Jun;29(2):100-6. doi: 10.1002/hon.960. Epub 2010 Aug 30. PMID: 20809477.

4. Shah AR, Muzzafar T, Assi R, Schellingerhout D, Estrov Z, Tamamyan G, Kantarjian H, Daver N. Hemophagocytic lymphohistiocytosis in adults: An under recognized entity. BBA Clin. 2016 Dec 20;7:36-40. doi: 10.1016/j.bbacli.2016.12.002. PMID: 28070498; PMCID: PMC5219626.

5. Zhang K, Chandrakasan S, Chapman H, Valencia CA, Husami A, Kissell D, Johnson JA, Filipovich AH. Synergistic defects of different molecules in the cytotoxic pathway lead to clinical familial hemophagocytic lymphohistiocytosis. Blood. 2014 Aug 21;124(8):1331-4. doi: 10.1182/blood-2014-05-573105. Epub 2014 Jun 10. PMID: 24916509; PMCID: PMC4141517.

6. Otrock ZK, Hock KG, Riley SB, de Witte T, Eby CS, Scott MG. Elevated serum ferritin is not specific for hemophagocytic lymphohistiocytosis. Ann Hematol. 2017 Oct;96(10):1667-1672. doi: 10.1007/s00277-017-3072-0. Epub 2017 Jul 31. PMID: 28762079.

7. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J, Janka G. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007 Feb;48(2):124-31. doi: 10.1002/pbc.21039. PMID: 16937360.

8. Otrock ZK, Daver N, Kantarjian HM, Eby CS. Diagnostic Challenges of Hemophagocytic Lymphohistiocytosis. Clin Lymphoma Myeloma Leuk. 2017 Jul;17S:S105-S110. doi:10.1016/j.clml.2017.02.017. PMID: 28760295.

9. Agbariah N, Sanz J, Rovó A. "A Dangerous Black Box:" Idiopathic Hemophagocytic Lymphohistiocytosis in Adult Patients-A Case Report and Review of the Literature. Case Rep Hematol. 2022 Dec 3;2022:5867129. doi: 10.1155/2022/5867129. PMID: 36510501; PMCID: PMC9741541.

10. Karlsson T. Secondary haemophagocytic lymphohistiocytosis: Experience from the Uppsala University Hospital. Ups J Med Sci. 2015;120(4):257-62. doi: 10.3109/03009734.2015.1064500. Epub 2015 Jul 25. PMID: 26212358; PMCID: PMC4816886.

Azhar Hussain:

Do we really need CMV prophylaxis in every aviremic high risk CMV-seropositive liver transplant recipients (D+/R+) in Pakistani population

Azhar Hussain[1], Abdul Wahab Dogar[1], Kaleem Ullah[1], Abdul Ghaffar[1], Shams-ud-din[1], Subhash Gupta[2]

[1] Liver Transplant and Hepatobiliary Unit, Pir Abdul Qadir Shah Jelani Institute of Medical Sciences, Gambat, Sindh, Pakistan

[2]Liver Transplant and Hepatobiliary Max Super Specialty Hospital, Saket (Max Saket), New Delhi, India

Background and aims: Cytomegalovirus (CMV) infection is a common complication after liver transplantation that can affect graft and patient survival. The aim of this study was to evaluate post-operative outcomes of living donor liver transplant recipients without any cytomegalovirus prophylaxis.

Methods: We retrospectively analysed 358 liver transplant recipients who underwent CMV PCR testing at 7th and 30th postoperative days after transplantation. We compared the clinical characteristics and outcomes of the post-op CMV PCR positive group and the negative group.

Results: Among 358 liver transplant recipients, 83(23.2%) had positive post-op CMV PCR at 7th post-op day [low titer (<1000 IU/mL) =79 & high titer (≥1000 IU/mL) =4]. Demographics and clinical characteristics were comparable in the study groups (Table1). On 1st post-operative day, various labs were similar in the study groups except albumin and gamma glutamyltrasnferase ($p<0.05$, for both) (Table 02). On 7th post-operative day, various labs were similar in the study groups ($p>0.05$) (Table 03). However, the post-op positive CMV PCR group had a higher incidence of portal vein thrombosis (25% vs 1.46%, p= 0.001) than the negative group, but biliary complications (biliary leak & biliary strictures), acute cellular rejection, and hepatic artery thrombosis (HAT) were similar ($p>0.05$, for all) (Table 04). There was no significant difference in the survival time among the post-op positive or negative CMV PCR groups (log-rank test p=0.143) (Figure 01).

Conclusion: Post-operative CMV PCR positivity were associated with increased risk of portal vein thrombosis (PVT) in living donor liver transplant recipients. Early detection and treatment of CMV infection may improve liver transplant outcomes.
Keywords: cytomegalovirus, polymerase chain reaction, liver transplantation, outcomes

Table 01: 1st Post-op Day Labs among different study subgroups (n=358)

Parameters	Post-op CMV PCR-Negative	Post-op CMV PCR Positive-Low Titer <1000 IU/mL	Post-op CMV PCR Positive-High Titer ≥1000 IU/mL)	P value

Mean AST (IU/mL)	1141.92 +/- 16293.94	166.58 +/- 196.73	132.50 +/- 61.43	0.865
Mean ALT (IU/mL)	114.10 +/- 132.57	122.57 +/- 163. 78	93.75 +/- 36.50	0.852
Mean Total Bilirubin (mg/dL)	4.63 +/- 3.20	5.56 +/-4.85	3.37 +/- 1.50	0.100
INR	1.77 +/- 0.74	1.70 +/- 0.65	2.21 +/- 0.23	0.359
Creatinine (mg/kg/24 hr)				
Albumin (g/dL)	1.80 +/- 0.55	2.09 +/- 0.72	1.45 +/- 0.12	0.000
Gamma glutamyltransferase (IU/mL)	45.81 +/- 48.73	51.76 +/- 45.89	202.50 +/- 370.34	0.000

Abbreviations: AST: Alanine aminotransferase; ALT: Aspartate aminotransferase; INR: International Normalized Ratio

Table 02: 7th Post-op Day Labs among different study subgroups (n=358)

Parameters	Post-op CMV PCR-Negative	Post-op CMV PCR Positive-Low Titer <1000 IU/mL	Post-op CMV PCR Positive-High Titer ≥1000 IU/mL)	P value
Mean AST (IU/mL)	100.79 +/- 146.84	125.14 +/- 233.31	66.67 +/- 33.82	0.497
Mean ALT (IU/mL)	188.38 +/- 205.24	211.35 +/- 271.48	124.67 +/- 57.76	0.627
Mean Total Bilirubin (mg/dL)	3.81 +/- 4.10	3.72 +/- 3.43	3.00 +/- 2.25	0.927
INR	1.69 +/- 2.22	1.67 +/- 1.76	1.45 +/- 0.24	0.979

Creatinine (mg/kg/24 hr)				
Albumin (g/dL)	5.35 +/- 51.36	2.21 +/- 0.34	2.16 +/- 0.15	0.861
Gamma glutamyltransferase (IU/mL)	182.70 +/- 166.18	139.59 +/- 116.47	262.00 +/- 173.58	0.066

Abbreviations: AST: Alanine aminotransferase; ALT: Aspartate aminotransferase; INR: International Normalized Ratio

Table 03: Post-op LDLT-related complications among different study subgroups (n=358)

Parameters	Post-op CMV PCR-Negative	Post-op CMV PCR Positive-Low Titer <1000 IU/mL	Post-op CMV PCR Positive-High Titer ≥1000 IU/mL)	P value
Biliary complications				0.680
Biliary leak	6 (23.07%)	1 (14.28%)	0	
Biliary stricture	20 (76.92%)	6 (85.71%)	1 (100%)	
Portal vein thrombosis				0.001
No	270 (98.54%)	79 (100%)	3 (75%)	
Yes, managed with coagulotherapy	3 (1.09%)	0	1 (25%)	
Yes, managed with surgery	1 (0.36%)	0	0	
Hepatic artery thrombosis				0.20

No	265 (97.06%)	77 (97.46%)	3 (75%)	
Yes, managed with medical treatment	2 (0.73%)	1 (1.26%)	0	
Yes, managed with intervention	3 (1.09%)	0	0	
Yes, managed with surgery	3 (1.09%)	1 (1.26%)	1 (25%)	
Acute cellular rejection				0.618
No	272 (99.27%)	78 (98.73%)	4 (100%)	
Yes, steroid pulse therapy used	2 (0.73%)	0	0	
Biopsy needed	0	1 (1.27%)	0	

Azhar Hussain:

Outcomes of liver transplantation in CMV-seropositive patients of South Asian descent: a retrospective cohort study

Azhar Hussain[1], Abdul Wahab Dogar[1], Kaleem Ullah[1], Abdul Ghaffar[1], Shams-ud-din[1], Subhash Gupta[2]

[1] Liver Transplant and Hepatobiliary Unit, Pir Abdul Qadir Shah Jelani Institute of Medical Sciences, Gambat, Sindh, Pakistan

[2]Liver Transplant and Hepatobiliary Max Super Speciality Hospital, Saket (Max Saket), New Delhi, India

Background: Human cytomegalovirus (CMV) plays an important role in solid organ transplants, especially liver transplants. It increases the morbidity and mortality of liver transplant patients, so the testing of CMV in both donors and recipients is useful to predict liver transplant outcomes.

Objectives: The purpose of this study is to investigate the risk factors and post-liver transplantation outcomes of CMV-seropositive liver transplant recipients of South Asian descent.

Materials and Methods: In this retrospective cohort study, 366 patients underwent liver transplantations at Gambat Liver Transplant Institute during 2020-2022. Their medical reports were analyzed to see the impact of CMV seropositivity on the outcomes of liver transplants. CMV infection was diagnosed by serological and PCR tests.

Results: In this study, 317 (86%) patients were male and 49 (14%) were female. In this study, 350 (95%) patients were pre-op CMV PCR-negative, 15 (4%) patients were pre-op CMV PCR-positive with low titer, and only 1 (0.2%) patient was pre-op CMV PCR-positive with high titer. There was no statistically significant difference between the mean of the rest of the lab reports on the 1st and 7th post-op day, and various liver transplant complications rate ($p>0.05$). There was no significant difference in the survival time among the study groups (log-rank test $p=0.143$).

Conclusion: The overall long-term survival rate was lower in pre-op CMV seropositive patients as compared to pre-op CMV seronegative patients.

Keywords: Cytomegalovirus, seropositivity, liver transplant, survival, South Asian

Azhar Hussain[1]

SEVERITY AND IMPACT OF GLUCOSE-6 PHOSPHATE DEHYDROGENASE DEFICIENCY IN LIVING RIGHT LOBE LIVER DONORS UNDERGOING RIGHT LOBE HEPATECTOMY

Azhar Hussain[1], Abdul Wahab Dogar[1], Kaleem Ullah[1], Abdul Ghaffar[1], Shams-ud-din[1], Subhash Gupta[2]

[1] Liver Transplant and Hepatobiliary Unit, Pir Abdul Qadir Shah Jelani Institute of Medical Sciences, Gambat, Sindh, Pakistan

[2]Liver Transplant and Hepatobiliary Max Super Speciality Hospital, Saket (Max Saket), New Delhi, India

Abstract:

Background: Glucose-6 Phosphate Dehydrogenase (G6PD) is the most common enzyme deficiency disorder which can cause a spectrum of post-operative complications among live liver donors.

Method: This cross-sectional study studied the prevalence and severity of G6PD deficiency among 152 live liver donors. We also evaluated the pre-and post-operative outcomes among 14 G6PD deficient donors with the 35 non-deficient donors who underwent right lobe hepatectomy. All patients were followed to check the hemolysis and other post-hepatectomy complications for 1 year.

Result: 14/152 (0.92%) live liver donors were G6PD deficient. Among 14 donors, four (28.57%) were WHO class-II G6PD deficient, while ten (71.42%) had WHO class-III G6PD deficient. None of the donors had WHO class-I G6PD deficiency. Pre-operative hemoglobin was comparable among G6PD deficient donors and non-deficient donors (13.18 ± 2.16 vs 13.20 ± 1.43, p=0.9), while post-operative hemoglobin was lower deficient donors compared to non-deficient donors (9.98 ± 1.58 vs 11.30 ± 0.82, p=0.021). Hemolysis was detected in three (21.14%). Moreover, total serum bilirubin was significantly elevated among G6PD deficient donors compared to non-deficient donors (3.89±2.67 vs 2.21±1.46, p=0.027), and the same trend was observed in serum indirect bilirubin. No blood transfusion was required.

Conclusion: Glucose-6 phosphate deficient donors undergoing right lobe hepatectomy should be screened for G6PD deficiency quantitatively as it poses a serious risk of hemolysis in deficient donors.

Keywords: Live donor liver transplantation (LDLT), G6PD deficiency, right lobe hepatectomy, post-operative hemolysis.

Table 01: Comparison of preoperative and postoperative parameters in G6PDd (n=14) vs Non-G6PDd (n=35) donor study groups.

Characteristics	G6PDd (n=14)	Non G6PDd (n=35)	p-value
Age (years)	20.68 ± 2.98	23.86 ± 6.74	0.191
Gender Male Female	 10(71.42%) 4(28.57%)	 22(62.85%) 13(37.14%)	0.762
BMI (kg/m^2)	20.40± 1.68	21.30 ± 2.28	0.372
LAI	10.50±4.20	11.26±4.97	0.648
Graft volume (g)	689.93 ± 129.42	696.56 ± 101.14	0.265
FLR (%)	36.73 ±3.72	35.78 ± 6.24	0.968
Blood loss (ml)	1163.33± 376.74	1167.18 ± 321.53	0.654
Hospital stays (days)	5.06 ± 0.25	5.05 ± 0.22	0.648
Pre-operative Hb (g/dl)	13.18 ± 2.16	13.20 ± 1.43	0.68
Immediate post-op Hb (g/dl)	9.98 ± 1.58	11.30 ± 0.82	0.021
Peak Total bilirubin (mg/dl)	3.89±2.67	2.21±1.46	0.027
Peak Indirect bilirubin (mg/dl)	2.22±1.38	1.40±0.89	0.046
Peak ALT (IU/l)	232.13 ± 114.25	213.21 ± 80.91	0.159

Peak AST (IU/l)	**256.73 ± 114.51**	**239.44± 82.60**	**0.560**
Peak INR	**1.69±0.16**	**1.81±0.34**	**0.135**
Blood transfusion	**1(6.67%)**	**1 (2.56%)**	**0.425**
Readmission	**0**	**1(2.56%)**	**0.571**
Mortality	**0**	**0**	**-**

Abbreviations: BMI: Body mass index, LAI: liver attenuation index, Hb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, INR: International normalized ratio.

Azhar Hussain[:]

Comparison of Outcomes of Liver Grafts Requiring Back-table Reconstruction Flushed with Histidine-Tryptophan-Ketoglutarate (HTK) Solution and Cold Normal Saline (NS)

Azhar Hussain[1], Abdul Wahab Dogar[1], Kaleem Ullah[1], Abdul Ghaffar[1], Shams-ud-din[1], Subhash Gupta[2]

[1] Liver Transplant and Hepatobiliary Unit, Pir Abdul Qadir Shah Jelani Institute of Medical Sciences, Gambat, Sindh, Pakistan

[2]Liver Transplant and Hepatobiliary Max Super Speciality Hospital, Saket (Max Saket), New Delhi, India

Abstract

Background: To asses feasibility and safety of selected liver grafts flushed with cold normal saline (NS) and compare their outcomes with Histidine-Tryptophan-Ketoglutarate (HTK) solution for grafts that require back-table reconstruction.

Methods: One hundred adult recipients who underwent right lobe LDLT at the Department of Liver Transplantation Surgery, Gambat, Pakistan, were studied. After informed and written consent, recipients were randomized via lottery method and assigned to receive either "Cold Normal Saline" (cases/non-HTK group, who require back table reconstruction; n=50) or "Histidine-Tryptophan-Ketoglutarate (HTK) solution" (controls/HTK group, who require back table reconstruction; n=50).

Early allograft dysfunction (EAD) [bilirubin, transaminases, & INR], postoperative complications (biliary & vascular), healthcare utilization (hospital stay & readmission), and three-year survival were compared. The direct cost of both approaches was reported.

.

Results: Demographics and clinical characters were comparable in the two groups (Table 1). Comparing cases vs. controls, mean bilirubin, ALT, AST, and INR on the 7th postoperative day were similar in the two groups. 5(10%) cases and 4(8%) controls developed EAD (*p=0.72*). Post-LT complications (biliary leak 2% in cases vs. 0 in control), strictures (12% in cases vs. 16% in controls), hepatic artery thrombosis (4% vs. 2%) and portal vein thrombosis (0 vs. 2%) were equally distributed. Mean hospital stay (11.02 $\pm$ 2.63 and 12.06 $\pm$ 3.68 days) and 30-day mortality (8% vs 8%) were also comparable in two groups. Finally, 1-year survival (92% vs 90%) based on Kaplan-Meier analysis was also comparable (*p= 0.71*). The cost of using a non-HTK/normal saline-based approach was much lesser than the HTK solution (1 USD vs 2000 USD).

Conclusion: In a selected cohort of right lobe LDLT recipients, preservation solutions can be avoided safely with comparable outcomes. In high-volume LDLT centers, avoiding the preservation use can also result in saving costs without impacting outcomes.

Keywords: HTK solution, right lobe donation, living donor, liver transplantation, survival rate, preservation solution

Word count: 300

Table 1: Recipient demographics, clinical characteristics, laboratory values, and postoperative complications.

Variables	non-HTK group (n=50)	HTK group (n=50)	p-value
Recipients			
Age(years)	39.18±11.69	36.84±6.77	0.224
Gender			0.741
Male	44(88%)	46 (92%)	
Female	6(12%)	4 (08%)	
BMI(kg/m^2)	22.46±4.29	22.84±4.24	0.657
Etiology			
Viral	47 (94%)	45 (90%)	
NASH	2 (04%)	1 (02%)	
Alcoholic	00 (00%)	00 (00%)	
Budd Chiari	00 (00%)	1 (02%)	
PBC	00 (00%)	1 (02%)	
Wilson	1 (02%)	1 (02%)	
PSC	00 (00%)	1 (02%)	
HCC	11 (22%)	02 (04%)	0.015
Co-Morbidities			
DM	4 (08%)	2 (04%)	0.67
HTN	00 (00%)	3 (06%)	0.24
CVD	00 (00%)	00 (00%)	0.00
CTP score			
A	3 (06%)	1 (02%)	0.59
B	9 (18%)	9 (18%)	
C	38 (76%)	40 (80%)	
MELD-Na	19.53±5.51	20.88±4.75	0.19
Operation time (min)	537±70.66	534.60±60.72	0.85
Blood loss(ml)	1622±317.70	1512±300.775	0.07
Hospital stays(days)	11.02±2.63	12.06±3.68	0.10
Mean Post-operative labs (at day 07)			
Total bilirubin (mg/dL)	2.96 ± 2.97	3.06 ± 3.24	0.91
INR (IU/L)	1.44 ± 0.24	1.39 ± 0.18	0.82
ALT (IU/L)	186.79 ± 144.95	137.69 ± 97.28	0.05
AST (IU/L)	119.69 ± 133.45	93.78 ± 85.65	0.26

Postoperative Complications

EAD	4 (8%)	5(10%)	0.727
PNF	00	1 (2%)	0.315
ACR	3(6%)	4 (8%)	0.695
HAT	2 (4%)	1(2%)	0.558
Sepsis	5 (10%)	4 (8%)	0.727
PVT	00	1 (2%)	0.315
Biliary complications			
Stricture	6 (12%)	8 (16%)	0.564
Leak	1 (2%)	00	0.315
Clavin-dindo Grade≥III	11 (22%)	13 (26%)	0.64
30-day Mortality	4 (8%)	4 (8%)	1.00
1-year mortality (excluding 1st month)	00	1 (2%)	0.315

Abbreviations:

BMI: body mass index; HCC: hepatocellular carcinoma; HTN: hypertension; CVD: cardiovascular disease; CTP: Child Turcotte Pugh; INR: international normalized ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase, EAD: early graft dysfunction; PNF: primary non-function; ACR: acute cellular rejection; HAT: hepatic artery thrombosis; PVT: portal vein thrombosis

Azhar Hussain[1]

Impact of Protein C, Protein S, Anti-thrombin-III deficiency, Anti-phospholipid Antibodies (APLA) and Leiden factor-V mutation in Venous Thromboembolic Events (VTE) and Overall Post-operative Donor Outcomes Undergoing Right Lobe Hepatectomy in LDLT.

Azhar Hussain[1], Abdul Wahab Dogar[1], Kaleem Ullah[1], Abdul Ghaffar[1], Shams-ud-din[1], Subhash Gupta[2]

[1] Liver Transplant and Hepatobiliary Unit, Pir Abdul Qadir Shah Jelani Institute of Medical Sciences, Gambat, Sindh, Pakistan

[2]Liver Transplant and Hepatobiliary Max Super Speciality Hospital, Saket (Max Saket), New Delhi, India

Abstract:

Background: The main aim of this study was to determine the frequency of hereditary thrombophilia in the Pakistani population and share our centers' safety and VTE prophylaxis protocols in live liver donors.

Materials & Methods: Thrombophilia testing that includes protein S (PS), protein C (PC), antithrombin (AT) III, and anti-phospholipid antibody (APLA) was done in 567 living donor candidates between July 2016 and April 2020. Donors were divided into the normal, borderline, and high-risk groups. The safety endpoints were VTE occurrence, bleeding complications, or mortality.

Results: Among them, 21 (3.7%) donors were deficient in protein C, 14(2.5%) were deficient in anti-thrombin-III, and 45(7.9%) had Leiden factor-V mutation. 31/416 (7.45%) were deficient in factor II. IgM & IgG Anti-phospholipids antibodies were positive in 2/567(0.4%) and 2/567(0.4%) respectively. IgM & IgG Lupus anticoagulant antibodies were positive in 3/567(0.5%) and 3/567(0.5%), respectively Donor operation was performed in 44 candidates in the borderline group and 7 in the high-risk group. Complications after surgery were comparable between the two groups. One donor in the normal donor group developed pulmonary embolism, but none of the donors in either borderline or high-risk group developed VTE.

Conclusions: Donor operation is safe in donors in either borderline or high-risk groups, although more evaluations are required to determine the necessity and lowest safe levels of PC, PS, and AT-III of thrombophilia testing before surgery among living donor candidates.

Keywords: Living Donors of Liver Transplantation, Thrombophilia Screening, Venous Thromboembolic Events

Table 01: Comparison of demographics and surgical features of LLDs in donor groups

Variables	Normal Group (n=516)	Borderline Group (n=44)	High Risk Group (n=7)	P value
Mean age (Years)	23.43 ± 5.53	23.91± 5.25	26.86 ± 6.54	0.17
Mean BMI (Kg/m^2)	21.40 ± 7.99	20.5 ± 2.71	21.53 ± 3.29	0.69
Gender				
Male	290(56.2%)	24(54.5%)	4(57.1%)	0.97
Female	226(43.7%)	20(45.4%)	3(42.8%)	
Marital status				
Unmarried	351(68.1%)	25(56.9%)	5(71.4%)	0.06
Married	165 (31.9%)	19 (43.1%)	2(28.5%)	
Donors relation to recipients				
Son	63 (12.2%)	6 (13.6%)	1(14.2%)	0.008
Brother	99 (19.1%)	5 (11.3%)	2(28.5%)	
Nephew	25 (4.8%)	5(11.3%)	1(14.2%)	
Daughter	35 (6.7%)	5 (11.3%)	0	
Sister	32 (6.2%)	5 (11.3%)	0	
Father	88 (17.1%)	3 (6.8%)	0	
Swap	10 (1.9%)	0	0	
Others	157(30.4%)	11 (25.0%)	3(42.8%)	
Type of Graft				
Modified right lobe graft	437 (84.6%)	36 (81.8%)	6(85.7%)	NS
Modified extended right lobe graft	62 (12.0%)	8 (18.1%)	1(14.2%)	
Left lobe graft	4 (0.7%)	7 (15.9%)		
Left lateral segment graft	11 (2.1%)	0	0	
	6(1.1%)	0	0	
GRWR	1.26 ± 0.63	1.4 ± 0.68	1.2 ± 0.63	NS

Mean warm ischemia time (minutes)	10.99 ± 6.09	10.68 ± 4.08	13.86 ± 7.26	
Mean operation time (hours)	407.94 ± 64.86	412.27 ± 89.11	422.86 ± 62.37	
Mean blood loss (ml)				NS
Blood transfusions (no of patients/ %)	516	44	7	0.76
Personal History of Thrombosis	0	0	0	_
Family History of Thrombosis	0	0	1	_

Abbreviations: BMI: Body mass index; GRWR: Graft to weight ratio

Table 02: Various outcomes in LLDs in donor groups

Variable	Normal Group (n=516)	Borderline Group (n=44)	High Risk Group (n=7)	P value
Total number of complications	62 (12.0%)	15 (34.1%)	2(28.5%)	0.43
Grade 1 & 2				
-Wound infections	20 (3.8%)	3 (6.8%)	2(28.5%)	
-Wound hematoma	2 (0.3%)	1 (2.2%)	0	0.001
-UTI	4 (0.7%)	2 (4.5%)	0	
-Fever	3 (0.5%)	2 (4.5%)	0	
-Paralytic ileus	2 (0.3%)	1 (2.2%)	0	
Grade 3A				
-Bile leakage	6 (1.1%)	1 (2.2%)	0	
-Bile duct stricture	3(0.5%)	0	0	0.15
-Post-op bleeding	3 (0.5%)	1 (2.2%)	0	
-Pleural effusion/Aspiration	9 (1.7%)	1 (2.2%)	0	
-ERCP & Stenting	3 (0.5%)	1 (2.2%)	0	
Grade 3B				
- Re-open	6(1.1%)	1 (2.2%)	0	0.45
Grade 4A				
- Need ICU care/ ventilator	1 (0.1%)	1 (2.2%)	0	0.95
Grade 4B				
-Multi-organ failure	0	0	0	--
Grade 5	0	0	0	--
Mean ICU stay (Days)	3 ± 1	2.53 ± 1	3 ± 1	0.15
Mean hospital stay (Days)	6 ± 2	5 ± 2	6 ± 2	0.17
Mortality	0	0	0	--

Abbreviations: UTI: Urinary tract infection; ERCP: Endoscopic retrograde cholangiopancreaticography; ICU: Intensive Care Unit

Bharat Rawlley:

Clinical outcomes in patients with Left ventricular assist device on Guideline directed medical therapy: A propensity score matched analysis

Bharat Rawlley[1], Andres Cordova Sanchez[1], Kartik Gupta[2], Matthew Ramm[1], Debanik Chaudhuri[1]

1 Department of Internal Medicine, State University of New York Upstate Medical University, Syracuse, New York

2 Department of Medicine, Henry Ford Hospital, Detroit, MI, USA

Introduction:

We investigate the benefit of Guideline Directed Medical Therapy [GDMT] in patients with Left Ventricular Assist Device (LVAD) using an insurance claims database.

Methods:

We queried Trinetx US collaborative network for patients with LVAD and created two groups; those who received ≥2 prescriptions of any GDMT medication and who did not receive any GDMT after implantation. These were matched by Propensity Score Matching (PSM) for age, race, sex, BMI, LVEF, SBP, DBP, ischemic heart disease, hypertension, disorder of pulmonary circulation, chronic kidney disease (CKD) and acute kidney injury (AKI). All diagnosis were identified using ICD codes. Patient demographics, LVEF, BMI, SBP and DBP were recorded as reported by TriNetX. We looked at primary and secondary outcome measures starting 90 days until 10 years post implantation, primary being all cause mortality and secondary being risk of decompensated heart failure, hypotension, AKI, odds of receiving heart transplant and LVAD explant.

Results:

We had 4514 patients with LVAD on GDMT and 687 without GDMT. After PSM, we had 651 patients in each group. Both were matched by PSM with Standardized mean difference (SMD) < 0.1 for all variables. Those with LVAD on GDMT had lower risk of all-cause mortality [233 (37.28%)] compared to those not on GDMT [157 (56.29%)] (hazard ratio [HR] 0.30, 95% confidence interval [CI] 0.24–0.37, P < 0.0001) [Figure 1] but at a higher risk of decompensation (RR 2.74, 95% CI 2.19-3.42), hypotension (RR 3.58, 95% CI 2.73 – 4.69) and AKI (RR 2.64, 95% CI 2.23-3.18). Patients receiving heart transplant and LVAD explant had higher odds of being on GDMT [Odds Ratio [OR], 95% CI: 2.86, 1.87 – 4.37; 4.29, 2.13 – 8.63, respectively).

Conclusions:

LVAD patients on GDMT have lower all-cause mortality, higher odds of receiving heart transplant and LVAD explant starting 90 days post implant. However, for reasons not clear to us, they are also at higher risk of decompensation, hypotension and AKI.

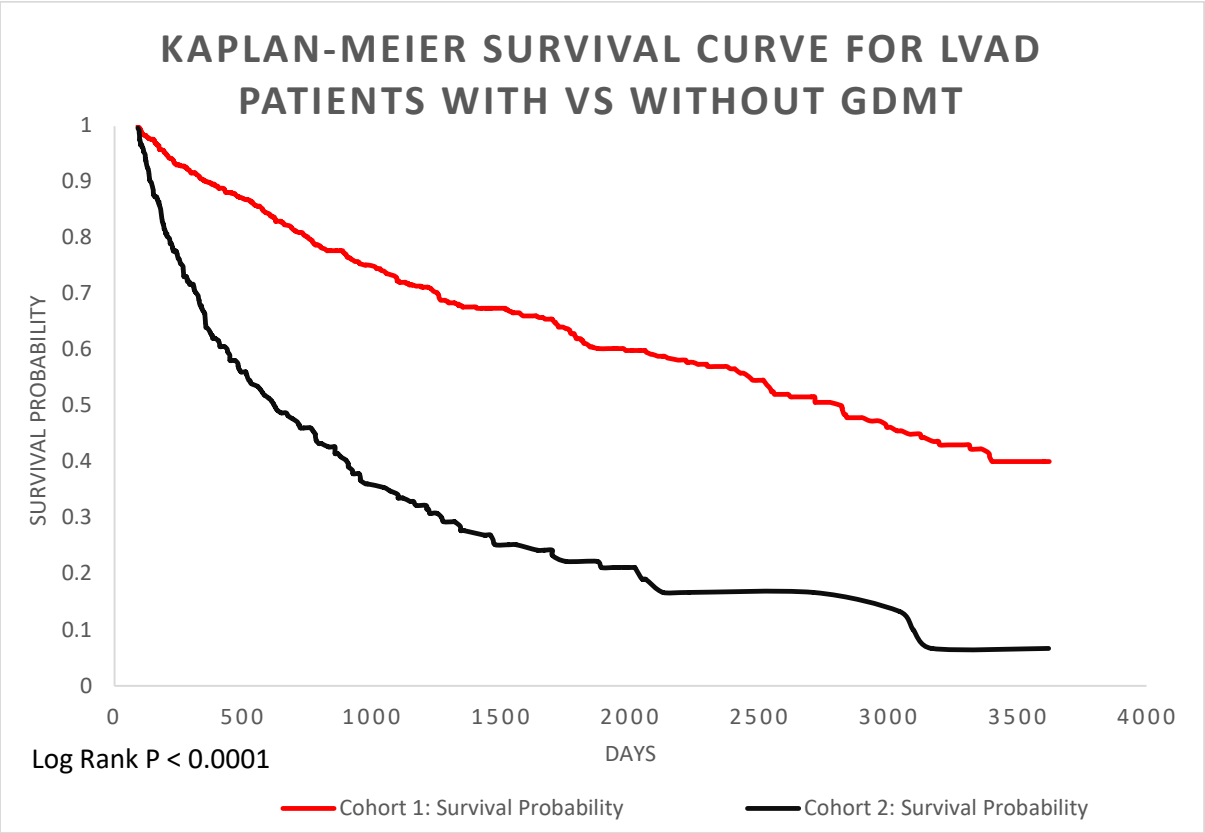


Figure 1: Kaplan Meier Survival Curve for LVAD patients with vs without GDMT

Binod KC:

A Rare Case Report of Rapidly Progressive Glomerulonephritis (RPGN) in a Patient with Goodpasture Syndrome Presenting with Concurrent Anti-GBM and ANCA Antibodies

Authors: Binod KC [1,] Marlene Marte[2] , Mahnoor Sherazi[1,] Hom Neupane[2]

Department of Medicine, State University of New York (SUNY) Upstate Medical University, Syracuse, New York.
Division of Rheumatology and Clinical Immunology, State University of New York (SUNY) Upstate Medical University, Syracuse, New York.

ABSTRACT:

Introduction:
Goodpasture syndrome (GPS) is a rare autoimmune disease with an annual incidence of 0.5-1.6 cases per million. On rare occasions, patients with Goodpasture's syndrome (GPS) are present with both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA). Rutgers, et al. reviewed Limburg renal biopsy registry (1978 -2003) which included 1373 cases of crescentic glomerulonephritis (CGN) and reported 10 double-positive cases. Concurrent ANCA and anti-GBM disease is rare with high mortality rate. Aggressive immunosuppression with steroids, cyclophosphamide and plasma exchange can induce remission and preserve renal function. Here we present a case of both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA) with RPGN in patients with Good Pasture Syndrome.

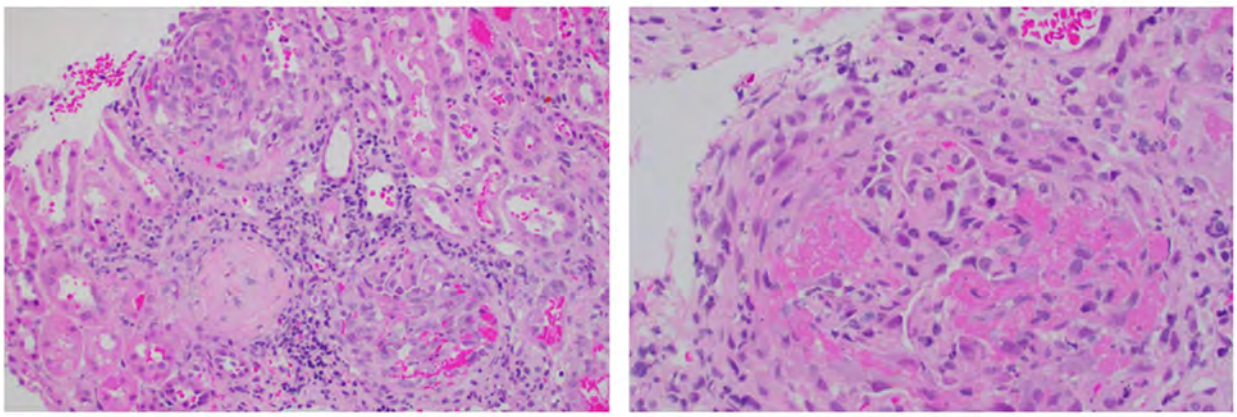
Case Presentation.
A 53-year-old female with a medical history of Mitral Valve Prolapse and asthma presented with intractable nausea, vomiting, fatigue, decreased urine output, and dark-colored urine. Physical examination revealed lower extremity edema, distended abdomen, and periorbital edema. Laboratory investigations showed elevated creatinine, significant hematuria, and proteinuria. CT Thorax without contrast showed Scattered focal irregular areas of lung consolidation most pronounced at the lung bases with small pleural effusion likely due to pneumonia. CT Abdomen showed a very small amount of ascites. Patient was Started on Intravenous fluid Normal Saline for presumed pre-renal AKI and antibiotics for pneumonia- IV Ceftriaxone, IV Azithromycin and IV Vancomycin. Day 3- Serum Creatinine worsened to 6.6 mg/dl rapidly with oliguria- 100cc/day. Nephrology and Rheumatology were consulted. Autoimmune workup revealed positive anti-glomerular basement membrane (anti-GBM) antibodies (55 U; normal value <20U) and positive p-ANCA. Infectious Disease Workup including HIV, HBV, HCV, QuantiFERON, Bartonella, Histoplasma, Coccidioides and Blastomyces were negative. The patient was started on pulse dose methylprednisolone with plasmapheresis as well as urgent Hemodialysis. Renal biopsy was consistent with acute crescentic glomerulonephritis. Direct immunofluorescence showed evidence of anti-GBM antibodies with linear deposits of IgG bound to the glomerular basement membrane. We planned prolonged course of plasmapheresis for at least 10-14 treatments until anti-

GBM becomes undetectable. She was clinically improving and discharged after 9th session of plasmapheresis, and she is also treated with immunosuppressive therapy with cyclophosphamide followed by extended-release prednisone taper and PCP prophylaxis with Bactrim. Patient was scheduled for further 3 sessions of plasmapheresis and dialysis at the time of discharge.

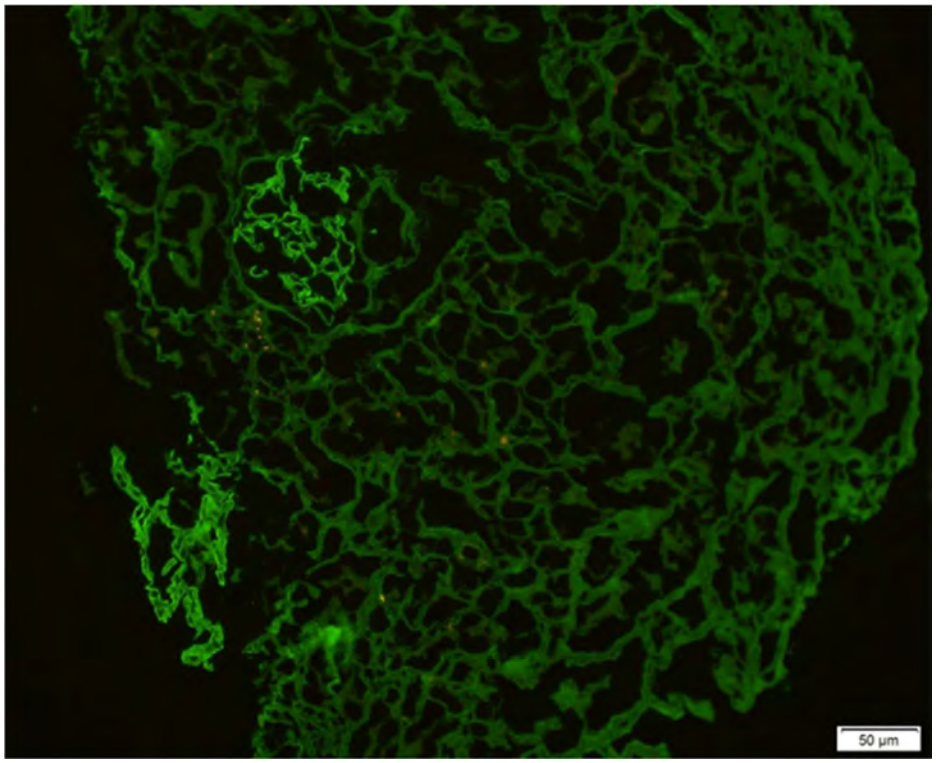
Discussion:

GPS is characterized by auto reactivity to antigens in type IV collagen chains present in the glomeruli and alveolar basement membrane capillaries resulting in crescentic glomerulonephritis and diffuse pulmonary alveolar hemorrhage. Additionally, ANCA is associated with GBM in 20-60% of the cases. The current treatment includes plasma exchange (PE) which involves removal of circulating anti-GBM antibodies and other mediators of inflammation, and immunosuppressants that minimize new antibody formation. Although Plasmapheresis is effective in the treatment of GPS, the efficacy of combined immunosuppressant with PE is not well established. Our case is unique in that the combined treatment with immunosuppressants, and plasmapheresis resulted in a significant improvement of renal function in a pANCA positive good pasture's disease. As GPS is associated with irreversible renal damage and high mortality rate, early and appropriate treatment may reverse the kidney damage and prevent the need for hemodialysis. For monitoring for response Anti-GBM levels are measured weekly for the first six weeks until undetectable on 2 consecutive occasions and then in 6 months. However, further multi-center clinical trials are required to establish its efficacy in the treatment of GPS.

FIGURE LEGEND:



A. B)



C)

Figure1: Kidney biopsy demonstrated a diffuse necrotizing and crescentic glomerulonephritis consistent with anti-GBM disease associated with MPO-ANCA. (A and B) demonstrate the cellular crescents in this rapidly progressive diffuse necrotizing glomerulonephritis. (C) Direct immunofluorescence findings of linear staining of the glomerular basement membrane of IgG support the diagnosis of anti-GBM

Binod KC:

A Rare Case of HMG-CoA Reductase Antibody Positive Statin Induced Necrotizing Autoimmune Myopathy

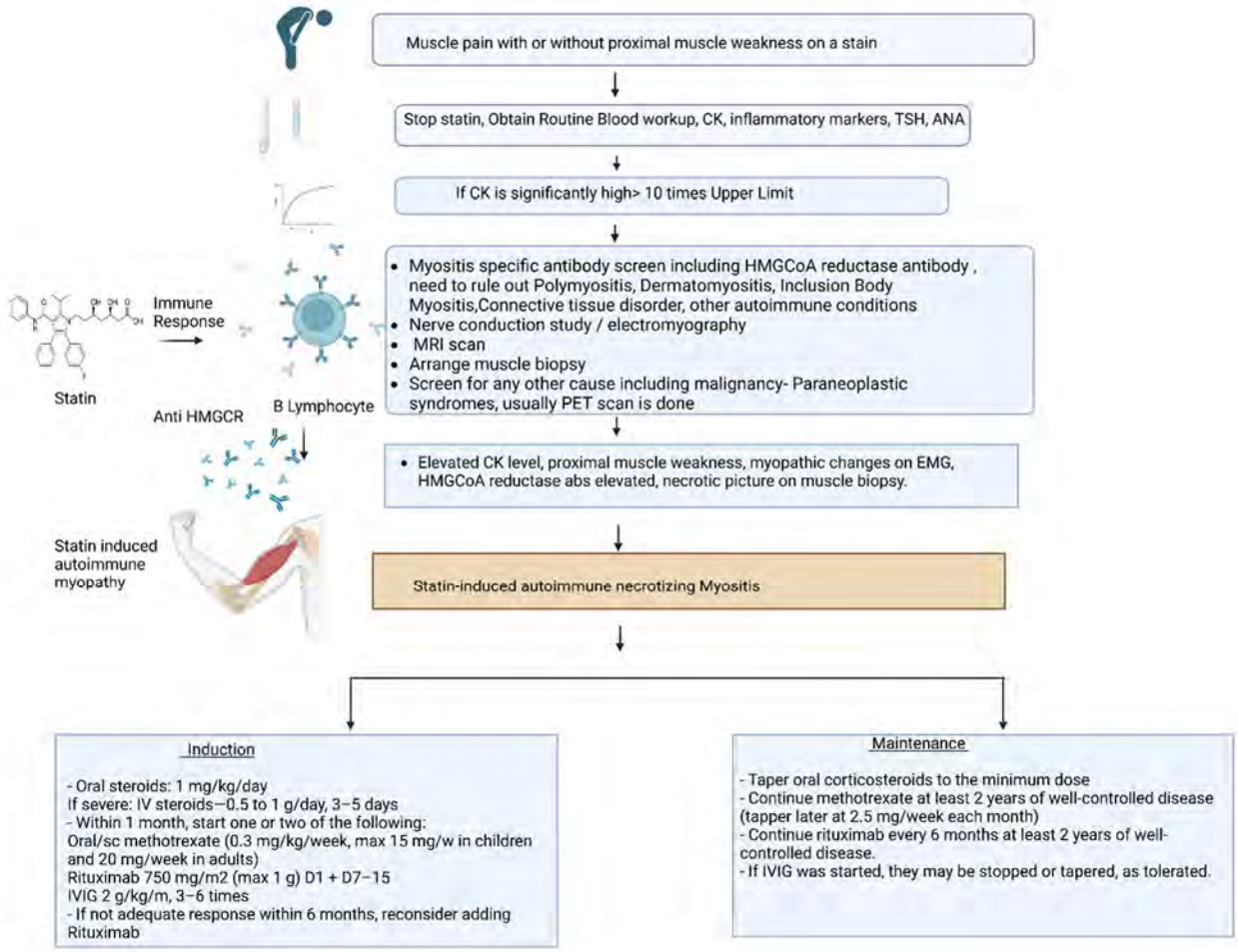
Binod KC MBBS [1] ,Ryan Ruia[2],Sistu KC MBBS [3] ,Fatme Allam MD [4]
[1]*Division of Medicine, State University of New York Upstate Medical University, Syracuse, New York;*
[2]Norton College of Medicine at Upstate Medical University, Syracuse, New York
[3]*Division of Medicine, Patan Academy of Health Sciences, Lalitpur, Nepal*
[4]*Division of Rheumatology, State University of New York Upstate Medical University, Syracuse, New York*

Abstract Version :

Statin-induced necrotizing myositis is a rare subtype of idiopathic inflammatory myopathy, with an estimated prevalence of 2-3 cases per 100,000 individuals. This case report describes the presentation, diagnosis, and management statin induced necrotizing myopathy of a 63-year-old male patient with a history of hypercholesterolemia, lacunar infarct, and hypertension, who presented with elevated liver enzymes and progressive weakness accompanied by myalgias in the proximal upper and lower extremities. Initial laboratory work revealed significantly increased CK level >30,000 with elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. The patient had self-discontinued statin therapy one month prior to the onset of muscle weakness. Rheumatology consultation led to the consideration of polymyositis (PM) , Dermatomyositis and statin-associated immune-mediated necrotizing myopathy (IMNM) in the differential diagnosis. Anti-HMGCR antibodies were strongly positive, confirming the diagnosis of statin associated IMNM. Muscle biopsy and electromyography findings supported the diagnosis. Intravenous methylprednisolone and subsequent oral prednisolone were initiated, but the patient deteriorated rapidly. Intravenous immunoglobulin (IVIG) therapy in combination with glucocorticoids was subsequently administered, leading to clinical improvement. Maintenance treatment with methotrexate and IVIG was initiated. After a period of remission, the patient experienced a flare when we started to increase the frequency of IVIG from every 4 weeks to 6 weeks, which was later successfully managed with oral prednisolone along with IVIG and methotrexate. Serial follow-up visits showed gradual improvement in muscle strength and laboratory markers. In the event of repeated flares, the addition of rituximab to the treatment regimen would be considered. This case highlights the importance of considering statin associated IMNM in patients presenting with myopathy symptoms and a history of statin use.

Proposed Algorithm for the Evaluation of Potential Cases of Statin-Associated Autoimmune Myopathy

Algorithm for the Evaluation of Potential Cases of Statin-Associated Autoimmune Myopathy



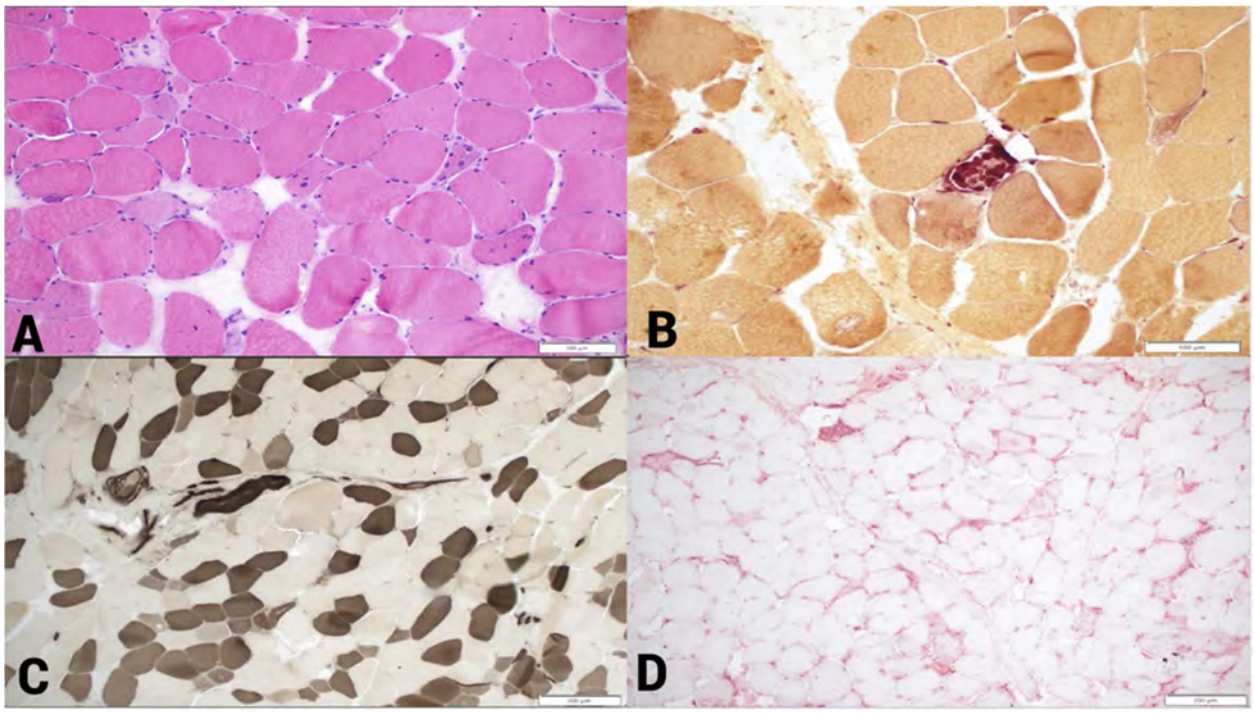


FIGURE 1

A: (Top Left) H&E cryostat sections demonstrate good technical preservation of the myofiber architecture. There is significant fiber size variation. The atrophic fibers are primarily round and polygonal. There are increased numbers of myofibers with internalized nuclei, increased regenerating fibers, and increased necrotic fibers. There are scattered fibers with central vacuoles, a minority of which appear to have basophilic rimming. The endomysial connective tissue is increased and there is focal fragmentation of the perimysial connective tissue. There are scattered mononuclear cells in the endomysial and perimysial compartments. There is no evidence of vasculitis, group atrophy, or selective perifascicular atrophy.

B: (Bottom Left) ATPase stains (pH 9.4, 4.6, 4.2) demonstrate no evidence of selective fiber type atrophy or fiber type grouping. The pH 4.2 preparation reveals increased numbers of type IIc fibers

C: (Top Right) The esterase stain highlights scattered necrotic cells.

D: (Bottom Right) Immunohistochemistry for MHC-I (HLA-ABC) reveals mildly increased staining in occasional fascicles. CD3 and CD20 demonstrate scattered endomysial lymphocytes, with more frequent B-cells compared to T-cells. CD68 highlights frequent macrophages, most prominently in the necrotic myofibers.

FIGURE 2: Disease trajectory: corresponding CK levels, AST, ALT and ESR with medications use. Vertical axis: CK level, AST, ALT, ESR; horizontal axis: timeline in days of treatment.

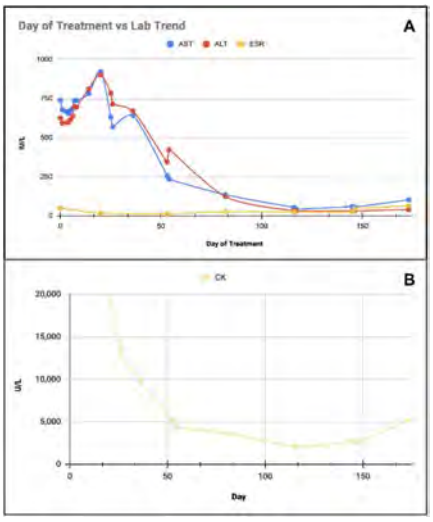
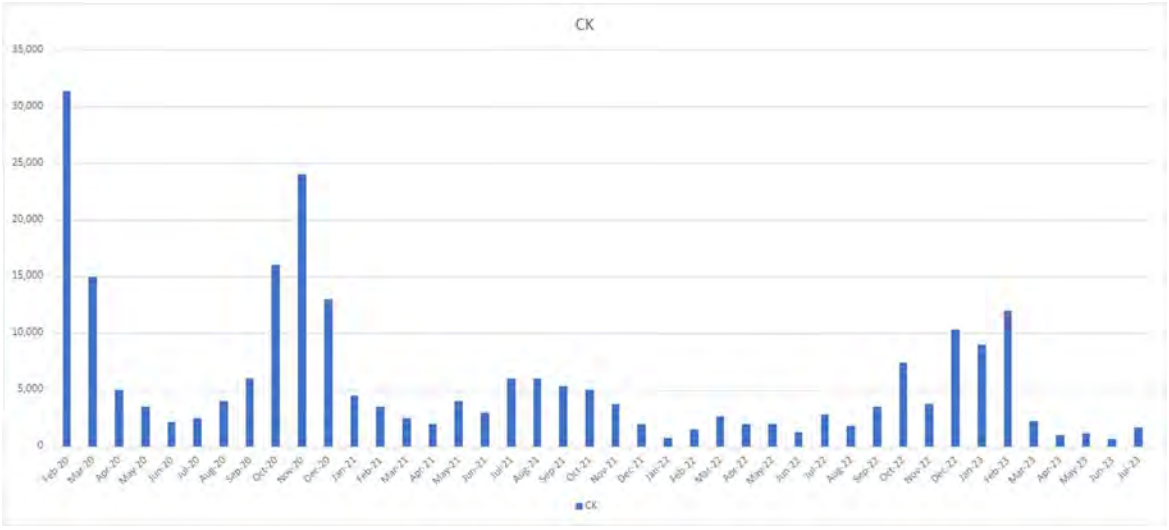


FIGURE 2: Disease trajectory in bar diagram: corresponding CK levels with timeline of treatment



Sreechandra Kruthiventi:

Legionella bozemanii (Fluoribacter bozemanae) brain abscess in a renal transplant recipient.

Sreechandra Kruthiventi MD[1], Abrar Khan DO[2], Rahul Mahapatra DO[2], Soma Sanyal, MD[3] and Wesley Kufel PharmD[4],

[1]Division of Medicine, State University of New York Upstate Medical University, Syracuse, New York; [2]Infectious Disease, State University of New York Upstate Medical University, Syracuse, NY, [3]Department of pathology, State University of New York Upstate Medical University, Syracuse, NY [4]Department of pharmacy, Binghamton University, Binghamton, New York.

Background: Legionnaires' disease is a potentially fatal multisystem disease caused by *Legionella* species. However, extrapulmonary *Legionella* disease is rare[1] and is typically associated with Legionella species other than *L. pneumophila*.

Case presentation: We present a 55-year-old male with history of renal transplant secondary to IgA nephropathy (day 0) which was complicated by T-cell mediated rejection requiring anti-thymocyte globulin and elotuzumab (day 130). He was then hospitalized on day 184 with community-acquired pneumonia and treated with piperacillin-tazobactam and azithromycin. Three weeks later (day 214), he presented with new-onset seizures and was found to have a frontal brain abscess on MRI. His clinical course and brain imaging worsened despite undergoing multiple operative drainage procedures and receiving broad-spectrum antimicrobials. *L. bozemanii* was first identified from cerebrospinal fluid (CSF) on buffered charcoal yeast culture from day 240 and was also later confirmed by 16S rRNA sequencing. Susceptibilities were unavailable due to poor organism growth. Of note, his allergy history was significant for rash with ciprofloxacin and levofloxacin. Based on the low severity of the allergic reaction and need for central nervous system penetration, moxifloxacin 400 mg^2 intravenously every 24 hours was initiated on day 244 in addition to broad-spectrum antibiotics. Subsequent CSF cultures were positive for *L. bozemanii* until the CSF culture on day 250. Due to poor clinical response, azithromycin and intrathecal polymyxin B were added for salvage therapy on day 255. His neurological status continued to progress and he eventually succumbed to his illness on day 262.

Conclusion: We present a diagnostically challenging case of *L. bozemanii* brain abscess in an immunocompromised patient[3,4]. To our knowledge, this is the first case of culture proven *L. bozemanii* brain abscess in the literature. Considering the fatal nature of the infection, *Legionella* infection should be considered in a multisystem disease in immunocompromised patients.

References:

1. Andersen BB, Søgaard I. Legionnaires' disease and brain abscess. Neurology. 1987 Feb;37(2):333-4. doi: 10.1212/wnl.37.2.333. PMID: 3808318.

2. Garau J, Fritsch A, Arvis P, Read RC. Clinical efficacy of moxifloxacin versus comparator therapies for community-acquired pneumonia caused by Legionella spp. J Chemother. 2010 Aug;22(4):264-6. doi: 10.1179/joc.2010.22.4.264. PMID: 20685631.

3. Jaeger TM, Atkinson PP, Adams BA, Wright AJ, Hurt RD. Legionella bozemanii pneumonia in an immunocompromised patient. Mayo Clin Proc. 1988 Jan;63(1):72-6. doi: 10.1016/s0025-6196(12)62667-6. PMID: 3275844.

4. Parry MF, Stampleman L, Hutchinson JH, Folta D, Steinberg MG, Krasnogor LJ. Waterborne Legionella bozemanii and nosocomial pneumonia in immunosuppressed patients. Ann Intern Med. 1985 Aug;103(2):205-10. doi: 10.7326/0003-4819-103-2-205. PMID: 4014902.

Sreechandra Kruthiventi:

Disseminated Cryptococcus in an immunocompromised patient.

Sreechandra Kruthiventi,M.D[1]., Bhavya Poudyal, M.B.B.S.[1], Rahul Mahapatra, D.O[2]

Background: *Cryptococcus neoformans* is an opportunistic encapsulated yeast that primarily infects immunocompromised hosts. Commonly reported sites of infection are the lungs and central nervous system. Cutaneous involvement is rare, affecting 10 to 20% of patients with disseminated cryptococcal infection[1], and can often be the first sign of disseminated infection. Cutaneous cryptococcosis should be part of the differential diagnostic workup in an immunocompromised patient presenting with a new rash or skin lesions[2].

Case presentation- We describe a case of a 63-year-old immunosuppressed female with systemic lupus erythematosus (SLE) and Crohn's disease on chronic belimumab, mycophenolate mofetil, and prednisone. She had a recent hospitalization for lupus cerebritis requiring plasmapheresis, rituximab, and methylprednisolone therapy. She developed progressive bilateral erosions and verrucous lesions on her bilateral thighs and calves. Her cutaneous lesions were refractory to broad-spectrum intravenous antibiotic therapy which prompted a skin biopsy. Culture from skin biopsy specimen evolved *Cryptococcus neoformans*. Further evaluation revealed positive serum and CSF cryptococcal antigen, suggesting systemic dissemination. Induction therapy was started with liposomal amphotericin B and flucytosine, followed by fluconazole consolidation therapy and secondary prophylaxis. She responded well with a gradual improvement of skin lesions.

Conclusion- Cryptococcal infection is a rare but often fatal opportunistic pathogen in immunosuppressed patients[3]. Umbilicated papules resembling molluscum contagiosum are commonly seen in disseminated cryptococcus infections, but a wide variety of skin lesions have been described in the literature, including nodules, ulcerations, phlegmon, whitlow, cellulitis, plaques, and maculopapular lesions[4]. Lesions are most likely to be seen on the face and neck, followed by extremities and trunk. Cutaneous lesions can be an early marker for disseminated cryptococcal infection, even in the absence of systemic signs or symptoms of infection. This case emphasizes having a low threshold for skin biopsy for the evaluation of cutaneous lesions in immunocompromised patients for an early diagnosis.

Keywords- Immunocompromised, SLE, Cryptococcus neoformans, cellulitis, skin biopsy

References:

1. Sivaraj V, Kulasegaram R, Rickaby W, Dwyer E. Rare presentation of cutaneous cryptococcosis in advanced HIV. BMJ Case Rep. 2018 Dec.

2. Daniel J. Anderson and others, Cryptococcal Disease Presenting as Cellulitis, Clinical Infectious Diseases, Volume 14, Issue 3, March 1992, Pages 666–672

3. Valente ES, Lazzarin MC, Koech BL, et al. Disseminated Cryptococcosis Presenting as Cutaneous Cellulitis in an Adolescent With Systemic Lupus Erythematosus. Infect Dis Rep. 2015;7(2):5743. June 2015.

4. Hayashida MZ, Seque CA, Pasin VP, Enokihara MMSES, Porro AM. Disseminated cryptococcosis with skin lesions: report of a case series. An Bras Dermatol. 2017;92(5 Suppl 1):69-72.

Sreechandra Kruthiventi:

Femoral artery graft infection with Mycobacterium bovis secondary to Bacille Calmette-Guérin (BCG) intravesical therapy for bladder cancer.

Sreechandra Kruthiventi MD[1], Wesley Kufel PharmD[2], Carina Hernandez MD PhD[1] and Kumar Priyank MD[3]

Introduction

Mycobacterium bovis infection is attributed to transmission from cattle and consumption of unpasteurized dairy. However, human infections can be secondary to intravesical Bacillus Calmette–Guérin (BCG) therapy[1,2]. Around 6.7 % of vascular involvement has been reported. Herein, we report a case of a *M. bovis* femoral artery graft infection secondary to intravesical BCG therapy for bladder cancer.

Case presentation

A Caucasian male in his mid-seventies from upstate NY, with a PMH of bladder cancer on intravesical BCG therapy (last administration was 4 weeks prior to presentation) presented with left groin swelling. He was diagnosed to have a common femoral artery aneurysm and underwent aneurysmal resection and graft placement by vascular surgery. One month later, he developed left groin swelling with drainage, which did not respond to levofloxacin. He presented three months after the graft procedure for progressive swelling and pain and was found to have a complex collection posterior to left Common femoral artery. Vascular surgery did an open incision and drainage with removal of the artificial graft and placement of an allograft. His graft PCR was positive for Mycobacterium tuberculosis complex with AFB culture growing *M. bovis*[3]. This was likely from his intravesical BCG treatments. M. *bovis* isolate showed isolated resistance to Pyrazinamide. He was on Ethambutol, Isoniazid (INH) and Rifampin for four months followed by five months of INH and Rifampin. He completed nine months of therapy without any adverse effects and clinically responded well without recurrence.

Discussion

We report a vascular graft infection by *M. bovis* following intravesical BCG treatments. This patient was managed with graft removal and antimycobacterial therapy, which was well-tolerated. Invasive infections after intravesical BCG are approximately 3-7% of patients[4]. *M. bovis* infection should be considered in patients with a history of intravesical BCG therapy and lack of clinical response to conventional antibiotics.

References:

1. Seelig MH, Oldenburg WA, Klingler PJ, Blute ML, Pairolero PC. Mycotic vascular infections of large arteries with Mycobacterium bovis after intravesical bacillus Calmette-Guérin therapy:

case report. J Vasc Surg. 1999 Feb;29(2):377-81. doi: 10.1016/s0741-5214(99)70391-5. PMID: 9950996.

2. Pérez-Jacoiste Asín M.A., et al. Bacillus Calmette-Guérin (BCG) infection following intravesical BCG administration as adjunctive therapy for bladder cancer. Medicine (Baltimore) 2014;93:236–254.

3. Sposito FL, Campanerut PA, Ghiraldi LD, Leite CQ, Hirata MH, Hirata RD, Siqueira VL, Cardoso RF. Multiplex-PCR for differentiation of Mycobacterium bovis from Mycobacterium tuberculosis complex. Braz J Microbiol. 2014 Oct 9;45(3):841-3. doi: 10.1590/s1517-83822014000300012. PMID: 25477916; PMCID: PMC4204967.

4. Kubica T, Agzamova R, Wright A, Rakishev G, Rüsch-Gerdes S, Niemann S. Mycobacterium bovis isolates with M. tuberculosis specific characteristics. Emerg Infect Dis. 2006 May;12(5):763-5. doi: 10.3201/eid1205.050200. PMID: 16704833; PMCID: PMC3374422.

Sreechandra Kruthiventi:

Paecilomyces empyema in a renal transplant patient on Carbozantinib.

Sreechandra Kruthiventi MD[1], Carina Hernandez MD PhD[1], SS Prasad Gadula MBBS[1] and Kristopher Paolino MD[2]

Introduction

Paecilomyces is a common saprobic filamentous fungus and is a member of the Thermoascaceae family, and a rare cause of human infections. The most frequent forms of infections are pulmonary, ophthalmic, sinus and skin infections but can cause disseminated infections in immunocompromised patients. We report a case of *Paecilomyces* empyema in a renal carcinoma patient on Carbozantinib.

Case presentation

We present the case of a male in 60s with a past medical history significant for stage IV left renal cell carcinoma on Carbozantinib initially presented persistent dyspnea and chest pain. Of note, he was treated with antibiotics for pneumonia twice prior to presentation. Infectious workup was negative (sputum and blood culture) at that time, and he was discharged shortly after.

During this admission, Computed Tomography demonstrated right sided pneumothorax, consolidation and lung nodules. He was started on broad spectrum antibiotics for pneumonia and underwent right sided chest tube placement. After two days, he developed left sided pneumothorax and had a left sided chest tube placed. Eventually, he became hypoxic, requiring mechanical ventilatory support. His pleural fluid analysis was suggestive of exudate and the cultures initially grew *Pseudomonas* and Zosyn was continued. On D5 pleural fluid grew mold and voriconazole was added for fungal coverage. He was extubated but continued to remain on high flow oxygen and intermittent positive pressure ventilation. He was transitioned to comfort care as per patient's wishes and he passed away the next day. Eventually mold in his pleural fluid was identified as *Paecilomyces* on D11.

Discussion

Paecilomyces is a rare fungal infection which causes invasive infections in immunocompromised patients[1]. Tyrosine kinase inhibitors augments risk for invasive fungal infections[2].This case emphasizes the importance of extended incubation or subcultures to detect fungal infections. Voriconazole has demonstrated good activity and other promising options are ravuconazole and posaconazole[3].

References

1. Pastor FJ, Guarro J. Clinical manifestations, treatment and outcome of Paecilomyces lilacinus infections. Clin Microbiol Infect. 2006 Oct;12(10):948-60. doi: 10.1111/j.1469-0691.2006.01481.x. PMID: 16961630.
2. Chamilos G, Lionakis MS, Kontoyiannis DP. Call for Action: Invasive Fungal Infections Associated With Ibrutinib and Other Small Molecule Kinase Inhibitors Targeting Immune Signaling Pathways. Clin Infect Dis. 2018 Jan 6;66(1):140-148. doi: 10.1093/cid/cix687. PMID: 29029010; PMCID: PMC5850040.
3. Chamilos G, Kontoyiannis DP. Voriconazole-resistant disseminated Paecilomyces variotii infection in a neutropenic patient with leukaemia on voriconazole prophylaxis. J Infect. 2005 Nov;51(4):e225-8. doi: 10.1016/j.jinf.2005.02.005. PMID: 16291275.

Deevyashali Parekh:

Nivolumab in platinum-refractory head-and-neck cancers: A retrospective observational audit from a tertiary cancer center

Abstract

Background:

Nivolumab and pembrolizumab are approved treatment options for platinum-refractory head-and-neck squamous cell cancer (HNSCC) based on the demonstration of improved outcomes in clinical trials. However, limited data exist on their efficacy in the real-world setting.

Objectives:

To determine the impact of immune checkpoint inhibitors in the treatment of platinum-refractory HNSCC and the associated outcomes in a real-world setting.

Materials and Methods:

This was a retrospective study conducted between August 1, 2016, and December 31, 2018 in the Department of Medical Oncology at the Tata Memorial Hospital, a tertiary cancer center in India. We included patients with advanced platinum refractory HNSCC who had been treated with nivolumab. Data regarding adverse events, response, overall survival (OS), and progression-free survival (PFS) were collected. Survival analysis was performed by the Kaplan–Meier method.

Results:

A total of 2796 patients qualified for potential treatment with immunotherapy, but only 41 (1.47%) were able to receive it. The dose used was 240 mg in seven patients (17.1%) and 3 mg/kg in the remaining 34 (82.9%). The response rate was 19.5% (n = 8). The median PFS and OS were 2.27 months [95% confidence interval (CI), 1.51–4.14] and 5.29 months [95% CI, 3.78–11.67], respectively. The 1 year OS was 33.6% (95% CI, 19.5–48.4). Oral cavity tumors were associated with a lower PFS (hazard ratio, 3.86; 95% CI, 1.67–8.92; *P* = 0.001) and OS (hazard ratio, 2.79; 95% CI, 1.26–6.17; *P* = 0.001).

Conclusion:

Nivolumab has a good impact on both OS and PFS even in the real-world setting of patients with extensively pretreated platinum-refractory HNSCC similar to what has been reported in the pivotal studies. Among the patients who are treated with nivolumab, those with oral cavity tumors have a worse OS and PFS relative to those of other sites.

Jenish Bhandari :

A rare single case of Covid-19 induced acute myocarditis and encephalopathy presenting simultaneously in a fully vaccinated patient

Jenish Bhandari Anas Abbas , Caitlin Ward , Mahnoor Sherazi , Maha Bayya

Abstract: The ongoing Coronavirus disease 2019 (COVID-19) pandemic may result in cardiovascular complications such as myocarditis, while encephalitis is a potentially life-threatening COVID-19-associated central nervous system complication. This case illustrates the possibility of developing severe multisystem symptoms from a COVID-19 infection, despite having received the COVID-19 vaccine within the year. Delay in treatment for myocarditis and encephalopathy can lead to permanent and possibly fatal damage. Our patient, a middle-aged female with a complicated medical history, initially came in without characteristic manifestations of myocarditis such as shortness of breath, chest pain, or arrhythmia, but with an altered mental status. Through further laboratory tests, the patient was diagnosed with myocarditis and encephalopathy which were resolved within weeks through medical management and physical/occupational therapy.

Conclusion: This case presentation describes concomitant COVID-19 myocarditis and encephalitis in fully vaccinated patient . Physicians should remain vigilant about the possibility of life-threatening complications from COVID-19 infection, even in fully vaccinated patients. Timely identification and proactive management of COVID-19 are crucial to minimize potential complications in such cases.

Jenish Bhandari :

The Discovery of an Intracardiac Thrombus Following a Mild COVID-19 Infection: A Case Report and Review of Literature

Authors: Jenish Bhandari MBBS , Mahnoor Sherazi MBBS, Syed Huda MBBS, Niranjan Ojha MBBS, Robert Carhart MD

Abstract :

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19) is a viral disease that predominantly affects the respiratory system, but extrapulmonary manifestations have been increasingly reported over the course of the pandemic. Common extrapulmonary manifestations include the gastrointestinal, cardiovascular, and neurological systems, such as diarrhea, rashes, loss of smell/taste, myalgia, acute kidney injury, cardiac arrhythmias, or heart failure. COVID-19 infection is associated with an increased risk of thromboembolic events, especially in the setting of severe disease. We present a case of a 42-year-old female who recently tested positive for COVID-19 infection and presented to the clinic with complaints of palpitations that started after her diagnosis. An electrocardiogram done in the clinic showed sinus rhythm, and the patient was placed on an event monitor, which showed no evidence of tachyarrhythmia. A transthoracic echocardiogram (TTE) done as part of the workup showed a large thrombus in the right ventricular outflow tract attached to the ventricular side of the pulmonic valve. The patient was started on a therapeutic dose of apixaban with complete resolution of her symptoms.

Conclusion: While intracardiac thrombi are typically linked to severe symptomatic cases of COVID-19, our cases underscore the uncommon connection between asymptomatic COVID-19 infections and intracardiac thrombi. Physicians should remain vigilant about these infrequent presentations to facilitate early detection and effective management.

Jenish Bhandari :

HIGH-DOSE STATIN GIVEN AS LOADING DOSE PRIOR TO PCI REDUCES NO-REFLOW PHENOMENON IN ACUTE CORONARY SYNDROME: A META-ANALYSIS OF 4829 PROCEDURES

Jenish Bhandari , Sonali Sachdeva, Udita Gupta, Avilash Mondal, Abdulrahman Hashem, Mahnoor Sukaina, Harshwardhan Khandait, Farah Yasmin, Rupak Desai, Akhil Jain, Hasnan M. Ijaz, Ankit Vyas

Abstract:

Background: No-reflow, a phenomenon characterized by inadequate myocardial perfusion despite an open epicardial vessel, is more commonly observed in emergency percutaneous coronary intervention (PCI) after acute coronary syndrome (ACS) compared to elective PCI. To mitigate this occurrence, some studies have proposed using a high-intensity statin loading dose before PCI.

Methods: A systematic literature search was conducted in PUBMED, Google Scholar, and SCOPUS databases to identify relevant studies reporting on the incidence of no-reflow after a loading dose of high-intensity statin compared to a control group before PCI. Data on the comparative incidence of no-reflow in both groups were extracted from the selected studies. A random-effects model was employed to calculate the pooled relative risk, and heterogeneity was assessed using I2 statistics.

Results: The initial search yielded 95 articles, with 11 studies meeting the inclusion criteria for the final meta-analysis. The combined sample size consisted of 4,829 patients (74.6% males, mean age 61.7±11.24 years). Among the sample population, the most prevalent comorbidities included hypertension (60.4%), smoking (37.8%), dyslipidemia (34.6%), and diabetes mellitus (28.3%). Meta-analysis results demonstrated that a loading dose of high-intensity statin before PCI significantly reduced the risk of no-reflow (Relative risk 0.510, p=0.02, I2=58.5%).

Conclusion: Administering a loading dose of high-intensity statin before primary PCI for ACS proves to be an effective strategy in reducing the incidence of no-reflow during the procedure.

Jenish Bhandari:

Lumbosacral Vertebral Osteomyelitis with Iliopsoas and Epidural Abscess Following Intravesical BCG Therapy

Jenish Bhandari MBBS, Mahnoor Sherazi MBBS, Binod KC MBBS, Anas Abbass MD, Niranjan Ojha MBBS

Abstract:

Intravesical BCG therapy is widely used for treating superficial or non-muscle-invasive bladder cancer, utilizing the antitumor properties of Mycobacterium bovis to combat malignant uroepithelial cells. Although effective, BCG therapy can lead to local or disseminated infections. In rare instances, it may cause vertebral osteomyelitis, particularly in the thoracolumbar spine, with a higher prevalence among older males. Here, we present the case of an 84-year-old male patient who developed L5-S1 osteomyelitis along with epidural and iliopsoas abscesses following BCG therapy. The patient experienced severe low back pain and bilateral lower extremity weakness. This paper aims to enhance awareness among spine surgeons about this infrequent complication and to emphasize the importance of considering a history of BCG therapy when diagnosing such cases.

Conclusion:

Intravesical BCG therapy is an effective treatment for non-muscle-invasive bladder cancer, but patients should be informed about potential adverse events associated with this treatment. The use of a live attenuated vaccine carries the risk of infection, and vertebral osteomyelitis mimicking spinal malignancy should be considered as a possible complication. Spine surgeons and oncologists should be vigilant regarding the potential for spinal infections in patients with a history of BCG therapy.

Jenish Bhandari:

HIGHER ODDS OF LONG-TERM ALL-CAUSE MORTALITY WITH PERSISTENT PULMONARY HYPERTENSION AFTER TRANSCATHETER AORTIC VALVE REPLACEMENT: A META-ANALYSIS

Jenish Bhandari, Sonali Sachdeva , Harshwardhan Khandait,, Sarvesh Naik, Abdulrahman Hashem, Mahnoor Sukaina , Rupak Desai , Ankit Vyas, Akhil Jain,

Abstract:

Background: Transcatheter aortic valve replacement (TAVR) is a preferred treatment for severe aortic stenosis (AS) in high-surgical-risk patients. However, the current risk models for assessing the likelihood of recovery after TAVR do not consider persistent pulmonary hypertension status post-procedure. This study aimed to evaluate the impact of persistent pulmonary hypertension after TAVR on long-term outcomes.

Methods: We conducted a systematic search in PubMed, Google Scholar, and SCOPUS to identify relevant studies reporting long-term outcomes in patients with persistent pulmonary hypertension after TAVR. Using a random-effects model, we calculated the pooled relative risk of long-term all-cause mortality between patients with persistent pulmonary hypertension after TAVR and those with improved pulmonary hypertension post-procedure. Heterogeneity was assessed using I2 statistics, and sensitivity analysis was performed using the leave-one-out method.

Results: Among 102 initially identified articles, 7 studies were included in the final analysis, with a total of 2,789 patients (49.31% males, mean age 80.991±2.528 years). The pooled and sensitivity analyses consistently demonstrated significantly higher odds of long-term all-cause mortality in patients with persistent pulmonary hypertension after TAVR compared to those with improved pulmonary hypertension after the procedure (HR 2.799, 95% CI: 2.068-3.789, p=<0.001, I2=25.51%).

Conclusion: The presence of persistent pulmonary hypertension after TAVR is associated with a poor prognosis, signifying increased odds of long-term all-cause mortality. This finding underscores the need for prospective validation and potential incorporation into future risk models to enhance outcome predictions for patients undergoing TAVR.

Kenopama Gyawali[i]

Not Everything that Smells fruity is Diabetic Ketoacidosis: A Case of Pancreatic Ketoacidosis

Kenopama Gyawali[1], Sanchit Panda[2], Kamal Gautam[1], Sagun Sthapit[1], Nayab Ahmed[2] and Dragos N. Manta[2]

Introduction:

Severe anion gap metabolic acidosis caused by ketoacidosis is commonly observed in the intensive care unit among patients with uncontrolled diabetes and high blood sugar levels. Starvation, alcoholism, and medication use are less common causes. Pancreatic ketoacidosis is a rare complication of acute pancreatitis and cause of ketoacidosis that poses a diagnostic and treatment challenge for Intensivists. This case report describes a 42-year-old patient with severe anion gap metabolic acidosis resulting from acute pancreatitis.

Case Presentation:

A 42-year-old female presented to the emergency department with abdominal pain, nausea, and vomiting for 4 days. Initial vitals were concerning for hypotension, tachycardia, and tachypnea. On examination she appeared confused and lethargic, epigastric tenderness was noted.

Initial laboratory values revealed serum sodium 125 mEq/L, chloride 90 mEq/L, undetectable serum bicarbonate and anion gap of 31 mmol/L. Serum potassium and glucose were normal. She had a new kidney injury with oliguria. Serum lipase 3600 U/L and beta hydroxybutyrate were significantly elevated more than 9 mmol/L. The arterial blood gas revealed severe anion gap metabolic acidosis with pH of 7.02 and pCO2 of 30 mmHg. Arterial lactate was 2.7 mg/dL. Urine analysis showed proteinuria, with ketonuria. Computed tomography of the abdomen showed diffuse pancreatic edema. Serum creatine kinase, acetaminophen, salicylate and ethanol levels were all normal.

She was admitted to the medical intensive care unit and was promptly resuscitated with intravenous fluids. Due to concern for toxic alcohol ingestion and severe metabolic acidosis with oliguria she underwent one session of hemodialysis. She was empirically treated with fomepizole for presumed ethylene glycol ingestion. Insulin and dextrose infusions were initiated for presumed euglycemic diabetic ketoacidosis.

Subsequent workup was negative for toxic alcohols, iron and lipid panels were normal. Her hemoglobin A1c was normal with a normal c-peptide level. Her insulin-associated antibodies, glutamic acid decarboxylase 65, insulinoma-associated protein 2 and zinc transporter antibodies were negative. She showed significant improvement with supportive treatment and was eventually discharged home with a diagnosis of pancreatic ketoacidosis secondary to acute pancreatitis.

Discussion: Pancreatic ketoacidosis (PKA) is considered a diagnosis of exclusion, and is thought to be caused by the release of free fatty acids from necrotic pancreatic tissue. The liver metabolizes these acids into ketones, leading to metabolic acidosis, which can be life-threatening. Some case reports suggest a positive correlation between serum lipase levels, anion gap, and serum pH [1,2]. With supportive treatment, ketogenesis ceases, metabolic acidosis improves, and serum lipase levels decrease, indicating that elevated pancreatic lipase in circulation may induce severe ketoacidosis through lipolysis. Aggressive fluid resuscitation, correction of electrolyte imbalances, and insulin supplementation are recommended to prevent catabolism and promote glucose uptake [2].Our patient's presentation and hospital course posed a diagnostic dilemma. However, we kept a broad differential diagnosis for anion gap metabolic acidosis and remained methodical in our diagnostic approach while providing supportive treatment. As the serum lipase level declines with supportive management, the process of ketogenesis stops and metabolic acidosis improves. (Figure 1).

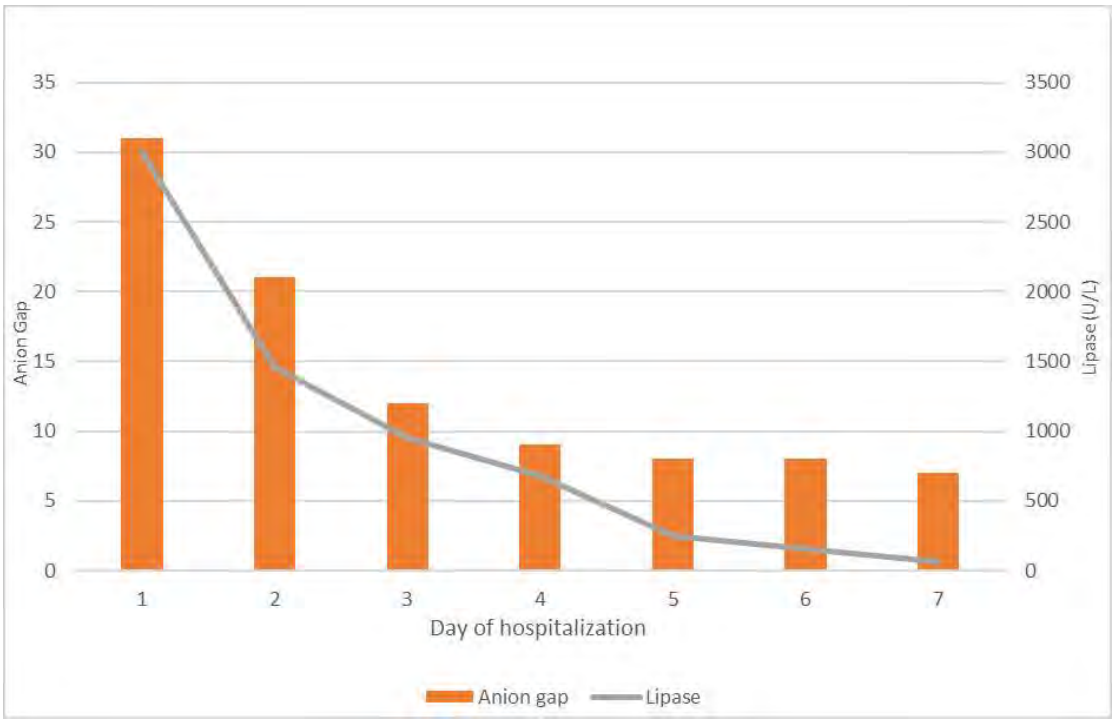


Figure 1: Trend of Lipase and Anion gap during our patient's hospitalization.

Conclusion:

PKA presents as a diagnostic challenge in severe ketoacidosis, requiring a methodical approach.

References:

1. Kabadi, U.M., 1995. Pancreatic ketoacidosis: ketonemia associated with acute pancreatitis. Postgraduate medical journal, 71(831), pp.32-35.

2. Kabadi, U.M., 2015. Pancreatic ketoacidosis (kabadi syndrome) mimicking diabetic ketoacidosis. Endocrine Practice, 21(10), p.1184.

3. Rajan, P. and Misra, D.S., 2020. Pancreatic ketoacidosis-a rare case report.

Kenopama Gyawali:

Acute Chest Syndrome in a patient with Sickle Cell Disease with COVID-19 Infection

Kenopama Gyawali,MBBS[1], Sanchit Panda, MD[2], Sagun Sthapit, MBBS[1], Nicholas Anand, MBBCH[1], Eric Merrell, MD[1], Manju,Paul, MD[2]

Introduction

Acute chest syndrome (ACS) is a severe complication of sickle cell disease and a leading cause of hospitalization and death in people with sickle cell disease (SCD), an inherited monogenic hematological disorder. We present a case of a 20-year-old young man who presented with ACS in the setting of COVID-19 pneumonia.

Case Presentation

A 20-year-old man from Colombia with HbSC genotype SCD and COVID-19 infection presented with severe lower extremities pain and fever. He was treated for pain crisis and COVID-19 with hydration, analgesics, oxygen therapy, and Remdesivir. Although initially he was also treated with broad spectrum antibiotics, it was discontinued as his sputum cultures were negative. On day 3, he developed respiratory distress and chest x-ray showed near complete consolidation of the left lung and atelectasis in the right lower lobe raising concern for ACS [Figure 1]. Computed tomography angiography of thorax ruled out pulmonary embolism and showed dense infiltrates involving entire left lung [Figure 2]. Immediate exchange transfusion was done, leading to resolution of respiratory symptoms and improved aeration in the left lung within the next 4 days [Figure 1].

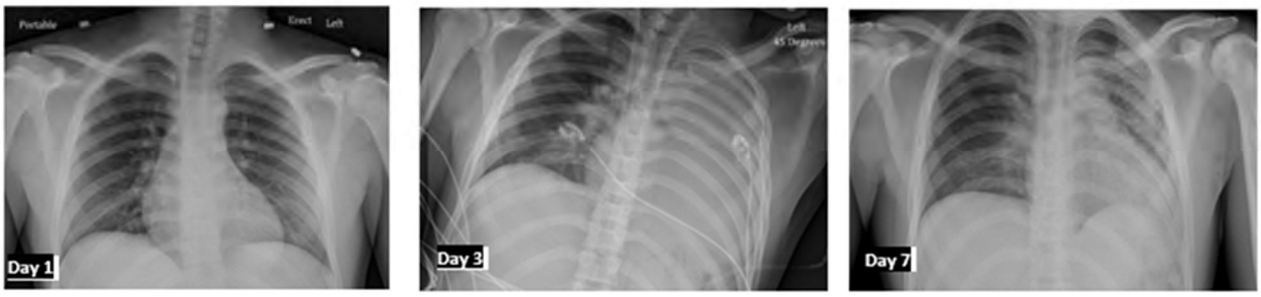


Figure 1: Chest x-ray images of our patient on different days. Patient had left sided lung consolidation on day 3 on comparison to day 1 which prompted the diagnosis of ACS. Day 7 shows improvement of left sided lung following treatments with exchange transfusion.

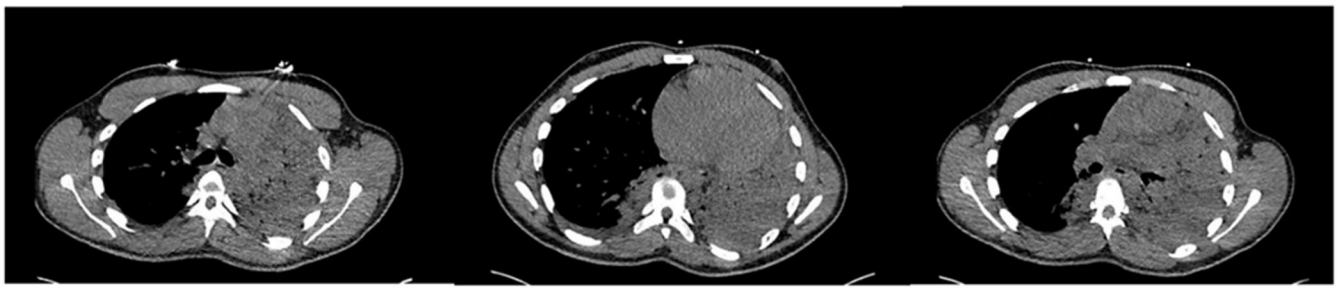


Figure 2 : Different coronal CTA thorax images of patient showing left sided consolidation that prompted diagnosis of ACS

Discussion. CS is a known complication of SCD, commonly seen in HbSS genotype, and can be triggered by various factors such as infections, thrombosis, and embolisms. It presents with new pulmonary infiltrate on chest imaging accompanied by fever and/or respiratory symptoms. Lung injury can range from interstitial infiltrates to alveolar condensation, including atelectasis, pleural effusion, and acute respiratory distress syndrome [1]. Radiological findings may include lung consolidation, ground-glass opacities, and atelectasis, with commonly affected lobes being the right and left inferior ones. Infiltrates may not appear until 2 or 3 days after admission for vaso-occlusive crisis [2]. Our patient was initially admitted for vaso-occlusive crisis triggered by COVID-19 viral infection and developed ACS on day 3 with a unique presentation of near complete lung consolidation. Rarely, near complete consolidation of the entire lung has been described in literature.In one study, 28% of the patients with SCD and COVID-19 had ACS [5]. Though limited data is available on COVID-19 infection and ACS in SCD genotype, one study showed that the HbSC genotype is a strong independent risk factor for mechanical ventilation or death in SCD patients with COVID-19. Pulmonary complications were seen more frequently in patients with HbSC genotype in this study [2,3]. It is worth noting that our patient was of HbSC genotype.ACS is treated with analgesics, fluids, oxygen, antibiotics, and blood transfusions. Exchange transfusions are used in severe cases as in case of our patient.

Conclusion. Limited data suggests that SCD patients with HbSC genotype and COVID-19 infection are at risk of developing ACS. Unilateral complete lung opacification is a rare radiographic finding. Severe cases of ACS are treated with exchange transfusion.

References:

1. Paul, R.N., Castro, O.L., Aggarwal, A. and Oneal, P.A., 2011. Acute chest syndrome: sickle cell disease. European journal of haematology, 87(3), pp.191-207.
2. Arlet, J.B., Lionnet, F., Khimoud, D., Joseph, L., de Montalembert, M., Morisset, S., Garou, A., Cannas, G., Cougoul, P., Guitton, C. and Holvoet, L., 2022. Risk factors for severe COVID-19 in hospitalized sickle cell disease patients: A study of 319 patients in France. *American Journal of Hematology*, *97*(3), p.E86.
3. Arlet, J.B., de Luna, G., Khimoud, D., Odièvre, M.H., de Montalembert, M., Joseph, L., Chantalat-Auger, C., Flamarion, E., Bartolucci, P., Lionnet, F. and Monnier, S., 2020. Prognosis of patients

with sickle cell disease and COVID-19: a French experience. The Lancet Haematology, 7(9), pp.e632-e634

M. Sandhu:

The Voice of the Patient: Transforming Residents into Patient Experience Champions

Sandhu M MD[1], Goodman A MD[2], Sweet J MD[1], Gambhir HS MD[1]

Each year, graduating residents enter the faculty workforce and are expected to know about the patient experience and HCAHPS scores. During a patient's hospital stay, they are evaluated and managed by multiple providers, with a plethora of information relating to the health care team, treatment options, medications, test results, and discharge planning being shared with the patient. This is overwhelming for our patients. During training, residents do not receive formal teaching on obtaining patient perspective when sharing critical information which impacts the quality of care that we provide for our patients as well as the patient experience. In our curriculum, through "Quality Rotation X" we developed a structured senior resident rounding experience, where they visit with patients planned for discharge to ascertain their perspective about their experience during the hospital stay. This session aims to bridge knowledge gaps and increase mindfulness of residents during their training in regards to the patient experience. During "the voice of the patient", we start by providing an overview of the patient experience and an introduction to HCAHPS scores. Subsequently, residents perform bedside patient rounds alongside the quality chief resident. During these rounds, residents meet with patients nearing discharge, inquiring about their experience in the hospital with a focus on communication. We recorded data over the past year and identified themes and gaps in communication. 67% of patients were able to identify their primary team during their hospital stay. Patients suggested writing on index cards, the whiteboard, and creating informational pamphlets to improve communication. Additionally, Patients expressed difficulty with understanding diagnosis (12%), medications (7%), and testing (6%). Patients provided positive feedback about face-to-face communication and families being updated. In 85% of cases, the rounding senior shared their findings with the primary team resident, with the patient's permission, to improve communication.

Mahnoor Sherazi:

Gastrointestinal Perforation, a dreaded side effect of Tocilizumab — Early Recognition in a Giant Cell Arteritis Patient

Mahnoor Sherazi MBBS, Binod KC MBBS, Jenish Bhandari MBBS, Omar Naser MD, Sandy Nasr MD and Christian Geier, MD

Introduction:
Tocilizumab, a recombinant humanized monoclonal antibody targeting the Interleukin-6 receptor, can effectively treat certain inflammatory diseases, including Giant Cell Arteritis (GCA). Despite its important therapeutic role, the drug is also associated with the gastrointestinal perforation (GIP), a potentially fatal complication. Because GIP requires immediate recognition its association with tocilizumab use deserves maximum awareness among all specialties.

Case Presentation:
An 84-year-old male with hyperlipidemia, hypertension, and relapsing GCA presented to the emergency department with abdominal pain and bloody bowel movements for two days. He had been on a two-month course of prednisone and received tocilizumab two weeks ago for giant cell arteritis. Upon admission, patient exhibited signs of peritonitis such as abdominal tenderness, distension and guarding. Lab results indicated leukocytosis and a positive Covid-19 PCR. Chest X-ray and CT Abdomen confirmed gastrointestinal perforation with free air and fluid in the abdomen. Surgery was performed to repair the sigmoid colon perforation emergently. Given its association with GIP, tocilizumab was discontinued, and the patient was discharged on prednisone therapy for GCA.

Discussion:
The use of tocilizumab comes with a rare but potentially life-threatening side effect of gastrointestinal perforations (GIP), with an estimated incidence of 2.7 - 3.0 per 1,000 patient-years. The exact mechanism of how IL-6 antagonism leads to GIP is not fully understood, but it is believed to involve a reduction in the expression of vascular endothelial growth factor (VEGF), which plays a critical role in maintaining intestinal mucosal integrity. In our patient, the occurrence of gastrointestinal symptoms without any known risk factors strongly suggests that tocilizumab is responsible for the GIP, especially considering the close temporal association between the use of tocilizumab and the onset of symptoms.

Conclusion:
Physicians should remain vigilant about GIP as a rare but serious adverse effect of tocilizumab. Early detection and prompt management of GIP are crucial to reduce potential complications in patients receiving this drug.

Mahnoor Sherazi:

Successful Use of Tocilizumab for Catastrophic Antiphospholipid Syndrome in an SLE Patient

Mahnoor Sherazi MBBS, Binod KC MBBS, Jenish Bhandari MBBS, Sarah Lubin, Sandy Nasr MD, Hom Neupane MD, Andras Perl MD PhD, Christian Geier MD

Case presentation:
A 69-year-old male with a history of SLE (ANA 1:160 speckled pattern) and raised antiphospholipid titers was admitted with bilateral pulmonary embolisms and started on a heparin drip. Within hours, sudden diffuse alveolar hemorrhage, profound thrombocytopenia, renal failure, and anemia developed. Laboratory results revealed strikingly elevated anti-cardiolipin IgG/IgA, β2-glycoprotein IgG/IGA, prolonged DRVVT, low C3, C4, CH50; consistent with Catastrophic Antiphospholipid Syndrome (CAPS). His mental status worsened, and he had increasing vasopressor requirements. He was clinically and serologically resistant to treatment with conventional anticoagulation, immunosuppression, and plasmapheresis. A head CT was suggestive of an acute stroke in multiple watershed areas, consistent with ongoing microvascular thrombus formation. C3, C4, and CH50 levels remained profoundly low suggestive of ongoing complement activation; rising APLA titers, predominantly of IgA and IgG isotype, suggested persistent autoantibody release from a plasma cell source. Attempts to inhibit complement activation with eculizumab had no effect on either clinical status or hypocomplementemia; serum cytokine profiling was performed. This revealed persistently elevated serum Interleukin-6, implicated in promoting plasma cell survival and function. Accordingly, we administered anti-IL-6 therapy with tocilizumab (8 mg/kg). Following the first dose of tocilizumab, we saw a remarkable clinical improvement in pressor requirements, hypocomplementemia, and IgA/IgG APLA titers. Soon after, our patient became alert and responsive; his residual encephalopathy resolved completely after sedation was weaned; corticosteroids could be tapered. Ultimately, he could be discharged on hydroxychloroquine 200 mg twice daily, and oral anticoagulation and followed for long-term therapy of SLE and APLS as outpatient.

Conclusion:
This challenging case highlights potential complications of catastrophic antiphospholipid syndrome. The apparent treatment response to tocilizumab suggests that the Interleukin-6 axis can play a key role in sustaining APLS production and complement activation resistant to conventional APLS therapies. It also underlines the potential utility of individually targeted treatment approaches in critical cases of systemic autoimmune disease.

Mahinbanu Mammadli:

Improving the coordination of care shortens the health care delays in cancer patients: A Quality project.

Mahinbanu Mammadli, Stephen Graziano, Alina Basnet, Danielle B, Julie Briggs, Harvir Singh Gambhir

Upstate Medical Universitty

Abstract

Cancer is one of the leading causes of mortality, morbidity and medical costs in healthcare system worldwide. Initial evaluation for cancer in timely and accurately manner is a critical step for in early detection which is currently facing with multiple challenges, including coordination of care. Standardization of the coordination in the healthcare system has been shown to improve the outcome in cancer patients. Here we showed that by decreasing the referral burden to the specialist by implementing APP teams, prioritizing the severity of the disease and improving the effectivity of coordination by inter-disciplinary meetings, we were able to improve the time elapsed from the referral to the initial encounter in patients with possible malignancy which could potentially lead to decreased mortality, improved survival and prognosis and help to provide care on timely manner.

By implementing our quality project, we improved the time elapsed between the referral to initial encounter with Hematology and Oncology specialists within 7 days from 31% to 58% within a year in patients with possible malignancy. We were able to improve the waiting period in a persistent manner when comparing data every month and every quarter. These data imply that by addressing effectivity of the coordination of care, by decreasing referral burden we can possibly shorten waiting time and shorten the diagnostic interval in patients with cancer.

M. Sandhu:

RN-MD Communication Series: An Interdisciplinary Approach to Bridge Communication Gaps

Sandhu M MD[1], Sweet J MD[1], Gambhir HS MD[1]

Nurses and resident physicians are two prominent frontline contributors to the care of patients in all academic healthcare institutions. It is critical to have effective communication between nurses and resident physicians to achieve excellent patient care. Quality reviews and safety alerts identified inadequate or fragmented communication between nurses and residents as the root cause of many adverse events. The quality team developed a platform to connect nurses and resident physicians through the RN-MD communication series to improve communication.

The goal of this session is to improve communication between residents and nurses, and to learn about each other's workflow. This session is built into a mandatory quality rotation in our curriculum, called "Rotation X", and occurs every week. The RN-MD session includes an intern, a senior resident, the quality chief resident, and a charge nurse or nurse manager from one of the medical or ICU floors. In each session, four scenarios are sequentially presented in an open forum and each participant provides perspective from their point-of-view. We then discuss strategies to improve communication going forward.

We surveyed all participants over the past year and have had resoundingly positive feedback from both residents and nurses. 96% of participants strongly agreed that nursing/resident communication is critical to creating a culture of patient safety. After the session, 100% of participants stated that they better understood the importance of RN-MD collaboration, and 96% of participants found the session valuable for improving teamwork and rapport between the healthcare team. 100% of participants stated that they would recommend continuing these sessions, with multiple participants recommending more frequent sessions and involving other teams within the hospital.

Mulham Ombada:

Hypermucoviscous klebsiella pneumonia: a hypervirulent strain masquerading as metastasis

SUMMARY

Hypermucoviscous klebsiella pneumoniae (hvkp) is a hypervirulent strain of klebsiella that causes metastatic spread and life-threatening infection. It is more common among patients of Asian descent but more recently it has been increasingly reported globally. We report a case of pan-susceptible hvkp infection in a patient of Asian descent that has been living in the US for 20 years. It caused liver abscess, peri-gastric abscess, peri-splenic abscess, multifocal pneumonia, septic emboli and tricuspid valve infective endocarditis. He was treated with ceftriaxone, but his septic shock was refractory leading to death. This case highlights the severity of infection caused by this strain, its ability to present with radiographic signs suggestive of malignancy with metastasis. This case also suggests that this strain can become pathogenic after very prolonged period of gastrointestinal colonization.

BACKGROUND

Metastatic spread is an unusual feature for enteric gram-negative bacilli, particularly in non-immunocompromised. Hypervirulent (hv) klebsiella pneumonia – also known as hypermucoviscous klebsiella pneumoniae - emerged as an exception to this rule. After first being described in Asian Pacific region. HMV klebsiella is now increasingly recognized globally. This strain might be more common in patient of Asian descent due to genetic susceptibility rather than geo specific acquisition, but this has not been confirmed. Along with its hypervirulence, this strain can acquire extensive antimicrobial resistance. This, along with its global spread, makes it a potential cause of devastating morbidity and mortality worldwide. Moving forward, this strain need to be considered when empirically treating devastating infections, including endocarditis, meningitis and endophthalmitis in the appropriate clinical and epidemiological setting.

CASE PRESENTATION

A male patient in his 60s, of Asian descent, previously healthy, presented to the emergency room via EMS for 5 days of fever associated with malaise, vomiting and decreased appetite. Patient is immunocompetent but with no routine medical follow up. Social history revealed that he drinks alcohol daily. He moved to the US 20 years ago.

Upon admission, patient was noted to have hyperglycemia, hypotension and hypoxic respiratory failure. His physical exam was positive for scleral icterus, abdominal tenderness, hepatomegaly and lower extremities edema. He was admitted for septic shock.

INVESTIGATIONS *If relevant*

Laboratory workup revealed leukocytosis with a wbc 17600/Ul, high anion gap acidosis with blood glucose of 544 mg/dl, corrected sodium of 127 meq/l, elevated total bilirubin at 6.6 mg/dl, direct component 5.2 mg/dl. His AST and ALT were within normal range. EKG showed ST elevation in multiple leads with no regional wall motion abnormalities on echocardiography, suggestive of pericarditis. CT abdomen and pelvis showed left hepatic lobe hypodense lesion and complex fluid collections in left upper quadrant adjacent to the spleen with mass effect on the stomach, suggestive of malignancy. CT chest showed multiple rounded masses and consolidations in both lungs with complex left side pleural effusion, also suggestive of malignancy (Fig 1).

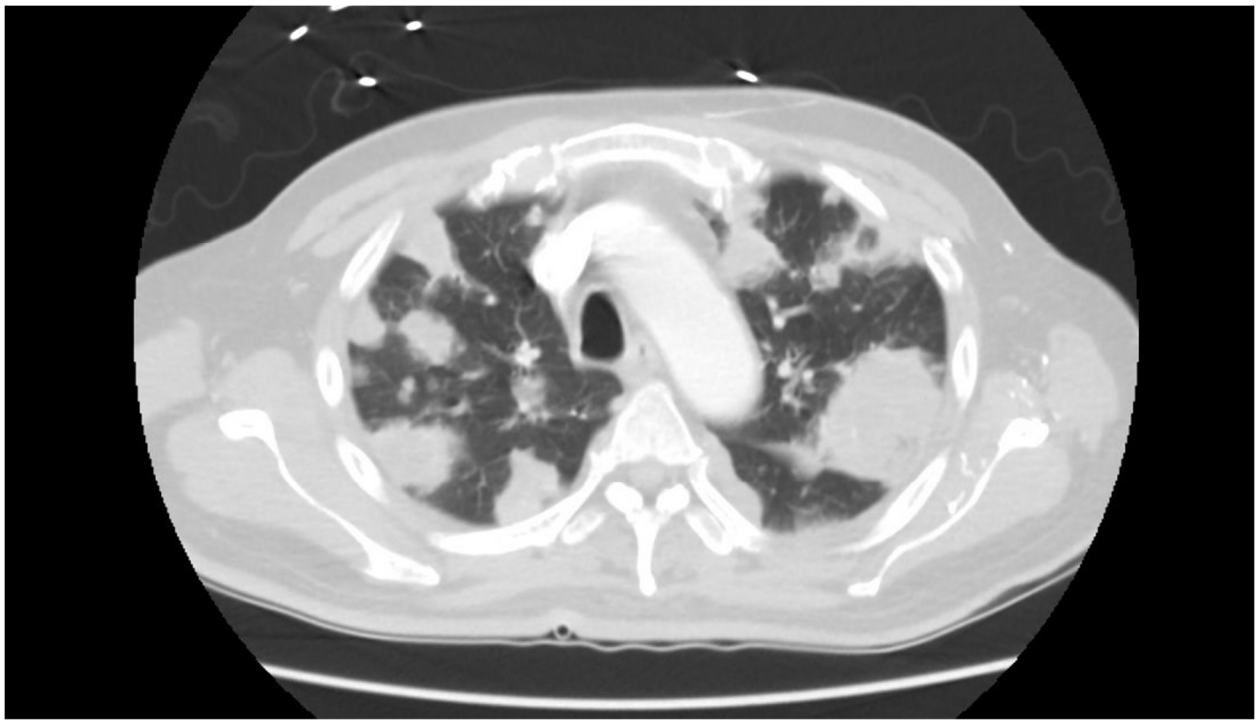


Fig 1. Coronal cut of CT (Computed Tomography) chest showing multiple rounded masses and consolidations

DIFFERENTIAL DIAGNOSIS *If relevant*

Due to concern for malignancy with multiple metastasis, a percutaneous sampling of the liver lesion was done yielding thick white material. This procedure was followed by percutaneous drains placement in peri-gastric and peri-splenic fluid collections, yielding pus. Cultures of all these samples, along with blood and sputum cultures grew Klebsiella pneumoniae. A transthoracic echocardiography was limited but showed very severe tricuspid regurgitation establishing the diagnosis of tricuspid valve endocarditis using modified Duke Criteria. Ophthalmological evaluation was negative for signs of endophthalmitis or retinal emboli.

A string test was done to evaluate for Hypermucoviscous klebsiella strain and was clearly positive (Fig 2).

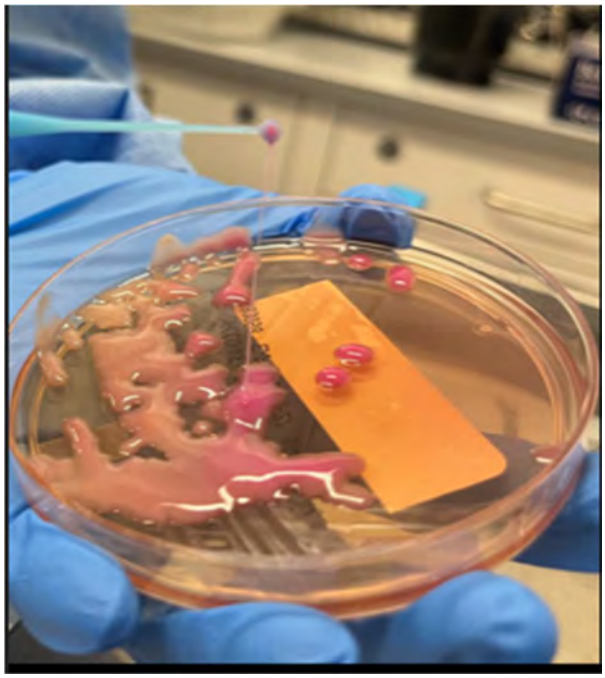


Fig 2. String test. String was more than 10 cm in length (positive test defined as >5 mm)

TREATMENT *If relevant*

Patient received resuscitation with intravenous fluids, insulin drip for DKA and new diagnosis of diabetes. He was diagnosed with shock and started on norepinephrine and empiric vancomycin and piperacillin-tazobactam IV.

Klebsiella pneumoniae was pan-susceptible with an MIC <1 to ceftriaxone (Fig 3). Patient was transitioned to ceftriaxone 2 g iv q24h.

	Klebsiella pneumoniae	
	SELECT MIC RESULTS REPORTED.	SELECT KIRBY BAUER RESULTS REPORTED.
Ampicillin + Sulbactam	8/4 Sensitive	
Cefazolin		Sensitive
Ceftazidime	<=1 Sensitive	
Ceftriaxone	<=1 Sensitive	
Ciprofloxacin	<=0.25 Sensitive	
Gentamicin	<=1 Sensitive	
Levofloxacin	<=0.12 Sensitive	
Piperacillin + Tazobactam	<=4 Sensitive	
Tobramycin	<=1 Sensitive	
Trimethoprim + Sulfamethoxazole	<=1/19 Sensitive	

Fig 3. Antimicrobial susceptibility of the klebsiella pneumoniae isolate

OUTCOME AND FOLLOW-UP

His hospital course was complicated by acute kidney injury requiring renal replacement therapy, limb ischemia, persistent shock leading to death.

DISCUSSION *Include a very brief review of similar published cases*

Metastatic spread is an unusual feature for enteric gram-negative bacilli, particularly in non-immunocompromised. Hypervirulent klebsiella pneumonia HV – also known as hypermucoviscous klebsiella pneumoniae HMV- emerged as an exception for this rule. After first being described in Asian Pacific region. HMV klebsiella is now increasingly recognized globally.

Its clinical features are defined by its ability to cause life threatening, community acquired infections, in immunocompetent and sometimes young hosts, including liver abscess, pneumonia, meningitis, endophthalmitis and endocarditis, many of which were confirmed in our patient.

The characteristics that enhance its virulence and distinguish it from other variants of klebsiella include its thick capsule thus its hypermucoviscous phenotype and immune evasion, along with its increased ability to acquire iron.

Despite that most patients affected by this hypervirulent strain are Asians, HMV klebsiella pneumoniae is now encountered in western countries. Racial distribution might represent a genetic predisposition or simply a geo specific strain acquisition.

Our patient has not left the US for 20 years. A more recent acquisition of the strain versus a chronic enteric colonization is difficult to discern.

Serotyping and molecular testing in this case were not done, but a string test (as shown in Pic 2) was clearly positive, with a thread of more than 10 cm.

Susceptibility of HMV strain to antimicrobials is variable, ranging from pan-susceptible, like in this case, to multidrug resistant.

Increase antibiotic use and emergence of advanced multidrug resistance in strains like the ones we describe will undoubtedly have fearful and devastating morbidity and mortality.

An early recognition of HMV metastatic syndrome is also key factor that should be recognized and should lead to empiric coverage, in the appropriate clinical and epidemiological setting, including coverage for multidrug resistant strains. In our patient, initial imaging was suggestive of metastatic malignancy, though this did not delay appropriate antimicrobial use.

Recognition of this strain, its metastatic spread and its global dissemination might cause a major epidemiological shift that needs to be accounted for when diagnosing and empirically treating infections such as endophthalmitis, meningitis and infective endocarditis where enteric gram-negative bacilli are usually not a common culprit.

REFERENCES

1. Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) Klebsiella pneumoniae: a new and dangerous breed. Virulence. 2013 Feb 15;4(2):107-18.

LEARNING POINTS/TAKE HOME MESSAGES *3-5 bullet points*

- Hypervirulent klebsiella pneumonia causes metastatic infections with extremely high mortality
- It is more common in patients of Asian descent, but its more recent global spread sounds the alarm for potential devastating impact
- Our patient had severe infection suggesting either local spread or that this strain can colonize the GI tract for years before causing its devastating effect

2. Li W, Sun G, Yu Y, Li N, Chen M, Jin R, Jiao Y, Wu H. Increasing occurrence of antimicrobial-resistant hypervirulent (hypermucoviscous) Klebsiella pneumoniae isolates in China. Clinical infectious diseases. 2014 Jan 15;58(2):225-32.
3. Sánchez-López J, García-Caballero A, Navarro-San Francisco C, Quereda C, Ruiz-Garbajosa P, Navas E, Dronda F, Morosini MI, Cantón R, Diez-Aguilar M. Hypermucoviscous Klebsiella pneumoniae: a challenge in community acquired infection. IDCases. 2019 Jan 1;17:e00547.
4. Zhan L, Wang S, Guo Y, Jin Y, Duan J, Hao Z, Lv J, Qi X, Hu L, Chen L, Kreiswirth BN. Outbreak by hypermucoviscous Klebsiella pneumoniae ST11 isolates with carbapenem resistance in a tertiary hospital in China. Frontiers in cellular and infection microbiology. 2017 May 16;7:182.
5. Namikawa H, Oinuma KI, Yamada K, Kaneko Y, Kakeya H, Shuto T. Differences in severity of bacteremia caused by hypermucoviscous and non-hypermucoviscous Klebsiella pneumoniae. International Journal of Antimicrobial Agents. 2023 Feb 28:106767.
6. Walker KA, Miller VL. The intersection of capsule gene expression, hypermucoviscosity and hypervirulence in Klebsiella pneumoniae. Current opinion in microbiology. 2020 Apr 1;54:95-102.

Omar Nasser:

A Case of Possible Acute Refeeding Syndrome after prolonged Fasting: A Rare but Potentially Life-Threatening Diagnosis

Omar Naser MD[1] , Binod KC MBBS[1], and Ilona Chepak MD [1]

Abstract:

Refeeding syndrome is a potentially life-threatening complication that can occur in individuals who have been fasting and are then abruptly re-fed. We present a case of a 42-year-old African American female who initially presented to the Adult Medicine Clinic with acute onset of generalized weakness and red color urine. She had been fasting for 21 days and started eating the day prior to presentation due to religious reasons. In the clinic, the patient was found to be bradycardic in the 40s with intermittently heart rate going to the 80s. BP was 120/80, afebrile, and she appeared very fatigued and ill on examination. EKG showed HR of 83 with frequent PVCs with bigeminy pattern, which was a new finding for her. Due to concern for refeeding syndrome in the setting of bradycardia with EKG changes, the patient was sent to the ED via EMS. Upon evaluation, she was found to have electrolyte abnormalities and metabolic derangements consistent with refeeding syndrome. She was subsequently admitted inpatient and managed with electrolyte replacement and gradual refeeding, with resolution of her symptoms. Prompt recognition and management of refeeding syndrome is crucial to prevent complications and mortality. Treatment includes close monitoring of electrolyte levels, gradual advancement of the diet, and correction of electrolyte abnormalities through intravenous supplementation. It is essential to educate patients on the potential risks of prolonged fasting and the importance of seeking medical attention before embarking on such practices, particularly in those with underlying medical conditions. Health care providers should also be aware of the potential complications of refeeding syndrome and promptly recognize and manage it to optimize patient outcomes.

Vidisha Desai:

Atraumatic Page Kidney After Initiation of Dual Anti-platelet Regimen Post Intracranial Stent Placement

Authors: Vidisha Desai, Devjani Ganesan, Viren Kaul (jishuviren@gmail.com)

Abstract

Page kidney is a rare condition that can cause hypertension due to compression of the renal parenchyma from a hematoma or a mass leading to activation of the renin-angiotensin-aldosterone system (RAAS).[5] The most common cause of Page kidney observed has been secondary to traumatic causes.[4] In this case, we describe a case of atraumatic Page kidney caused by initiation of antiplatelet agents.

A middle-aged woman with a history of hypertension, and intracranial aneurysm presented to the hospital for an elective intervention of the intracranial aneurysm. Post procedure, the patient was placed on ticagrelor and aspirin to prevent thrombosis of the intracranial stent. Immediately after the procedure, she developed profound hypotension, and severe left upper quadrant pain. Computer Tomography (CT) showed a large left perinephric hemorrhage with associated displacement and mass effect upon the left kidney. Due to persistent hypotension despite adequate fluid resuscitation, bedside ultrasound was done which demonstrated rapid enlargement of the peri-renal hematoma prompting emergent embolization of involved renal artery by interventional radiology after discussions with urology to prevent complete nephrectomy. Post embolization, patient was transferred back to the ICU where she rapidly developed severe hypertension requiring initiation of nicardipine drip. This development of uncontrolled hypertension was attributed to Page kidney.

Historically, cases of Page kidney were attributed to sports-related trauma or blunt trauma of the abdomen. Assessment of cases after 1991 demonstrated an etiological evolution towards iatrogenic renal subcapsular hematoma frequently occurring as complications of performing a renal biopsy or lithotripsy. In the past, the definitive therapeutic management was radical nephrectomy. With advent of minimally invasive techniques such as arterial isolation and embolization, CT-guided intervention is often the first line approach in acute situations. Although patients with Page kidney typically present with new onset flank pain and hypertension, it is important to note that our patient's case was unusual as she was initially in hypovolemic shock due to the catastrophic bleeding after initiation of dual-antiplatelet therapy.

Vidisha Desai:

Evaluating the readability of the publicly available information related to ARDS

Authors: Vidisha Desai, Gabriella Primera, Nayab Ahmed, Harvir Singh Gambhir, Viren Kaul

Abstract

As seen during the COVID-19 pandemic, ARDS is a prominent cause of intensive care unit (ICU) admissions and the need for mechanical ventilation.[5] This resulted in increased public awareness of this syndrome and as per the Pew Research Center, 61% American adults look online for health information[1]. We sought to evaluate the accessibility of currently available informational material in terms of readability.

We searched for "ARDS" using a Virtual Private Network (VPN)-enabled google search. To assess the "readability" of a website, we evaluated each webpage using the Flesch-Kincaid Reading Ease score (FRE), the Gunning-Fog Index (GFI), and the International English Language Testing System (IELTS) readability formula, amongst others.[4] We further evaluated components of the prose including paragraph count, word count, letter count and composites of these individual metrics. We used Readable (Added Bytes Ltd.) to acquire these metrics of readability.[3]

The mean FRE score for the included webpages was 41.3 which correlates to a college or "difficult to read" reading level. The mode for FRE was 52.7 which correlates to the 10^{th}-12^{th} grade reading level. To provide granular context on the complexity of the written pages, the mean paragraph count was 8, words per paragraph 34.6, sentences per paragraph 2.13, and words per sentence 14.89. The average reading time per page was 1 minute and 50 seconds.

When evaluating the top publicly available webpages regarding the readability of information on ARDS, we found that the webpages were difficult to read and well above the AMA-recommended sixth-grade reading level.[4] These public resources are not accessible for a large proportion of the American population. The next step in our ongoing research is to better identify what factors drive the readability of these webpages to better inform the creation of future material by healthcare organizations and institutions.

Ashwini K. Ashwath:

A STEMI patient in Refractory Cardiogenic Shock and Complete heart block

Ashwini K. Ashwath, Atika Azhar, Anderson Anuforo, Muhammad Malik, Debanik Chaudhuri.

History and Physical Exam: A 61-year-old lady with hypertension, diabetes mellitus, and Coronary artery disease (CAD) status post percutaneous coronary intervention (PCI) to left anterior descending (LAD) in 2006 presented with cardiogenic shock. ECG showed ST elevation in lead 1, aVL, and ST depression in the precordial and inferior leads. Norepinephrine was started, and cardiac catheterization indicated 100% occlusion in the Distal Left Main (LM) and Left circumflex (LCx), & >90% in the distal LAD.

Interventional Management: To stabilize the refractory cardiogenic shock, an Impella CP device was inserted. PCI was performed and was treated with angioplasty. Due to an enormous thrombus burden, mechanical thrombectomy was performed via Penumbra CAT device, and flow to the LAD was restored. We noted >90% distal LAD stenosis and a ruptured plaque in the proximal LCx with 100% occlusion, both of which were stented and had a TIMI-3 flow distally. Intravascular ultrasound (IVUS) showed good stent expansion and apposition. Despite these efforts, right heart catheterization showed severe cardiogenic shock with a Cardiac Index (CI) of 1.37 L/min/m2. The patient also developed a complete heart block necessitating the insertion of a temporary venous pacemaker. Due to refractory shock, Extracorporeal Membrane oxygenation (ECMO) was started, and the patient survived the acute event.

This case illustrates the principle of instituting mechanical circulatory support early to stabilize refractory cardiogenic shock. Without initial Impella support, the patient could not have undergone the required revascularization, but it was still inadequate, as illustrated above. Hence Mechanical circulatory support was escalated to VA-ECMO, with Impella being left intact for LV venting.

Ashwini K. Ashwath:

Concurrent Intracardiac thrombus and Cerebral venous thrombosis (CVT) despite therapeutic anticoagulation in Acute Promyelocytic Leukemia

Ashwini K. Ashwath, Atika Azhar, Ryan Denley

Background: Thrombotic events in APL are known to occur, but hemorrhagic complications predominate in the literature as they are the leading cause of mortality. Therapeutic all-trans retinoic acid (ATRA) has dramatically improved cure rates in APL, but it may alter the hemostatic balance, increasing hypercoagulability and atypical thromboses.

Aim: Describe rare concurrent thrombotic events in an APL patient undergoing treatment.

Methods: A 28-year-old lady was diagnosed with pulmonary embolism (PE) in the setting of leukopenia. Bone marrow biopsy confirmed APL with t(15;17). She was initiated on ATRA and arsenic trioxide for low-risk disease and received anticoagulation for her PE. During induction, she developed headaches, diplopia, and papilledema. MRI of the brain showed transverse sinus thrombosis requiring urgent mechanical thrombectomy. Days later, she complained of chest pain, prompting CT angiography. A new intracardiac thrombus was seen fixed to the right ventricular wall, which cardiac MRI and echocardiogram confirmed. Due to poor candidacy for thrombolysis or mechanical retrieval, she continued anticoagulation as the primary management.

Results: Intracardiac thrombus and CVT in APL are sparsely reported in the medical literature. We are writing the first case of their coexistence.

Conclusions: Thrombotic events in APL occur in 2-15% of patients and are almost exclusively myocardial infarctions, strokes, or DVT/PE. Sixty percent of these events occur following ATRA therapy. This may be explained by ATRA-mediated IL-1ß, CD2, and CD15 expression leading to leukocytosis, leucoagglutination, tissue damage by microvascular occlusion, and thrombosis. The onset of our patient's symptom suggests her thrombi occurred during anticoagulation for her pulmonary embolism, underscoring APL's potent thrombogenic potential. Patients presenting with acute symptoms during or following ATRA treatment should additionally be evaluated for atypical sites of thrombosis.

Hiba Zafar:

A case of LV thrombus lysis with simultaneous neurologic deficits during bedside sonography Authors: Zafar, Hiba; Russo, Ronald; Weinberg, Andrew

ABSTRACT: A 52-year-old male with history of tobacco use was brought to the hospital after a syncopal episode. The patient was eating prior to being found diaphoretic and confused by his coworkers. During transport to the hospital a 12-lead electrocardiogram (ECG) obtained showed inferolateral ST elevation myocardial infarction (MI) with anterior Q waves. Angiography revealed single vessel coronary artery disease with 100% occlusion to the mid-LAD. Due to plaque morphology and presence of distal collaterals, balloon angioplasty was attempted however no further attempts were made at revascularization due to likely limited benefit. CT Head was obtained for altered mentation with no acute intracranial abnormality. 2D transthoracic echocardiogram (ECHO) revealed a large, highly mobile thrombus on the mid-apical anteroseptal wall, with mid anterior-anteroseptal wall aneurysm with a wide mouth containing the thrombus. The patient began to display acute focal neurological deficits with flaccid quadriparesis, right gaze field cut and aphasia. CTA head and neck and MRI brain were obtained with small infarcts in both cerebellar hemispheres. Patient's neurologic status improved in hours with complete resolution of symptoms prior to discharge. Repeat limited ECHO 2 days after the first reported no visualization of previous thrombus with interval improvement in aneurysm.

While neurologic symptoms have been reported in the presence of left ventricular (LV) thrombus, this is a unique case of neurologic symptom onset with lysis of LV thrombus. During the patient's stroke code, sonography was being completed and lysis was visualized on ECHO (Figure 1). Of note, ECHO transducer frequencies range 1.5-7MHz, while those of EKoSonic (EKOS)endovascular systems are 2MHz. Given known lytic properties of sonographic waves this case may open further discussion regarding the time duration of sonographic imaging of highly mobile LV thrombi

Hiba Zafar:

A rare case of air embolus in the presence of bilateral pulmonary emboli

ABSTRACT Case Presentation: A 70-year-old male with cardiac risk factors, cirrhosis, stage II cholangiocarcinoma, and a right internal jugular port-a-catheter, presented to the hospital following an unwitnessed syncopal episode one day after undergoing a therapeutic paracentesis. On presentation he was hemodynamically unstable and endorsed severe substernal chest pain. Diagnostic work-up revealed large bilateral pulmonary emboli, and large amounts of intravascular gas in the right brachial vein, superior vena cava (SVC), right atrium and ventricle (Figure A). He was immediately placed on supplemental oxygen, given intravenous fluids, and started on vasopressors. He was a poor candidate for mechanical thrombectomy thus tissue plasminogen activator (tPA) was administered, and he was admitted to the medical intensive care unit for further management. Discussion: Venous air emboli occur as rare complications of trauma or intravascular procedures when air or gas enters the vasculature. Symptoms are generally non-specific making them difficult to recognize. In this patient, a central port-a-catheter had been placed two months prior for chemotherapy administration. A central line provides a direct connection between the air and the vasculature. The sub-atmospheric pressures in the SVC, where these lines often terminate, create a pressure gradient conducive to the development of air emboli. Hypovolemic states as seen in cirrhosis and pulmonary emboli) can further magnify this gradient. Interestingly, the presence of a large venous air embolism and concurrent massive bilateral pulmonary emboli, has rarely been previously reported. Caution should be taken in prevention, early detection, and treatment to avoid potentially fatal complications

Ravi B. Singh[1]

Impella versus Intra-Aortic Balloon Pump for Mechanical Circulatory Support in Acute Myocardial Infarction Complicated by Cardiogenic Shock: A Systematic review and Meta-Analysis

Authors: Muhammad Hanif[1], Vikash Jaiswal[2], Shiva Gupta[3], FNU Sundas[4], Ravi B. Singh[1], Debanik Chaudhauri[1]

Affiliations

Department of Internal Medicine, SUNY Upstate Medical University Syracuse, NY, USA.
Department of Research, Larkin Community Hospital, FL, USA
Department of Internal Medicine, KGMC Lucknow, India
Khyber Medical College, Peshawar, Pakistan.

Abstract

Background: Acute myocardial infarction complicated by cardiogenic shock (AMICS) requires mechanical circulatory support, with IABP and Impella being commonly used options. The IABP's survival benefit is uncertain, and guideline recommendations differ. Studies comparing Impella and IABP have yielded mixed results and reported varying complication rates.

Aim: This meta-analysis aims to comprehensively evaluate the effectiveness and safety of Impella versus IABP in AMICS.

Methods: A systematic search was conducted in PubMed, EMBASE, Cochrane, and clincialtrials.gov from inception to April 2023 to identify studies comparing Impella and IABP in AMICS. A meta-analysis was performed to assess the short-term mortality (in-hospital and 30day) as the primary efficacy endpoint, along with major bleeding, limb complications, acute kidney injury (AKI), stroke, and hemolysis as safety endpoints of interest.

Results: A total of 10 studies (2 RCTs, 8 observational) with 6,634 patients were included into the final analysis. No significant difference was found in 30-day mortality (OR=1.03; 95% CI=0.741.42; p=0.87), in-hospital mortality (OR=1.14; 95% CI=0.45-2.85; p=0.79) and all-cause mortality (OR=1.00; 95% CI=0.55-1.81; p=0.99) between Impella and IABP. However, the analysis revealed a higher risk of major bleeding with Impella compared to IABP (OR=2.12; 95% CI=1.323.42; p=0.002) and an increased likelihood of limb complications (OR=3.86; 95% CI=1.57-9.48; p=0.003). There was no significant difference in the incidence of AKI (OR=0.91; 95% CI=0.561.48; p=0.70) and stroke (OR=0.72; 95% CI=0.42-1.24; p=0.24) between the two groups. Notably, the risk of hemolysis was significantly higher in the Impella group (OR=11.35; 95% CI=1.9964.69; p=0.006).

Conclusion: Impella and IABP showed similar short-term mortality, AKI, and stroke rates in AMICS patients. However, Impella was associated with a higher risk of major bleeding, limb complications, and hemolysis.

Ravi B. Singh:

Infective Endocarditis post-Transcatheter edge-to-edge mitral valve repair: A Systematic Review

Authors: Muhammed Hanif[1], Vikash Jaiswal[2], Vibhor Agrawal[3], FNU Sundas[4], Ravi B. Singh[1] , Debanik Chaudhuri[1]

Affiliation

1. Department of Internal Medicine, SUNY Upstate Medical University, Syracuse, NY, USA
2. Department of Cardiovascular Research, Larkin Community Hospital, South Miami, FL, USA
3. Department of Medicine, King George's Medical University, Lucknow, India
4. Khyber Medical College, Peshawar, Pakistan

Abstract

Background: Infective Endocarditis (IE) post-MitraClip procedure has not been well recognized, with very limited reports published to date.

Objective: We aim to systematically evaluate the clinical characteristics, management, outcomes, and prognosis among IE patients after mitral valve repair with MitraClip device.

Methods:

We conducted a systematic literature search in PubMed, Embase, and Scopus from inception till 10th March 2023 by using predefined MESH terms and "AND" and "OR." The following search terms were used: "Infective Endocarditis" AND "Transcatheter mitral valve repair".

Results:

A total of 26 publications describing 29 cases of IE following percutaneous edge-to-edge mitral valve repair were identified. The mean age of the patients was 72.62 ± 12.76 years, of which 62.96% were male. The etiology of MR was mostly functional/secondary in 54.55% of cases, while the mean number of implanted clips was 1.65 ± 0.68 (Mode = 1), and the most common location for MitraClip® implantation was the A2-P2 segment. The mean duration from MitraClip® intervention to readmission with IE was 44.44 ± 57.11 weeks. Echocardiography findings showed severe MR in 70.83% of patients. *Staphylococcus aureus* was the most common infectious organism involved in 56% of cases. Surgical mitral valve replacement with a bioprosthesis was performed in 55.17% of the patients, and 34.48% were managed medically. The most common antibiotic regimen was vancomycin, rifampicin, and gentamycin. Mortality was higher in the medically managed patients than those who underwent surgical MVR (40% vs. 37.5%).

Conclusion: IE post-TEER of the mitral valve is a rare complication but is associated with a higher rate of mortality. Aggressive antibiotic medication and proper prophylaxis during index procedures can be beneficial.

Ravi B. Singh

Procedural Safety of Transcatheter Aortic Valve Replacement with Portico Valve: A Systematic Review

Authors: Muhammad Hanif [1], Vikash Jaiswal[2], Vinay Suresh[3], FNU Sundas[4], Ravi B. Singh[1], Debanik Chaudhuri1

Affiliation:

1. Department of Internal Medicine, SUNY Upstate Medical University, Syracuse, NY, USA.
2. Division of Cardiovascular Research, Larkin Community Hospital, South Miami, Fl, USA. 3. Department of Medicine, King George's Medical University, Lucknow, India
4. Khyber Medical College Peshawar, Pakistan.

Abstract

Background:

The Portico transcathater aortic heart valve is a self-expandable, fully resheathable bioprosthetic valve with a nitinol frame and porcine pericardial sealing cuff. It has been used among symptomatic severe aortic stenosis who are at high or extreme surgical risk. However, till date very few studies has been reported with inconclusive evidence for its post-procedure safety outcomes.

Objective: We aim to evaluate the safety of the Portico transcatheter aortic valve replacement system among patients with aortic stenosis.

Methodology:

We conducted a systematic literature search on PubMed, Embase, and Scopus from inception till 10th April 2023 by using predefined MESH terms using "AND" and "OR." The following search terms were used: "Aortic Stenosis" AND "Transcatheter aortic valve replacement" OR "Portico valve." Finally, descriptive statistics were used to summarize the data in this paper. The mean and standard deviation were adopted to describe continuous variables, whereas frequencies and percentages were used for dichotomous data.

Results:

A total of 7 studies with 2782 patients were included in the analysis. The mean age of patients was 82.3 years, and 54.63% were female. The most common comorbidity was hypertension (65.21%) and diabetes mellitus (26.45%). Among patients of AS with Portico valve implants, 6.47% reported all-cause mortality at a follow-up. Post-procedural outcomes including 30-day mortality (2.32%), cardiovascular mortality (2.37%), stroke (2.23%), myocardial infarction (0.94%), major bleeding (3.97%), major vascular

complications (4.91%), acute kidney injury (AKI) (1.37%), and permanent pacemaker implantations (PPI) in 15.73% patients were reported. Overall, device success was observed in 95.82% of patients.

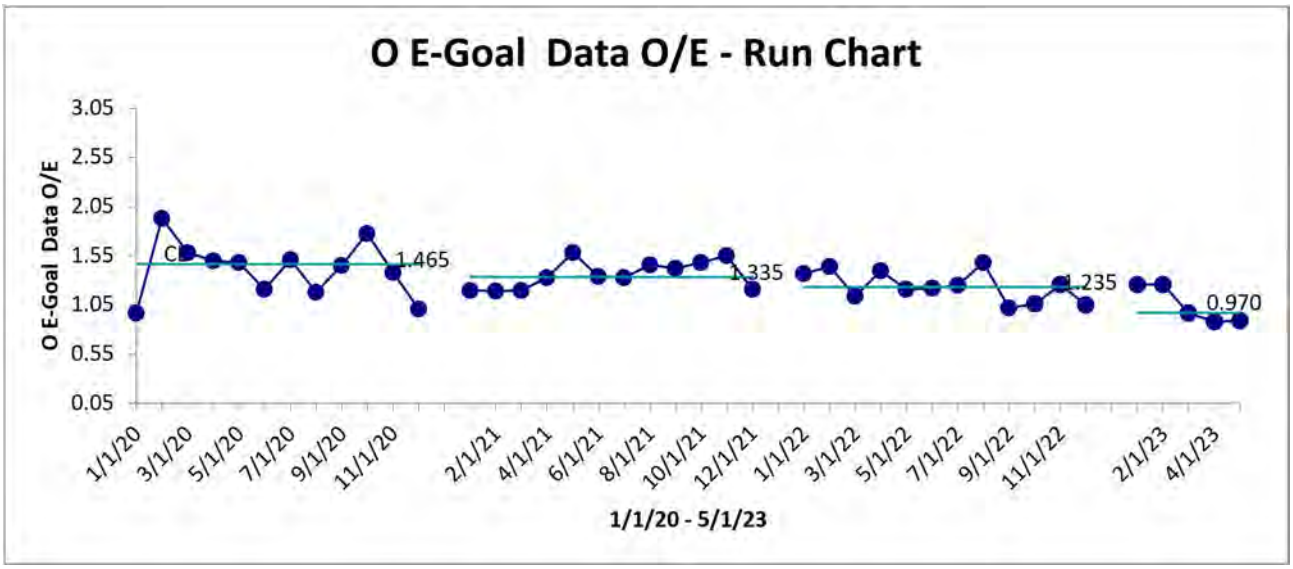
Conclusion: Transcatheter aortic valve replacement with the repositionable Portico valve, a new bioprosthesis, appears to have a low post-procedural mortality rate and other clinical outcomes in high-risk patients with severe AS.

H. S. Gambhir:

Think Sepsis, STOP Sepsis: Save Lives

Background: Sepsis is a leading cause of in-hospital mortality in the United States, associated with approximately 250,000 deaths annually [1,2]. AdopEng early goal-directed therapy, which involves the early idenEficaEon of at-risk paEents and prompt treatment with anEbioEcs, hemodynamic opEmizaEon, and appropriate supporEve care, has contributed significantly to overall improved outcomes [2]. Sepsis was the leading cause of death at Upstate and the Department of Medicine in 2019. A sepsis campaign was iniEated as a quality and process improvement from September 2020 to Ell today to increase sepsis awareness, early recogniEon, and treatment of sepsis syndrome. The campaign had mulEple levels of intervenEon and collaboraEon with teams. The primary goal: increase the uElizaEon of standardized tools (sepsis order and sepsis note) when sepsis is diagnosed, and the secondary goal is to evaluate the impact on mortality and length of stay.

Results: The primary goal was met with increased uElizaEon of sepsis orders and notes from 13 % in 2019 to 30, 35, 45, and 60 % in 2020,2021,2022 and 2023, respecEvely. In addiEon, Sepsisrelated mortality rates decreased within the Department of Medicine. Our quality improvement iniEaEve improved the sepsis mortality observed to the expected (O/E) raEo from 1.50 in 2019 to 1.465, 1.335, 1.235, and 0.970 in 2020, 2021, 2022, and 2023 respecEvely. Conclusion: The primary goal of the sepsis campaign was met, and the intervenEons demonstrated an improvement in hospital-related sepsis mortality. To the current, sepsis is one of the top 10 diagnoses at SUNY Upstate Medical University and in the Department of Medicine, saving lives. This is a paradigm shi^ in the quality of care provided to paEents with diagnoses of Sepsis at SUNY Upstate and in the Department of Medicine.



References 1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS. The third internaEonal consensus definiEons for sepsis and sepEc shock (Sepsis-3). Jama. 2016 Feb 23;315(8):801-10. 2. Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Iwashyna TJ, Kadri SS, Angus DC, Danner RL, Fiore AE, Jernigan JA. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. Jama. 2017 Oct 3;318(13):1241-9.

H.S. Gambhir;

The baking of quality into Internal Medicine Residency Program: A Transformation.

Many healthcare institutes follow quality metrics, i.e. CMS, Vizient, Leap Frog, US News, etc. All of these have metrics to monitor clinical performance and outcomes. Some are publicly reported, and others are utilized for internal improvement. These directly impact star ratings and compensation. All have these organization bodies measure domains for quality improvement and patient safety [1]. The Vizient Quality and Accountability scorecard is a tool that measures academic medical centers' (AMCs) clinical performance year over year, focusing on quality and safety in comparison with similar hospitals while targeting specific opportunities for improvement. The Vizient quality domains include Mortality, Efficiency, Effectiveness, Equity, Patient experience, and Patient safety [2]. In an academic setting, the frontline healthcare providers are resident physicians.

As per the ACGME, all residency programs must integrate a curriculum with resident participation in patient safety and quality improvement initiatives, ultimately improving the quality of care and service provided to patients. Engaging residents in the institutional or departmental quality metrics is also challenging[3]. In the medicine department, we developed a longitudinal curriculum to build foundations of quality improvement and engage residents from the beginning of their journey in internal

medicine residency. Our curriculum has a stepwise and structured approach. In addition, all curriculum integrates & aligns with the institutional and departmental quality initiatives within the residency program.

Conclusion

Through the longitudinal survey results, we identified that awareness and education to residents through this rotation promoted engagement in the quality improvement initiatives of the department. This is a symbiotic approach for fortifying our residents' skillsets while aligning with institutional and national quality improvement metrics benefiting the healthcare system. This curriculum serves as a WIN-WIN situation for our patients, learners, department, and institution.

References

1. Sinaiko AD, Eastman D, Rosenthal MB. How report cards on physicians, physician groups, and hospitals can have greater impact on consumer choices. Health Aff (Millwood). 2012 Mar;31(3):602-11. doi: 10.1377/hlthaff.2011.1197. PMID: 22392672.
2. Bernard A. Birnbaum, MD, Quality Leadership. (n.d.). https://vizientincdelivery.sitecorecontenthub.cloud/api/public/content/3c34c949b89e4120b91d4023e065c885
3. Bodenheimer T, Dickinson WP, Kong M. Quality Improvement Models in Residency Programs.
   J Grad Med Educ. 2019 Feb;11(1):15-17. doi: 10.4300/JGME-D-18-00556.1. PMID: 30805091; PMCID: PMC6375330.

QI Curriculum

IM RESIDENCY

PGY 1

QI OP WORSHOP

Institute for Healthcare Improvement

Flipped Classroom

QI Activity

Rotation X

SWAT Team QI

Basic Certification in Quality

Resident Quality Council

QUICKSTARTER

PGY 2

M & M

RCA : DT & VA

OP : Case review

Resident Quality Council

QUICKSTARTER

PGY 3

Rotation X

RCA

CDI

Voice Of Patients

GEMBA WALK: CAUTI, CLABSI

Quality Dashboard

MD/RN Communication

Pharmacy QI

Resident Quality Council

QUICKSTARTER

QI Distinction Award
Micro-crendentialing

ENDOCRNOLOGY

Akshata Chaugule[1]

Predictors of Readmission and Mortality in Adults with Diabetes or Stress Hyperglycemia after Initial Hospitalization for COVID-19.

A. Chaugule[1], K. Howard[2], D.C. Simonson[3], M.E. McDonnell[3], R. Garg[4], G. Gopalakrishnan[2], J. Mitri[5], J. Lebastchi[2], N.E. Palermo[3], G. Westcott[5], R.S. Weinstock[1] for the CovidEastDM Consortium

[1]SUNY Upstate Medical University, Syracuse, NY, [2]Brown University, Rhode Island Hospital, Providence, RI, [3]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [4]University of Miami, Miller School of Medicine, Miami, FL*, [5]Joslin Diabetes Center and Harvard Medical School, Boston, MA

*Current affiliation: Harbor-UCLA Medical Center, Torrance, CA

Our consortium previously reported that older age, elevated glycemic gap, higher BMI and DKA on admission predicted mortality in adults with diabetes or stress hyperglycemia (glucose >180 mg/dl twice in 24 hrs) admitted with COVID-19 from March 2020 - February 2021 to 5 university hospitals. Here we examine those from this cohort who were readmitted (19.4%) after their initial discharge (Table). Of those readmitted 90.3% were readmitted within 30 days [median (IQR) 4 (0,14) days]. Older age, lower eGFR, comorbidities, ICU admission, mechanical ventilation, DKA and longer length of stay during the initial hospitalization were associated with readmission. Higher A1c and admission glucose, diagnosed diabetes, glycemic gap and BMI did not predict increased risk of readmission. Hispanics were less likely to be readmitted. Mortality during readmission was 8.0%. Those who died were older than those who survived (74.9±9.5 vs 65.2±14.4 yrs, p= 0.002) and were more likely to have had DKA during the first hospitalization (p< 0.001). Mortality analyses were limited by the small number of deaths (n=23). In conclusion, in adults with diabetes or stress hyperglycemia hospitalized with COVID-19, older age and non-glycemic comorbidities were associated with the risk of readmission, while glycemic gap and higher A1c were not. These results are important for guiding treatment strategies.

Initial Admission Total (n=1502)	Readmitted (n=292) % or mean (SD)	Not readmitted (n=1210) % or mean (SD)	*p* *
Age (yrs)	66.0 (14.2)	63.8 (14.5)	0.018
Gender (% male)	46.9 %	52.6 %	0.083
Race			ns
White	56.9 %	50.6 %	
Black	15.8 %	19.8 %	
Asian	2.7 %	3.1 %	
Other/Missing	24.6 %	26.5 %	
Hispanic	22.0 %	31.7 %	0.001

BMI (kg/m^2)	31.0 (7.6)	31.7 (7.9)	ns
ICU admission	36.3 %	30.2 %	0.045
Mechanical ventilation	26.7 %	12.5 %	< 0.001
Diagnosed diabetes	88.0 %	92.8 %	0.007
Any diabetes medication	54.5 %	49.2 %	ns
HbA1c (%)	7.70 (1.96)	8.22 (2.30)	<0.001
DKA	19.1 %	12.8 %	0.019
Admission glucose (mg/dl)	191.2 (106.1)	217.2 (133.7)	0.002
Glycemic gap (mg/dl)	16.5 (89.7)	27.5 (111.2)	ns
Any comorbidity	80.5 %	75.5 %	0.069
Length of stay (days) – median (IQR)	8 (4, 13)	6 (4, 11)	0.005
eGFR (ml/1.73m^2/ min)	52.6 (29.4)	59.8 (29.1)	0.001

* t-test for continuous variables, chi-square for categorical variables, Wilcoxon rank sum test for medians (IQR)

GASTROENTEROLOGY

Aloysius Madhock:

Cancer-specific survival in non-mucinous appendiceal adenocarcinomas after local resection versus right hemicolectomy: A Surveillance, Epidemiology, and End Results database study.

Aloysius M, Nikumbh T, Singh A, Shah N, Wang Y, **Aswath G, John S**, Cheryala M, Goyal H.

Surgery. 2023 Jul 13:S0039-6060(23)00321-5. doi: 10.1016/j.surg.2023.05.026. Online ahead of print.
PMID: 37453862

Background: Adenocarcinomas of the appendix are rare cancers for which no National Comprehensive Cancer Network guidelines exist, and for patients who undergo resection with curative intent, there is a paucity of data on prognostic factors affecting long-term cancer-specific survival. We aimed to compare the cancer-specific survival outcomes in adult patients with appendiceal non-mucinous adenocarcinoma undergoing either local resection versus right hemicolectomy.

Methods: This was a retrospective study from the National Cancer Institute Surveillance, Epidemiology, and End Results of patients who underwent curative resection over a 15-year period (2004-2019) for primary appendiceal adenocarcinoma. Out of 16,699 patients, 14,945 were excluded (exclusion criteria were non-adenocarcinoma histological types and patients with regional or distant metastasis as per National Cancer Institute Surveillance, Epidemiology, and End Results stage). Effects of factors (age, race, tumor biology [mucinous versus non-mucinous tumors], the extent of resection of the primary lesion, and lymph nodes) on cancer-specific long-term survival were studied. Survival analysis was performed using the Kaplan-Meier method. Survival outcomes were reported as mean survival (months).

Results: Of 1,754 patients, 827 (47.1%) were women, and 927 (52.1%) were men. The mean age in years (± standard deviation)was 62.43 ± 14.3. The racial distribution was as follows: Black 237 (13.5%), White 1,398 (79.7%), and Other 119 (6.8%). A total of 771 (44.6%) underwent local resection (appendectomy or segmental resection of colon without lymph node resection), and 983 (55.4%) underwent hemicolectomy with lymph node resection. Favorable survival prognosticators were age <50 years, White race, and well-differentiated histology. Patients with mucinous tumors experienced better survival. Patients who underwent right hemicolectomy with lymph node resection experienced better survival than those with an appendectomy or segmental colonic resection for non-mucinous tumors rather than mucinous tumors.

Conclusion: We report novel demographic, tumor-related, and operative prognostic factors impacting long-term cancer-specific survival in patients who undergo resection for appendiceal adenocarcinoma. The extent of resection of the primary lesion with draining lymph nodes determines long-term cancer-specific survival in non-mucinous appendiceal adenocarcinomas.

Aloysius Madhock

Fibrolamellar hepatocellular carcinoma: An epidemiologic and 5-year cancer survival assessment based off SEER data.

Aloysius MM, Iskander P, Ahmed K, Asija U, Mohammed E, Iskander A, Shah NJ, Goyal H, Khurana V, Simin N, **Aswath G, John S.**

Clin Res Hepatol Gastroenterol. 2023 Jun 10;47(7):102162. doi: 10.1016/j.clinre.2023.102162. Online ahead of print. PMID: 37307948

The fibrolamellar variant of hepatocellular carcinoma makes up a small percentage of liver tumors. Despite being a subset, it has been noted in the literature to have variations in terms of its epidemiology and intervention recommendations. Using the Surveillance, Epidemiology, and End Results database, 339 cases from 1988 to 2016 were studied. Favorable prognostic epidemiological factors included male sex, younger ages, and white race. Those who underwent any lymph node resection (combined with liver resection) did better than those without lymph node resection; chemotherapy proved beneficial for those where surgery was contraindicated. To our knowledge, this report is the largest conglomerate dataset analyzing prognostic profiles and treatment strategies for fibrolamellar hepatocellular carcinoma.

Aloysius Madhock:

Demographic profile, management, and survival of primary Gastrointestinal Kaposi Sarcoma: A USA Nationwide SEER-based study.

Shah NJ, Aloysius MM, Bhanat E, Gupta S, **Savio J, Aswath G,** Schafer DC, Goyal H.

Cancer Epidemiol. 2022 Oct 10;81:102277. doi: 10.1016/j.canep.2022.102277. Online ahead of print.PMID: 36228566

Kaposi Sarcoma (KS) is a Human Herpes Virus-8 (HHV-8) associated angio-proliferative disorder commonly seen in patients with HIV. It most commonly involves the skin as classic purple lesions but occasionally involves the gastrointestinal (GI) tract. To date, published data is scarce on primary GI KS. Using a national database, this study analyzes the incidence, demographics, and survival of primary GI KS. We conducted a retrospective analysis (1975–2019) on biopsy-proven primary GI KS cases from 17 registries from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. A total of 685 patients with GI KS were identified. Female gender, Non-Hispanic Asian or Pacific Islander (NHAPI), married marital status, and large bowel site-specific primary KS to have better overall survival. Luminal gastrointestinal KS was more frequent (84.96%) than solid organ involvement (3.07% of all cases). This study is the most extensive population-based study about the epidemiological and survival data of patients with primary GI KS, revealing GI KS to be a young male disease with the best outcomes in extraintestinal GI KS.

Aloysius Madhock:

Epidemiology and outcomes of gastrointestinal mucosal melanomas: a national database analysis.

Shah NJ, Aloysius MM, Bhanat E, Gupta S, **Aswath G, John S**, Tang SJ, Goyal H.

BMC Gastroenterol. 2022 Apr 9;22(1):178. doi: 10.1186/s12876-022-02254-5.PMID: 35397529

Aim: Gastrointestinal malignant melanoma is a rare mucosal melanoma (MM). Other MM include the respiratory and the genitourinary tract. All mucosal melanomas have a poor prognosis when compared to cutaneous melanomas. Ano-rectal melanomas are by far the most common and most studied gastrointestinal MM. Large-scale clinical data is lacking due to the rarity of the disease. We aim to analyze epidemiology and survival of the Gastrointestinal (G.I.) MM over 45 years using a national database.

Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried to identify patients with biopsy-proven G.I. Melanomas. We selected tumor site, intervention, and survival information for oncology codes as per the international classification of diseases. Survival analysis was performed using the SPSS v 27 ® IBM software.

Results: Of the 1105 biopsy-proven confirmed cases of primary G.I. melanoma's, 191 (17.3%) received chemotherapy (C.T.), 202 (18.3%) received radiotherapy (R.T.), 63 (5.7%) received both C.T and R.T., while 684 (61.9%) of the population received surgery alone or combined with C.T. and/or R.T. Statistically significant improvement in survival was noted in all treatment strategies that utilized surgery and also when site-specific MM cohorts underwent a surgical approach with or without C.T and/or R.T.

Conclusion: This is the most extensive study reporting epidemiological and survival data of treatment strategy outcomes of primary G.I. mucosal melanoma elucidating best overall survival with a management strategy involving surgical intervention.

Ahmad Nawaz:

NATIONAL PATTERNS AND SHIFTS IN UTILIZATION OF ESOPHAGEAL STENTS: INSIGHTS FROM NATIONAL INPATIENT SAMPLE DATABASE 2016 TO 2020

Ahmad Nawaz[1], AbdelKader Chaar[2], Shanti Patel[2], **Rabia Rizwan**[2], Fatima Khalid[3], Dhruv Mehta[4]

[1] SUNY Upstate university, [2] Yale University School of Medicine, [3] FMH College of Medicine and Dentistry
[4] UT Health San Antonio

Introduction

Esophageal stents (ES) are extensively used for palliating dysphagia from malignant obstruction. They are increasingly being used in the management of esophageal perforation and benign strictures from a variety of causes. Our study aims to analyze national patterns and shifts in utilization of ES focusing on both benign and malignant causes. Additionally, we also investigated trends in systemic complications associated with hospitalizations requiring ES.

Methods

A retrospective cohort study was conducted using the National Inpatient Sample (NIS) database from 2016 to 2020. All adult patients that require endoscopic placement of ES were included. The Cochrane-Armitage trend test was used to assess statistical significance in the number of hospital discharges, demographics and systemic compilations over the study period.

Results

We identified an increase in hospitalizations requiring ES for benign etiology as compared to malignant etiology, but the trend was not statistically significantly. There was a significant increase in hospitalizations requiring ES for esophageal perforation as seen in the Figure 1 (27.45% in 2016 to 46.05% in 2020; p=0.008). From 2016 to 2020, an increased rate of systemic complications was noted in the patients that were admitted requiring ES; cardiac complications (10.78% in 2016 to 36.84% in 2020; p=0.001), pulmonary complications (44.12% in 2016 to 59.21% in 2020; p=0.040), gastrointestinal (GI) complications (28.43% in 2016 to 43.42% in 2020; p=0.029) and infectious disease (ID) complications (35.29% in 2016 to 50.00% in 2020; p=0.034).

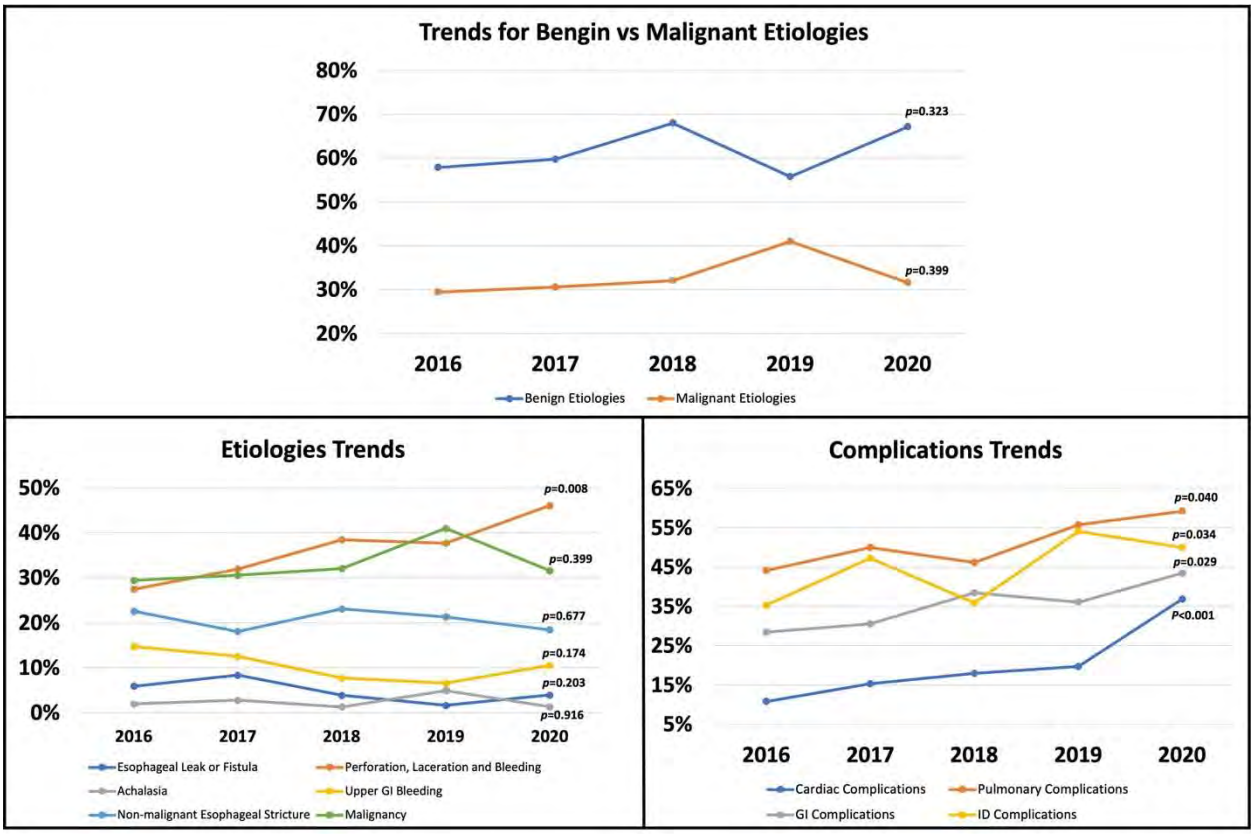
Discussion

We observed a trend showing increase utilization of ES for benign etiologies, most significantly for esophageal perforation, laceration and bleeding. We also noticed a significant increase in pulmonary, GI, cardiac and ID complications during hospital admissions requiring ES. This increased rate in systemic complications need further research as to clear out whether hospitalized patients that required ES were more morbid or rate of complications for ES have increased.

5-year trend of hospitalizations in patients that required Esophageal Stent.

	2016	2017	2018	2019	2020	p-value
Age (mean)	60.86	60.27	63.00	60.59	61.75	
Male, %	61.76	58.33	57.69	62.30	65.79	0.849
Race, %						0.563
White	77.42	73.77	72.37	76.27	76.71	
Black	16.13	9.84	7.89	10.17	10.96	
Hispanic	5.38	11.48	10.53	6.78	10.96	
Hospital region, %						0.359
Northeast	17.65	22.22	23.08	29.51	11.84	
Midwest	28.43	31.94	23.08	24.59	30.26	
South	35.29	23.61	26.92	21.31	34.21	
West	18.63	22.22	26.92	24.59	23.68	
Hospital location and teaching status, %						0.019
Rural	3.92	4.17	0.00	0.00	1.32	
Urban nonteachting	15.69	4.17	19.23	6.56	9.21	
Urban teaching	80.39	91.67	80.77	93.44	89.47	
Median household income, %						0.685
Quartile 1	36.00	22.54	26.92	20.00	24.32	
Quartile 2	22.00	29.58	32.05	30.00	28.38	
Quartile 3	25.00	22.54	23.08	25.00	24.32	
Quartile 4	17.00	25.35	17.95	25.00	22.97	
Etiology, %						
Malignancy	29.41	30.56	32.05	40.98	31.58	0.399
Perforation, Laceration and Bleeding	27.45	31.94	38.46	37.70	46.05	0.008

Non-malignant Esophageal Stricture	22.55	18.06	23.08	21.31	18.42	0.677
Upper GI Bleeding	14.71	12.50	7.69	6.56	10.53	0.174
Esophageal Leak or Fistula	5.88	8.33	3.85	1.64	3.95	0.203
Achalasia	1.96	2.78	1.28	4.92	1.32	0.916
Systemic Complications, %						
Pulmonary Complications	44.12	50.00	46.15	55.74	59.21	0.040
GI Complications	28.43	30.56	38.46	36.07	43.42	0.029
ID Complications	35.29	47.22	35.90	54.10	50.00	0.034
Cardiac Complications	10.78	15.28	17.95	19.67	36.84	0.001



Graph: 5-year trend of etiology and complications of patients that required ES during hospitalization.

Ahmad Nawaz:

Prevalence of Depression Is Higher in Irritable Bowel Syndrome Compared to Chronic GI and Non-GI Disorders

Ahmad Nawaz1, AbdelKader Chaar2, Shanti Patel2, Rabia Rizwan2, Badr Al Bawardy2,3

1 SUNY Upstate university, 2 Yale University School of Medicine, 3 King Faisal Specialist Hospital and **Research Center**

Introduction

Irritable bowel syndrome (IBS) is a chronic multifactorial gastrointestinal condition that substantially affects the quality of life. IBS has been associated with a high prevalence of psychological disorders including depression. In this study, we investigated the prevalence of depression IBS compared to chronic GI and non-GI disorders.

Methods

We utilized the national inpatient sample (2018- 2019) to calculate the rate of depression among adult pts with a history of IBS and different chronic disorders. ICD-10 codes were used to identify pts with history of IBS, depression, and different chronic conditions. Using multivariate logistic regression, we assessed the odds of having a co-diagnosis of depression in IBS pts compared to other chronic disorders commonly associated with depression. We also assessed odds of having a co-diagnosis of depression in IBS pts compared to other chronic disorders after excluding pts with co-diagnosis of fibromyalgia, chronic pain syndrome and/or anxiety.

Results

The analysis included 632,570 pts with a diagnosis of IBS; 29.86% of them had a co-diagnosis of depression. IBS pts who had co-diagnosis of depression were mostly females (84.7%) and mean age was 60.48 +/- 17.34 years. The prevalence of depression in the general population without IBS was 14.05%. IBS pts had more than double the chances of having a diagnosis of depression when compared to the general population (OR 2.23, 95% CI 2.19-2.26; p< 0.001). When compared to other chronic disorders, IBS pts had higher odds of having depression than those with congestive heart failure (OR 1.72, 95% CI 1.68-1.75; p< 0.001), chronic ischemic heart disease (OR 1.59, 95% CI 1.56-1.62; p< 0.001), diabetes (OR 1.64, 95% CI 1.61-1.66; p< 0.001), end-stage kidney disease on dialysis (OR 1.98, 95% CI 1.93-2.03; p< 0.001), HIV (OR 1.46, 95% CI 1.40-1.52; p< 0.001), IBD (OR 1.74, 95% CI 1.70-1.78; p< 0.001), leukemia (OR 2.22, 95% CI 2.14-2.29; p< 0.001), metastatic cancer (OR 1.49, 95% CI 1.42-1.55; p< 0.001), multiple sclerosis (OR 1.17, 95% CI 1.14-1.20; p< 0.001) and osteoarthritis ((OR 1.28, 95% CI 1.25-1.30; p< 0.001). After excluding pts with co-diagnosis of fibromyalgia, anxiety and chronic pain syndrome, IBS pts still had higher odds of having depression as compared to other chronic diseases (except for alcohol-related disorders and MS).

Discussion. The prevalence of depression in IBS is high compared to other chronic medical disorders. Depression symptomatology should be systematically checked in IBS pts.

Depression rates among patients with IBS and different chronic conditions				
Population	Prevalence of depression	Adjusted Odds Ratio#* [Risk of depression in IBS compared to different chronic conditions]	95% CI	p-value
IBS	29.86%	--	--	--
Congestive heart failure	13.99%	1.72	1.68 - 1.75	< 0.001
Chronic ischemic heart disease	14.33%	1.59	1.56 - 1.62	< 0.001
Diabetes	15.38%	1.64	1.61 - 1.66	< 0.001
End-stage kidney disease on dialysis	12.90%	1.98	1.93 -2.03	< 0.001
Inflammatory bowel disease	18.15%	1.74	1.70 - 1.78	< 0.001
Osteoarthritis	19.27%	1.28	1.25 - 1.30	< 0.001
HIV	17.49%	1.46	1.40 - 1.52	< 0.001
Leukemia	13.29%	2.22	2.14 - 2.29	< 0.001
Lymphoma	12.38%	2.42	2.35 - 2.50	< 0.001
Metastatic cancer	11.95%	2.50	2.44 - 2.56	< 0.001
Obesity	17.34%	1.59	1.56 - 1.62	< 0.001
Alcohol-related disorders	26.25%	0.91	0.89 - 0.93	< 0.001
Smoking	19.71%	1.47	1.45 - 1.50	< 0.001
Multiple sclerosis	25.98%	1.17	1.14 - 1.20	< 0.001
Fibromyalgia	35.94%	0.76	0.74 - 0.77	< 0.001
Depression rates among patients with IBS and different chronic conditions after excluding patients with co-diagnosis of fibromyalgia, chronic pain syndrome and anxiety				
IBS	18.06%	--	--	--
Congestive heart failure	9.49%	1.49	1.45 - 1.53	< 0.001

Chronic ischemic heart disease	9.66%	1.42	1.38 - 1.45	< 0.001
Diabetes	10.51%	1.35	1.31 - 1.38	< 0.001
End-stage kidney disease on dialysis	9.18%	1.59	1.55 -1.64	< 0.001
Inflammatory bowel disease	10.72%	1.63	1.57 - 1.68	< 0.001
Osteoarthritis	12.08%	1.27	1.24 - 1.30	< 0.001
HIV	13.24%	1.07	1.01 - 1.13	0.011
Leukemia	13.29%	2.22	2.14 - 2.29	< 0.001
Lymphoma	8.17%	2.09	2.01 - 2.18	< 0.001
Metastatic cancer	8.76%	1.93	1.85 - 2.01	0.033
Obesity	10.96%	1.38	1.34 - 1.41	< 0.001
Alcohol-related disorders	17.74%	0.78	0.76 - 0.80	< 0.001
Smoking	12.39%	1.37	1.33 - 1.40	< 0.001
Multiple sclerosis	18.22%	0.93	0.90 – 0.97	0.016

[#] Multivariate logistic regression after adjusting for age, gender, and race. The chronic condition is the reference.

[*] Patients who had both IBS and the specific chronic disease together were excluded.

Ahmad Nawaz:

OBESITY AND MORBID OBESITY IS ASSOCIATED WITH AN INCREASED RISK OF MORTALITY IN PATIENTS WITH COLON ISCHEMIA

Ahmad Nawaz, Abdelkader Chaar, Rabia Rizwan, Karthik Gnanapandithan, Abdul Q. Bhutta, Adil S. Bhutta, Muhammad Sohail Mansoor, Marc Fenster, Olga C. Aroniadis, Savio John, Paul Feuerstadt

Introduction Colon Ischemia (CI) is the most common ischemic injury to the gastrointestinal tract and obesity is a rapidly growing global health concern with considerable impact on life expectancy. The impact of obesity on outcomes in patients(pt) with CI is, however, unknown. We hypothesize that CI pts with obesity will have worse outcomes compared with those without obesity.

Methods We conducted a multicenter retrospective cohort study of consecutive inpatients with biopsy-proven CI admitted between 2005 and 2019 to Yale- New Haven Health Hospital, Montefiore Medical Center, Weiler Medical Center and SUNY- Upstate Medical Center. For each pt, we recorded a wide range of factors including the ACG guideline severity scoring system. Pts were divided into two cohorts: CI pts with obesity **(CI-O, BMI ≥30)** and pts who were not obese **(CI-NO, BMI < 30).** Primary outcomes included 30- and 90-day colectomy and mortality. Secondary outcomes included length of hospital stay (LOS), recurrence of CI, readmission (30- and 90-day) and segment of colon involved. The obesity cohort was further divided and compared based upon morbid obesity (**CI-MO, BMI ≥40**) and non-morbidly obese status (**CI-NMO, BMI < 40**). Multivariate logistic regression was performed adjusting for age, gender, race, Charlson Comorbidity Index (CCI), location and the severity of CI. **Results** 835 pts were identified with biopsy- proven CI, of which, 278 and 557 were CI-O and CI-NO, respectively. CI-O pts were more often woman with higher frequencies of coronary artery disease, diabetes mellitus (DM) and hypertension (Table 1). There were no differences between CI-O and CI-NO pts when considering ACG severity scoring, colonic segmental distribution, 30- and 90-day readmis- sion, recurrence, colectomy, or mortality. When adjusting for age, gender, race, location, colonic distribution, CCI and severity, pts with CI-O were at greater risk for 90-day mortality [OR 2.9 (95% CI: 1.2-6.5), p<0.011] than CI-NO pts. 45 and 789 pts were classified as CI-MO and CI-NMO, respectively. CI-MO pts were more often younger with higher frequen- cies of atrial fibrillation, DM and hypertension, but with a lower frequency of peripheral vascular disease compared with CI-NMO pts (Table 2). When adjusting for age, gender, race, location, distribution, CCI and severity, CI-MO pts were at higher risk for 30-day mortality [(OR 7.8 (95% CI: 2.0-30.1), p=0.003] and 90-day mortality [OR 4.7 (95% CI: 1.2-17.3), p=0.019] compared with CI-NMO pts.

Conclusion CI pts with obesity have increased mortality compared with those who are non-obese after confounding for multiple factors. Obese pts with CI and BMI ≥30 have a 2.9 OR for 90-day mortality, while those with a BMI≥40 have an OR of 7.8 for 30-d and 4.7 for 90-d mortality. Further research is needed to best tand the pathophysiologic mechanisms for these worsened outcomes.

Table 1: Baseline demographics, clinical characteristics, and outcomes of patients in CI-O and CI-NO groups

Abbreviations: CI, Colon Ischemia; ICU, Intensive Care Unit

Parameter	CI-O (n=278)	CI-NO (n=557)	*p* value
Demographics			
Age (median, (IQR))	**68 (59-75)**	**72 (62-82)**	**≤0.001**
Females, n (%)	**214 (76.9)**	**393 (70.5)**	**0.050**
Medical comorbidities			
Atrial Fibrillation, n (%)	45 (16.9)	79 (15.0)	0.487
Cerebral Vascular Disease, n (%)	28 (10.1)	65 (11.6)	0.522
Coronary Artery Disease, n (%)	**96 (34.9)**	**154 (27.8)**	**0.036**
Diabetes Mellitus, n (%)	**114 (41.3)**	**135 (24.2)**	**≤0.001**
Hypertension, n (%)	**227 (82.2)**	**410 (73.6)**	**0.006**
Peripheral Vascular Disease, n (%)	18 (6.5)	53 (9.5)	0.145
Bowel involvement			
Small bowel involvement, n (%)	9 (5.4)	24 (6.8)	0.544
Pancolitis, n (%)	9 (3.6)	24 (5.0)	0.393
Any right colon involvement, n (%)	57 (26.2)	95 (24.9)	0.719
Right colon only, n (%)	39 (17.8)	67 (17.4)	0.880
CI severity			
Mild/Moderate, n (%)	132 (48.1)	282 (50.9)	**0.445**
Severe, n (%)	142 (51.8)	271 (49.0)	
Charlson Comorbidity Index, median (IQR)	5 (3-7)	4.5 (3-7)	0.144
ICU requirement, n (%)	68 (25.1)	111 (20.4)	0.121
Outcomes			
Length of stay (mean, (SD))	3 (1-7)	3 (1-6)	0.490
30-day readmission, n (%)	29 (10.5)	59 (10.6)	0.990
90-day readmission, n (%)	61 (22.2)	107 (19.2)	0.309
30-day recurrence of CI, n (%)	3 (1.0)	14 (2.5)	0.169
90-day recurrence of CI, n (%)	9 (3.2)	28 (5.0)	0.240
30-day colectomy, n (%)	37 (13.4)	55 (10.0)	0.137
90-day colectomy, n (%)	33 (12.0)	53 (9.6)	0.299
30-day mortality, n (%)	14 (5.1)	22 (3.9)	0.453
90-day mortality, n (%)	23 (8.4)	29 (5.2)	0.081
	OR* (CI-O vs CI-NO)	**95% C.I. of OR**	**Adjusted** *p* value**
30-day readmission	0.96	[0.58 – 1.59]	0.899
90-day readmission	1.15	[0.78 – 1.69]	0.478
30-day recurrence of CI	0.599	[0.15 – 2.25]	0.449
90-day recurrence of CI	0.67	[0.26 - 1.69]	0.397
30-day colectomy	1.50	[0.77 – 2.90]	0.223
90-day colectomy	1.44	[0.72 - 2.87]	0.290
30-day mortality	1.72	[0.68 – 4.38]	0.250
90-day mortality	**2.90**	**[1.21 – 6.59]**	**0.011**

* CI-NO is the reference

**Multivariate logistic regression for the outcomes of CI-O compared to CI-NO. Analysis adjusted for age, gender, race, Charlson co-morbidity index, location, and CI severity

Ahmed Nawaz:

There Is No Difference in Frequency or Outcome of Colon Ischemia Based Upon the Season of Presentation

Ahmad Nawaz, MD1, Rabia Rizwan, MD1, Abdelkader Chaar, MD1, Houssam Alnahhas, MD, MPH2, Karthik Gnanapandithan, MD3, Muhammad Sohail Mansoor, MD4, Abdul Qadir Bhutta, MD5, Adil Bhutta, MD6, Marc Fenster, MD7, Olga Aroniadis, MD, MSc, FACG8, Savio John, MD9, Lawrence Brandt, MD, MACG10, Paul Feuerstadt, MD, FACG11.
1Yale University School of Medicine, New Haven, CT; 2Syria Public Health Network, London, England, United Kingdom; 3Mayo Clinic Florida, Jacksonville, FL; 4GI Specialists of Georgia, Marietta, GA; 5SUNY Upstate Syracuse University Hospital, Syracuse, NY; 6Yale New Haven Health, Hamden, CT; 7Jacobi Medical Center, Bronx, NY; 8Stony Brook Medicine, Stony Brook, NY; 9State University of New York Upstate University Hospital, Syracuse, NY; 10Montefiore Medical Center, Bronx, NY; 11PACT Gastroenterology Center and Yale University School of Medicine, New Haven, CT

Introduction: Colon Ischemia (CI) is the most common ischemic injury to the gastrointestinal tract. Studies from Asia have shown a seasonal variation of CI with an increased incidence in the summer months. Our study hypothesizes that in a United States population focusing within a northeastern group of hospitals, where there is a significant variation in the seasonal climate, there is a seasonal variation in the incidence and outcome for CI.

Methods: We conducted a multicenter retrospective cohort study of pts admitted with biopsy-proven CI admitted to Yale-New Haven Hospital, Montefiore Medical Center, Weiler Medical Center, and SUNY-Upstate Medical Center from 2005 through 2017. For each patient, demographics, medical co-morbidities, treatments, and outcomes were recorded. Using a meteorological definition of seasons, we subdivided the population into the onset of CI during the spring (SP-CI; March to May), summer (SU-CI; June to Aug), fall (FA-CI; Sept to Nov), and winter (WI-CI; Dec to Feb). We then compared the seasonal cohorts. Our primary outcome was incidence of CI based upon the season. The secondary outcomes included combination of 30-day colectomy and mortality (i.e., poor outcome), segmental involvement, intensive care unit (ICU) requirements, length of the hospital stay (LOS), 30-day readmission and recurrence.

Results: A total of 685 pts met inclusion criteria. There were no differences in incidence based upon season: CI-SP (27%), CI-SU (24.5%), CI-FA (22%) and CI-WI (26.4%). There were also no differences with regards to age, gender, or BMI. No differences were observed in the presentation, medical comorbidities, Charlson Comorbidity Index, or treatment patterns among the four groups. When considering outcomes, 30-day colectomy was observed 10.3%, 8.2%, 9.2% and 11.1% in the CI-SP, CI-SU, CI-FA and CI-WI group, respectively (p50.84). There were also no significant differences when considering 30-day mortality or poor-outcome. LOS, ICU requirements, segmental involvement, 30-day readmission and 30- day recurrence were not significantly different between the four groups (Table).

Conclusion: Our study showed no difference in the distribution of biopsy-proven cases of CI based upon seasonal change. This contrasts with Asian based studies. It is possible that the severity of the cases considered in our study are different than the Asian studies and that mild cases might have a seasonal variation that are less likely to undergo a colonoscopy to confirm the diagnosis.

Table 1. **Baseline characteristics and outcomes**

Outcomes	Spring (SP-CI) 27.0% (185)	Summer (SU-CI) 24.5% (168)	Fall (FA-CI) 22.0% (151)	Winter (WI-CI) 26.4% (181)	*p* value
Demographics					
Age (years), median (IQR)	70 (63 - 80)	69 (61 - 79)	72 (64 - 80)	70 (60 - 80)	0.988
Female	135 (72.9%)	125 (74.4%)	114 (75.5%)	133 (73.4)	0.957
BMI, median (IQR)	27.68 (23.83-32.14)	26.78 (22.86-30.67)	28.22 (24.80-31.7)	27.06 (23.39-32.11)	0.935
Presentation					
Tachycardia	17.8% (33)	17.8% (30)	20.5% (31)	20.4% (37)	0.857
Hypotension	6.4% (12)	8.3% (14)	5.3% (8)	9.4% (17)	0.485
Peritoneal signs	7.6% (14)	6.6% (11)	7.2% (11)	11.6% (21)	0.316
Medical comorbidities					
Chronic pulmonary disease	19.4% (36)	24.4% (41)	22.5% (34)	21.5% (39)	0.727
Colon cancer	2.1% (4)	1.1% (2)	1.3% (2)	2.2% (4)	0.837
Coronary artery disease	30.8% (57)	26.3% (44)	32% (48)	27.2% (49)	0.616
Diabetes mellitus	30.2% (56)	32.7% (55)	34.4% (52)	29.2% (53)	0.738
Hypertension	73.5% (136)	78.5% (132)	81.4% (123)	76.8% (139)	0.364
Hemodialysis	10.1% (9)	10.3% (10)	5.8% (5)	12.6% (11)	0.510
Hypercoagulable state	0.5% (1)	0.6% (1)	0.7% (1)	1.1% (2)	0.915
Malignancy (any)	14% (26)	18.4% (31)	14% (21)	17.7% (32)	0.557
Malignancy with metastasis	3.8% (1)	6.4% (2)	9.5% (2)	9.3% (3)	0.837
Peripheral vascular disease	10.3% (19)	5.3% (9)	6.6% (10)	7.2% (13)	0.324
Stroke	8.1% (15)	8.3% (14)	11.9% (18)	13.8% (25)	0.226
Calculated Charlson Score, mean (SD)	5 (2.7)	5 (2.8)	5.2 (2.8)	5.1 (3.0)	0.979
Bowel Segment Involvement					
Small bowel involvement	6.8% (8)	7.2% (7)	4% (4)	7.3% (8)	0.732
Pancolitis	5.6% (10)	2.5% (4)	4.8% (7)	8.3% (15)	0.122
Any right colon involvement	24.8% (40)	27.3% (41)	21.8% (29)	28.6% (45)	0.564
Right colon only	13.5% (23)	16.6% (26)	10.6% (15)	14.7% (25)	0.500
CI Severity					
Mild CI	0.5% (1)	0% (0)	0% (0)	1.12% (2)	0.390
Moderate CI	46.9% (86)	49.1% (82)	56.3% (84)	49.1% (88)	
Severe CI	52.4% (96)	50.9% (85)	43.6% (65)	49.7% (89)	
Presence of necrosis on colonoscopy	9.8% (16)	10.4% (16)	8.2% (11)	5.4% (9)	0.372
ICU requirement	22.5% (41)	24.2% (39)	18.2% (27)	25.9% (46)	0.400
Outcomes					
30-day colectomy	10.3% (19)	8.3% (14)	9.2% (14)	11.1% (20)	0.842
30- day mortality	5.4% (10)	3.5% (6)	4% (6)	6.6% (12)	0.546
Combined poor outcome (30- day colectomy and/or 30-day mortality)	13.5% (25)	9.5% (16)	11.3% (17)	15% (27)	0.437
Length of stay (mean, (SD))	6.2 (16.9)	10.3 (56.6)	8.4 (31.2)	10.1(55.2)	0.137
C Difficile as a complication	3.4% (6)	2.5% (4)	2.8% (4)	3.1% (5)	0.97

Ahmed Nawaz:

The Evolving Epidemiology of Colonic Ischemia: A Multi-Center Study

Kanika Sehgal MBBS, Rabia Rizwan MD , Abdelkader Chaar MD , Ahmad Nawaz MD , Karthik Gnanapandithan MD , Abdul Q Bhutta MD , Marc Fenster MD , Savio John MD, AGAF, FACG , Lawrence J. Brandt MD, MACG, AGAF, FASGE , Paul Feuerstadt MD, FACG, AGAF

Introduction

Colon ischemia (CI) is the most common cause of ischemic injury to the GI tract but pertinent recent epidemiologic data are limited. We therefore conducted a multi-center study to evaluate changes in demographics, disease severity and outcomes in pts with CI.

Methods

A retrospective study of biopsy-proven CI pts admitted to Yale-New Haven Hospital (YNHH), Montefiore Medical Center (MMC), and SUNY-Upstate Medical University. The data base was divided into two-time frames, 2008-2012 and 2013-2017, and epidemiologic factors and outcomes were compared for all pts and for inter-institution differences among CI pts during these periods.

Results

401 and 225 pts were included in the 2008-2012 and 2013-2017 time periods respectively. Woman predominated but a decrease in female predominance was seen during 2013-2017 (75.8% in 2008-2012 vs 63.1% in 2013-2017; p=0.001). Comparing the older to the more recent time frame, CI severity decreased (45.4% vs 59.9%; p=0.023), rectal involvement increased (12.4% vs 20.8%; p=0.031), 30-da (8.0% vs 16.4%; p=0.001) and 90-day colectomy rates increased (8.5% vs 13.6%; p=0.043), and 90-da recurrence rate decreased (5.5% vs 0.4%; p=0.001).

Most CI patients were from YNHH (n=295) and MMC (n=215). Both sites held a female predominance, however this was not significant within the 5- ear time frames. At YNHH, disease severity increased (47.2% vs 64.9%; p=0.012), while at MMC there was no difference in disease severity ((45.0% vs 52.5%; p=0.327). A greater proportion of pts received antibiotics recently (p=0.008) at YNHH, though this was not significant change at MMC (p=0.251). At YNHH, the more recent time period had increases in rectal (13.6% vs 28.9%; p=0.017), isolated right-CI (7.6% vs 19.2%; p=0.027) and ascending colon involvement (15.6% vs 30.5%; p=0.008). There were no significant changes in regional involvement at MMC. At YNHH, there were increasing rates of ICU stay (27.5% vs 40.0%; p=0.043), 30- day (14.4% v 31%; p=0.001) and 90-day colectomy (15.4% vs 26.6%; p=0.023) in the more modern time frame. At MMC, 30-day colectomy rate increased though this was not significant (2% vs. 3.12%; p=0.613) and 90-da recurrence decreased (9.3% vs 1.6%; p=0.042).

Discussion

5-year epidemiologic trends in pts with CI showed a decrease in the disease severity, with an increase in rectal involvement, with increasing rates of colectomy at 30 and 90 days. Some institutional site differences were noted but large studies are needed to characterize national trends.

Ahmed Nawaz:

Incidence and Outcomes of C. di!cile Infection Following Colon Ischemia

Ahmad Nawaz, MD1, Abdelkader Chaar, MD1, Rabia Rizwan, MD1, Karthik Gnanapandithan, MD2, Muhammad Sohail Mansoor, MD3, Abdul Qadir Bhutta, MD4, Adil Bhutta, MD5, Marc Fenster, MD6, Olga Aroniadis, MD, MSc, FACG7, Savio John, MD8, Lawrence Brandt, MD, MACG9, Paul Feuerstadt, MD, FACG10.
1Yale University School of Medicine, New Haven, CT; 2Mayo Clinic Florida, Jacksonville, FL; 3GI Specialists of Georgia, Marietta, GA; 4SUNY Upstate Syracuse University Hospital, Syracuse, NY; 5Yale New Haven Health, Hamden, CT; 6Jacobi Medical Center, Bronx, NY; 7Stony Brook Medicine, Stony Brook, NY; 8State University of New York Upstate University Hospital, Syracuse, NY; 9Monte!ore Medical Center, Bronx, NY; 10PACT Gastroenterology Center and Yale University School of Medicine, New Haven, CT.

Introduction: Colon Ischemia (CI) is the most common ischemic injury to the gastrointestinal tract. Clostridioides difficile infection (CDI) is the most common healthcare-associated infection. There is limited knowledge of the risk of CDI after CI. Our hypothesis is that CI patients who develop CDI have worse outcomes compared with CI patients who don't develop CDI. (Figure)
Methods: We conducted a multicenter retrospective cohort study of patients admitted with biopsy-proven CI to Yale-New Haven Health Hospital, Monte!ore Medical Center, Weiler Medical Center, and SUNY-Upstate Medical Center from 2005 to 2019. For each patient, we recorded numerous factors including the ACG severity scoring system. Patients who had CDI within 3 months following CI (CI1CDI) were compared to patients who did not develop CDI (CI-CDI). Primary outcome was to measure frequency of occurrence CDI in the CI population, secondary outcomes included comparing 30-day and 90-day colectomy, recurrent CI, readmission, and mortality from the time of diagnosis of CI, and segmental involvement of CI1CDI to CI-CDI. Multivariate logistic regression was performed after adjusting for the age, gender, race, Charlson Comorbidity Index (CCI) and the severity of CI.

Results: 906 patients met inclusion criteria with Bx proven CI. 3.2% developed CDI between 2005 and 2019 Figure. There were no differences between CI1CDI (n529) and CI-CDI groups (n5877) with regards to gender, BMI, medical co-morbidities, or severity. CI1CDI patients had more isolated right-colon involvement (38.8% vs 16.5%, p50.013), 30-day readmission (51.7% vs 9.3%, p, 0.001), 90-day readmission (65.5% vs 18.1%, p, 0.001), 30-day reoccurrence of CI (17.2% vs 1.6%, p, 0.001), 90-day reoccurrence of CI (24.1% vs 3.6%, p, 0.001) and 90-day mortality (17.8% vs 7.5%, p50.047) than CI-CDI. When adjusting for age, gender, race, CCI and severity, patients with CI1CDI were at higher risk for 30-day readmission [OR 10.62 (95% CI: 4.2-26.3), p, 0.001], 90-day readmission [OR 10.45 (95% CI: 4.0-26.8), p, 0.001], 30- day reoccurrence CI [OR 7.3 (95% CI: 1.9 -27.3), p50.003] and 90-day reoccurrence CI [OR 5.7 (95% CI: 1.8-17.2), p50.003] compared with CI-CDI group (Table).

Conclusion: CI patients who developed CDI had higher rates of CI recurrence, more frequent readmission, and were more likely to have isolated right colon involvement than CI-CDI. When a patient with a recent history of CI is diagnosed with CDI, they might benefit from more aggressive therapy to try to improve these outcomes.

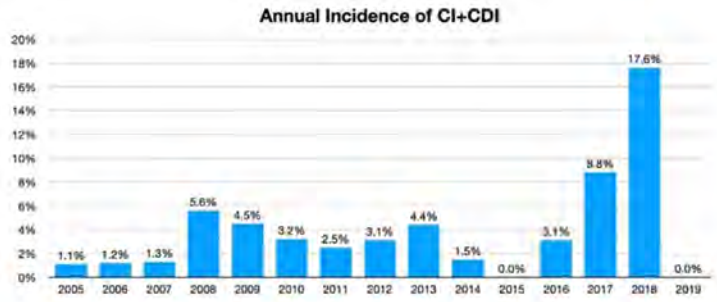


Figure 1. Annual incidence of CI+CDI. Abbreviations: BMI, Body mass index; CI, colon Ischemia; ICU, Intensive Care Unit

Ahmed Nawaz:

Development of a Clinically Applicable Prognostication Severity Score for Colon Ischemia (CAPSSCI) in Hospitalized Patients

Rizwan R, Amjad W, Feuerstadt P, Chaar A, Nawaz A, Gnanapandithan K, Bhutta AQ, Fenster M, John S, Sehgal K, Brandt LJ

Introduction

Colon Ischemia (CI) manifests a range of severity from reversible to fulminant disease requiring colectomy or resulting in death. Our goal was to develop a 30-day prediction score to triage the risk of progression of severe disease to colectomy or mortality in patients hospitalized with CI.

Methods

A multicenter retrospective study of patients hospitalized with biopsy-proven CI from 1/2005 to 7/2017. Patients with age < 45 yrs, the extreme elderly (> 90 yrs), and those with colon cancer were excluded. Patients requiring colectomy and/or dying within 30 days of presentation were classified as having severe disease**.** A multivariable Cox- proportional hazard model was used to identify risk factors for severe CI*.* Beta coefficients of independent risk factors were used to generate the scoring system. Coefficients were rounded to the nearest decimal value multiple of 0.25 to generate a clinically applicable prognostication severity score for CI (CAPSSCI). We calculated area under receiver operating curve (AUROC) of predicted and observed severe CI.

Results

713 pts with biopsy-proven CI met study criteria. Of these, 82 (11.3%) developed severe CI within 30 days of presentation. Their mean age was 70.1 ± 10.9 yrs, and 74.7% were male. The severe CI group had a higher percentage of women (41.5 vs. 23.3, p=0.001), coronary artery disease (CAD; 46.3 vs. 31.0, p=0.007) and COPD (18.3 vs. 9.8, p=0.030). The multivariable model showed the following to be associated with severe CI: ages 45 to 54 yrs and advanced age (compared to reference: 55 to 64 yrs); CAD (HR: 3.01, 95% CI: 1.10 – 8.30, p=0.03), shock index (HR: 5.65, 95% CI: 1.11 – 28.8, p=0.04), lower albumin, imaging findings of pan-colon and right-colon involvement, pneumatosis, and portal venous gas. A 45-point score (0 to 11.25 with 0.25 increment) CAPSCI was generated using point estimates (β) of these risk factors. **(Table 1)** AUROC to predict severe CI was 0.90 (95% CI: 0.85 – 0.93) at 30 days, and 5-fold internal cross-validation AUROC to predict 30-day severe CI was 0.87 (95% CI: 84 – 0.94). A cut-off of 3.25 accurately calibrated the risk for severe CI (sensitivity = 80.65%, 95% CI: 75.57% – 85.72% and specificity= 81.68%, 95% CI: 76.72% – 86.65%). **(Figure 1)**

Conclusion

CAPSCI is a simple-to-use risk score integrating baseline clinical variables and available diagnostic data. Healthcare providers can use this calculation to easily assess risk for severe outcomes of CI in hospitalized patients and direct therapy based upon this risk.

Variable	Hazard ratio (HR)	Beta-coefficient	p-value	Risk score
Age risk per 10 year (reference 55 to 64)	1			0
45 – 54	5.89 (0.94 – 36.91)	1.77 (-0.06 – 3.61)	0.058	1.75
65 – 74	5.18 (1.07 – 24.99)	1.64 (0.07 – 3.22)	0.04	1.75
75 -84	2.58 (0.49 – 13.55)	0.95 (-0.71 – 2.61)	0.26	1.00
≥ 85	4.45 (0.70 – 28.41)	1.49 (-0.36 – 3.35)	0.11	1.50
SI (reference <0.8)	1			0
SI (0.80 – 0.89)	2.71 (0.72 – 10.11)	1.00 (-0.32 – 2.31)	0.14	1.00
SI (0.90 – 0.99)	2.33 (0.57 – 9.50)	0.84 (-0.56 – 2.25)	0.24	1.00
SI (1.00 – 1.19)	2.68 (0.31 – 23.49)	0.98 (-1.19 – 3.16)	0.37	1.00
SI (≥ 1.20)	2.04 (0.44 – 9.50)	0.71 (-0.83 – 2.25)	0.36	0.75
CAD	2.11 (0.85 – 5.27)	0.75 (-0.17 – 1.66)	0.11	0.75
Pan colon	1.85 (0.53 – 6.50)	0.62 (-0.64 – 1.87)	0.34	0.75
RCI involvement	3.42 (1.32 – 8.89)	1.70 (0.29 – 3.11)	0.07	1.75
Pneumatosis	5.47 (1.34 – 22.4)	1.23 (0.27 – 2.18)	0.02	1.25
PV gas	4.04 (0.87 – 18.74)	1.40 (-0.14 – 2.93)	0.07	1.50
Albumin (g/dL) 3.5 to 5.5	1			0
1 – 2.1 gm/dl	10.76 (1.51 – 76.7)	2.38 (0.41 – 4.34)	0.02	2.5
2.2 – 2.4 gm/dl	2.27 (0.27 – 19.26)	0.82 (-1.32 – 2.96)	0.45	1.00
2.5 – 2.9 gm/dl	6.80 (2.17 – 21.3)	1.92 (0.77 – 3.06)	0.001	2.00
3.0 – 3.5 gm/dl	2.88 (0.85 – 9.80)	1.06 (-0.17 – 2.28)	0.09	1.00

Table 1: Component of CAPSCI

Variables included in model are age, history of coronary artery disease (CAD), lower albumin level, shock index (ratio of heart rate and systolic blood pressure), and imaging findings.

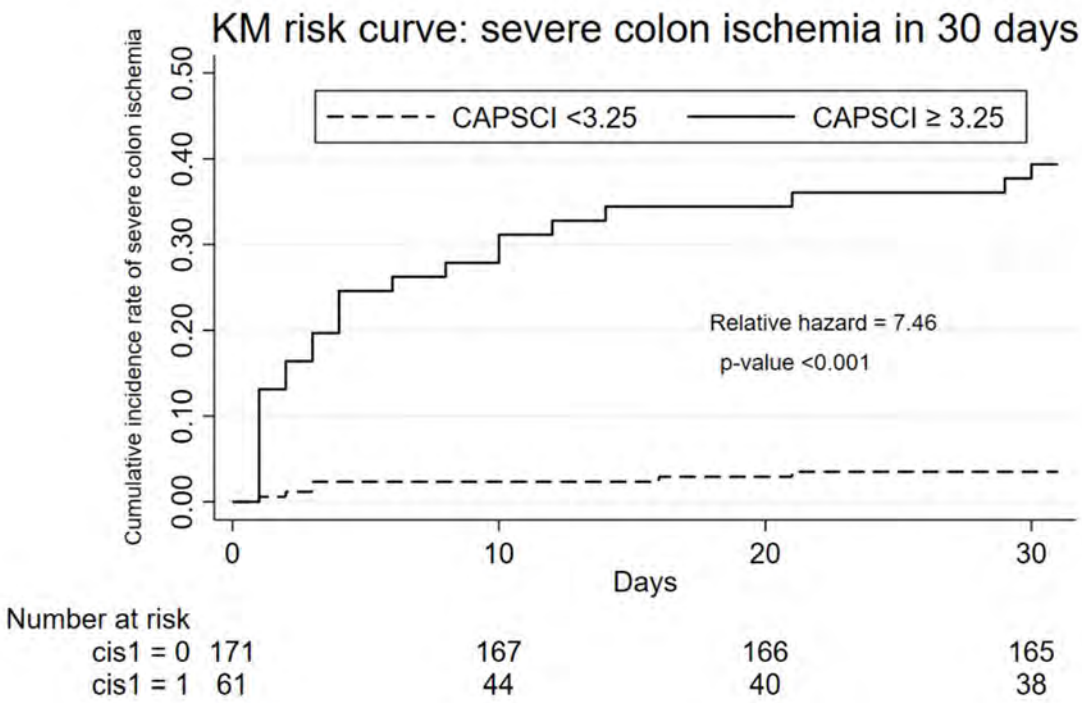

KM risk curve: severe colon ischemia in 30 days
Cumulative incidence rate of severe colon ischemia
0.00
0.10
0.20
0.30
0.40
0.50
CAPSCI <3.25
CAPSCI ≥ 3.25
Relative hazard = 7.46
p-value <0.001
0
10
20
30
Days
Number at risk
cis1 = 0 171 167 166 165
cis1 = 1 61 44 40 38

Figure: 1

Gayatri Pemmasani

10-Year Atherosclerotic Cardiovascular Disease Risk Scores In Patients With Non-Alcoholic Fatty Liver Disease and Sex differences

Gayatri Pemmasani, MD,[1] Wilbert Aronow, MD,[2] Raffi Karagozian, MD,[3] Srikanth Yandrapalli, MD,[4] Savio John, MD[1]

[1] SUNY Upstate Medical University, Syracuse, NY
[2] New York Medical College, Valhalla, NY
[3] Tufts University School of Medicine, Boston, MA
[4] Brown University- Warren Alpert School of Medicine, Providence, RI

Background: Non-alcoholic fatty liver disease (NAFLD) is increasing in prevalence in the US. NAFLD shares risk factors with atherosclerotic cardiovascular disease (ASCVD). The 10-year ASCVD risk score is traditionally used in patients over 40 years of age to make a recommendation for statin use to reduce the risk of future cardiovascular events. It is currently unclear how ASCVD risk scores are distributed in patients with NAFLD and if there are sex differences.

Methods: We used the National Health and Nutrition Examination Survey (NHANES) database (2017–March 2020) to identify patients with NAFLD. NAFLD was identified by transient elastography (FibroScan®) data, by using controlled attenuation parameter ≥302 dB/m using Youden's index. In the final NAFLD sample, ASCVD 10-year risk scores were calculated by identifying individual components of the ASCVD equation including sex, race, presence of diabetes mellitus, taking hypertension medications, smoking status, systolic blood pressure, total cholesterol and high-density lipoprotein cholesterol levels.

Results: We studied 986 patients with NAFLD and age>= 40 years. Mean patient age was 61+- 11 years, 50.7% study population was female, and 20.5% individuals were of non-Hispanic Black race. The mean 10-year ASCVD risk score was 4.5%+-46% and the median score was 14% [IQR 24% – 40%]. Overall, 32% patients had ASCVD score < 7.5% (statin not recommended for primary prevention of cardiovascular events), 29 % had scores 7.5%-19.9% (statin to be considered based on shared decision making and considering other risk factors), and 38.9% had 10-year ASCVD risk score >20% (strong recommendation for statin prescription). When stratified by sex, more females than males had a ASCVD score < 7.5% (40% vs 23%; P<0.01).

Conclusion: The majority of patients with NAFLD have a high risk for ASCVD events. Around a third of patients are considered low ASCVD risk based on the 10-year risk score and do not meet criteria for statin prescription for primary prevention, and this proportion was higher in females (4 in 10). Future sex specific outcome studies to evaluate the role of NAFLD as an independent risk factor for ASCVD events could support statin prescription in most patients with NAFLD to improve cardio

Gayatri Pemmasani:

Six-month cardiovascular prognostic impact of type 1 And type 2 myocardial infarction in patients hospitalized for gastrointestinal bleeding

Gayatri Pemmasani [1], Ashwini Ashwath [1], Wilbert S Aronow [2], Srikanth Yandrapalli [3], Jonathan Leighton [4], Savio John [1]

[1] SUNY Upstate Medical University, Syracuse, NY
[2] New York Medical College, Valhalla, NY
[3] Brown University- Warren Alpert School of Medicine, Providence, RI
[4] Mayo Clinic, Phoenix, AZ

Background: Patients with gastrointestinal bleeding (GIB) are at an increased risk of cardiovascular events and myocardial infarction (MI). Myocardial supply-demand mismatch results in type 2 MI(T2MI) and atherosclerotic plaque rupture leads to type 1 MI(T1MI). Data comparing the prognostic impact of these MI types in GIB are sparse.

Methods: Patients hospitalized for GIB were identified in the 2019 US Nationwide Readmissions Sample. In this population, we studied the differences in management of T1MI and T2MI, and the association of these MI types with in-hospital mortality and risk for 6-month MI and MI-related mortality.

Results: Of 444,475 patients admitted for a GIB, 12,860 (2.9%) had an MI (1.7% T2MI, 1.2% T1MI). Patients with T1MI were more likely to receive coronary angiography and revascularization than patients with T2MI. In-hospital mortality occurred in 2.0% patients, at a significantly higher rate in patients with an MI (7.9% vs 1.8%; $P < 0.001$), and higher with T1MI (11.9%) than T2MI (5.3%; $P < 0.001$). Among the survivors, 2.2% patient had an MI within 6 months, at a significantly higher rate in patients with index MI (13.1% vs 2.0%, adjusted OR 4.3 95% CI 3.83-4.90; $P < 0.001$). Mortality during the subsequent MI occurred in 0.3% of all patients (12% with an MI), at a 6-fold higher rate in patients with index MI (1.7% vs 0.3%; adjusted OR 3.69 95% CI 2.75-4.95; $P < 0.001$). The elevated risks were associated with both MI types. The risks for 6-month MI and related mortality were similar between T1MI and T2MI (6-month AMI: adjusted OR for T2MI = 1.03, 95% 0.83-1.29; fatal MI: adjusted OR for T2MI = 1.5, 95% CI 0.85-2.7).

Conclusion: The occurrence of an MI is associated with a substantially elevated risk for subsequent AMI and related mortality in patients hospitalized for a GIB. This future prognostic impact was similar between T1MI and T2MI.

Pujita Kudaravalli:

COMPARISON OF ADENOMA RECURRENCE RATE BETWEEN STANDARD ENDOSCOPIC MUCOSAL RESECTION VS ENDOSCOPIC MUCOSAL RESECTION WITH ADJUVANT THERMAL ABLATION INCLUDING THE NOVEL HYBRID APC: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Pujitha Kudaravalli MBBS1, Vishnu Charan Suresh Kumar MBBS1, Babu P. Mohan MD2, Kelita Singh MD1, Douglas G. Adler MD, FACG, AGAF, FASGE3, Bishnu Sapkota MD1

1. Division of Gastroenterology and Hepatology, SUNY Upstate Medical University, Syracuse, NY
2. Division of Gastroenterology and Hepatology, University of Utah School of Medicine, Huntsman Cancer Center, Salt Lake City, UT
3. Center for advanced therapeutic endoscopy, Porter Adventist Hospital, Centura Health, Denver, CO

Introduction:

Endoscopic mucosal resection (EMR) is the established treatment method for large (>20 mm) non-pedunculated colon polyps. However, an adenoma recurrence rate of 10-30% is reported. Local ablative therapy of the resection edges +/- base to treat any microscopic residual seem to reduce lesion recurrence. Ablation techniques include snare tip soft coagulation (STSC) of edges, argon plasma coagulation (APC) of edges, and the novel hybrid-APC to ablate edges and the base. In this systematic review and meta-analysis, we aim to compare the outcomes of various EMR adjuvant ablative therapies with standard EMR.

Methods:

We conducted a comprehensive search of several databases, including MedLine, Embase, Scopus (inception to November 2022), to identify studies reporting on the use of adjuvant ablative therapy in EMR. Outcomes of interest were the pooled rates of lesion recurrence, post-EMR bleeding, and post-polypectomy syndrome. Standard meta-analysis methods were employed using the random-effects model. Heterogeneity was assessed by I2% values and 95% prediction intervals.

Results:

28 studies with 3786 polypectomies were included in the final analysis (11 studies with standard EMR, 9 studies with STSC of polypectomy edges, 3 studies with APC of polypectomy margins and 5 studies with hybrid APC) . Mean patient age was 65.8 years and 48.6% were females. 56% of polyps were located in ascending, 9% in transverse and 35% in descending colon with a mean polyp size of 3.2 cm. The first follow up surveillance colonoscopy was performed at an average of 6.8 months.

Cumulative rates of adenoma recurrence on endoscopy/histology for EMR with no adjuvant thermal therapy was 26.4% [95% confidence interval (CI) (20.9-32.6); I2=65%], 5.3% [3.3-8.4; I2=80%] with STSC, 6.8% [3-14.5; I2=48%] with APC of margins and 3.1% [1-9.2%; I2=0%] with hybrid APC. The recurrence rate was significantly higher in EMR without ablation ($p<0.001$).

The post-polypectomy bleeding rate was 8.3% [4.6-14.5; I2=55%] in EMR without ablation, 6.8% [5.6-8.2; I2=0%] with STSC, 4.8% [2-11.2; I2= 55%] with APC; and 6.7% [3.4-12.8; I2=0%] with hybrid APC. The incidence of post-polypectomy syndrome was 3.7% [0.5-23.1; I2=55%] in EMR without ablation, 3.6% [1.8-7.2; I2= 0%] with STSC , and 5.6% [1.8-15.9; I2=75%] with APC. No statistically significant difference was noted in these outcomes of interest between STSC, APC and hybrid APC.

Conclusion:

Our study demonstrates that adjuvant thermal ablation of EMR margins is an effective technique in reducing adenoma recurrence when compared to standard EMR. Of the described adjuvant therapies, hybrid APC with ablation of base and margins was associated with the lowest adenoma recurrence rate. Future studies with direct comparisons and cost-analyses are warranted to optimize techniques for EMR.

Vishnu Kumar:

Comparison of no-show rates between telemedicine and in-person clinic appointments: A tertiary center experience.

Vishnu Kumar, MBBS, Pujitha kudaravalli, MBBS, Ganapathy Palanimuthu, B.Com, Ganesh Aswath, MD
Savio John, MD

Introduction

The COVID-19 pandemic had significantly disrupted the provision of timely outpatient care. This was promptly addressed with the widespread implementation of telemedicine after important issues, including insurance reimbursement, provider licensing, and patient privacy, were adequately addressed. We aimed to study the impact of telemedicine on no-show rates compared to in-person clinic visits.

Methods

This study was conducted at a large tertiary center clinic catering to a large catchment area. The number of appointments scheduled and the number of appointments that were successfully completed pre-COVID and once telemedicine was fully implemented were collected retrospectively. Data was analyzed descriptively, and a two-tailed t-test was used to compare the means, with a p-value < 0.05 considered statistically significant.

Results

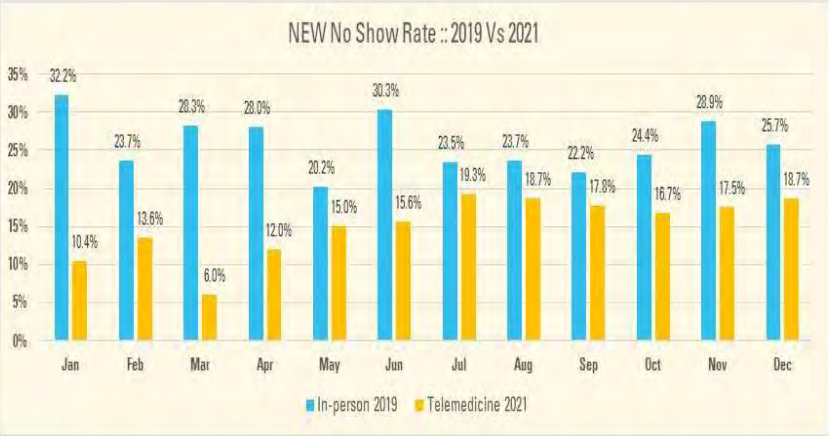
A total of 3325 new appointments (NEW) and 4805 follow-up appointments (FOL) were scheduled in 2019 prior to the pandemic with a no-show rate (NR) of 25.9% ± 3.6% and 21.2% ± 2.2%, respectively. All these were in-person visits. In 2021, when we had a full calendar year of telemedicine services, 2524 NEW and 3350 FOL were scheduled with a mean NR of 15.1% ± 4.0% and 9.7% ± 2.1%, respectively. There was a significant difference in NR between in-person and telemedicine visits for both NEW and FOL ($p< 0.0001$). NR was typically the highest in January, which is the coldest month in Upstate, NY, and in June, when the weather became warm for the first time. Telemedicine visits seemed to negate the winter weather effect, and NR was comparable to that of other months (Figure 1). The results are summarized in Table 1.

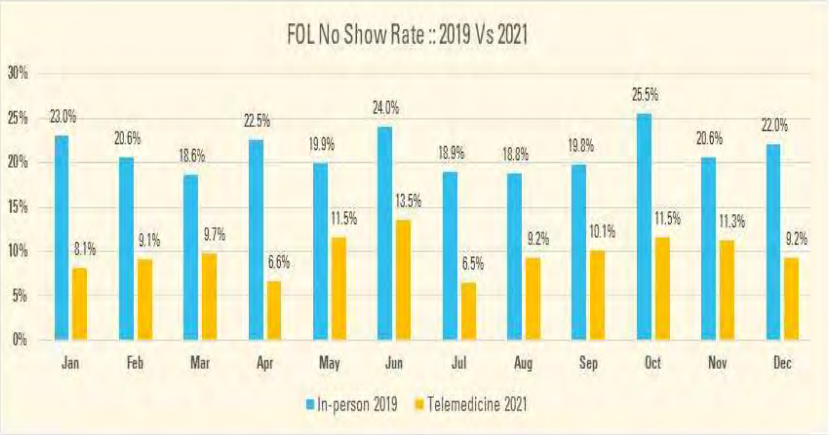
Discussion

Our study showed that the no-show rates for both new and follow-up appointments significantly improved with the incorporation of telehealth services. Telemedicine is helpful during harsh weather conditions, which may prevent patients from traveling to their appointments. Several studies have

reported high patient satisfaction with telehealth programs. Although physical examination is a key component in our assessment of a patient, telemedicine may improve patient care and outcomes in patients with chronic diseases who do not require repeated physical examinations. Our study provides further evidence that telemedicine should be routinely incorporated into the healthcare system, particularly for outpatient care.

Figure 1: NEW and FOL no-show rates





Vishnu Kumar:

IMPROVEMENT IN LIVER FIBROSIS AND SURROGATE MARKERS OF NAFLD WITH ENDOSCOPIC BARIATRIC THERAPIES: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Vishnu Charan Suresh Kumar MBBS[1], Abinash Subedi MBBS[1], Gayatri Pemmasani MBBS[2], Dayana Nasr MD[2], Ganesh Aswath MD[1], Bishnu Sapkota MD FACG[1], Violeta Popov MD PhD FACG[3]

1. Division of Gastroenterology and Hepatology, SUNY Upstate Medical University, Syracuse, NY
2. Department of Medicine, SUNY Upstate Medical University, Syracuse, NY
3. NYU Langone Medical Center and VA NY Harbor Healthcare System, New York University School of Medicine, New York

Introduction:

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the Western world, and approximately 5–10% body weight loss has been shown to improve liver steatosis(LS) and liver fibrosis(LF). Endoscopic bariatric therapies (EBT) offer a less invasive option for weight reduction than bariatric surgery and are more effective than lifestyle modifications. Recent studies have reported improvements in liver-related outcomes. We conducted a systematic review and meta-analysis to study the effects of EBT on NAFLD and NAFLD surrogate markers.

Methods:

We searched MedLine, Embase, and Scopus through October 2022. A search strategy using a combination of subject headings and text words was constructed to find articles that reported the effect of EBTs on liver-related outcomes, specifically LS and LF.

The pre-defined NAFLD surrogate markers included measures of LS (assessment of steatosis by transient elastography(TE) or MRI, hepatic steatosis index); LF surrogates(liver stiffness by TE or MRI, NAFLD fibrosis score (NFS), FIB-4); and other metabolic measures: aspartate aminotransferase(AST), alanine aminotransferase(ALT), body mass index(BMI), Hemoglobin A1c(A1c), and Homeostatic Model Assessment for Insulin Resistance(HOMA-IR). The primary outcome was defined as the pooled standard difference in means (SMD) of the change from baseline to final values for changes in LF and LS following EBT. The secondary outcomes included changes in AST, ALT, HOMA-IR, A1c, and weight. A random-effects model was used. Heterogeneity was assessed using I2% and 95% prediction intervals.

Results:

EBT was associated with a significant decrease in LF by SMD: -0.38 [(-0.54, -0.21) I2% = 0, p = 0.000, 9 studies] and LS, SMD: -0.56 [(-0.77, -0.36] I2%=0, p = 0.000, 4 studies]). Other surrogate markers of

NAFLD also improved after EBT; ALT: -13.11 [(-19.87, -6.36) I2%=54.7, p=0.000, 7 studies]; AST: -5.47 [(-10.62, -0.32) I2%=58.4, p=0.04, 5 studies]. The change in BMI after EBT was -5.60[(-6.64, -4.56) I2%=0, p=0.000, 8 studies]. EBT had a significant effect on reducing HOMA-IR, -0.62 [(-0.90, -0.35) I2%=0, p=0.000, 5 studies] and A1c, -0.61[(-0.82, -0.41) I2%=0, p=0.000, 8 studies]. Table 1.

Subgroup analysis and meta-regression performed showed no significant effect of baseline BMI, change in BMI, and % total weight loss on outcomes.
Visual inspection of the funnel plots and results of Eggers test (p=0.39) revealed no publication bias. Fig 1.

Conclusion:

EBT resulted in improvement in liver fibrosis, liver steatosis, and other surrogate markers of NAFLD. Based on the current findings, EBT may provide an additional treatment option for patients with NAFLD as part of a multidisciplinary approach. Large-scale, long-term, high-quality studies, including those examining the cost-effectiveness of EBT, are needed to establish EBT as a treatment for NAFLD.

Vishnu Kumar:

Comparison of the efficacy of different Hemostatic Powders for the Management of Gastrointestinal Bleeding: A Systematic Review and Meta-Analysis.

Vishnu Charan Suresh Kumar MBBS[1], Fathima Keshia Suhail MD[1], Babu Mohan MD[2], Prateek Harne MD[3],

Pujitha Kudaravalli MBBS[1], Ganesh Aswath MD[1], Douglas G. Adler MD, FACG, AGAF, FASGE[2]

Division of Gastroenterology and Hepatology, SUNY Upstate Medical University, Syracuse, NY

Division of Gastroenterology and Hepatology, University of Utah School of Medicine, Huntsman Cancer Center, Salt Lake City, UT

Division of Gastroenterology and Hepatology, UT Rio Grande Valley, McAllen, TX

Introduction:
Gastrointestinal (GI) bleeding is a common indication for endoscopy. Hemostatic powders have been found to be efficacious, generally safe and well tolerated. Hemospray(HS), Endoclot(EC), and NexPowder(NP) are currently approved for use in the US. We conducted a systematic review and meta-analysis to compare the efficacy of different hemostatic powders.
Methods:
We conducted a comprehensive search of several databases (inception to November 2022) to identify studies reporting the use of different hemostatic sprays in the treatment of gastrointestinal bleeding. Random-effects model was used to calculate the outcomes; I2% values and 95% prediction intervals were calculated to assess heterogeneity. All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 3 (BioStat, Englewood, NJ).
Results: A total of 24, 8, and 5 studies on HS, EC, and NP, respectively, were included in the final analysis. The cumulative rates of successful immediate hemostasis for HS, EC, and NP were 91.2% [(84.6-95.2); I2=84%], 89.9% [(81-94.8); I2=15%], 88.8% [(32.5-99.2); I2=95%], and cumulative long-term success rates were 70.6% [(63.8-76.6); I2=70%], 81% [(65.3-90.6); I2=59%], and 92% [(86.6-95.4); I2=20%], respectively. Subgroup analysis showed that NP had the highest immediate hemostasis rate (96.1 % [92-98.1]; I2 = 0 %) in upper GI bleeding (UGIB) compared to HS (91.8 % [84.8-95.7]; I2 = 86 %) and EC (91.1 % [81.5-96]; I2 = 15 %). NP also had higher long-term success in treating UGIB [92.7% (84.8-96.7); I2=39%], lower rebleeding rates [11.6% (5.4-23.2); I2=63%], and lower IR/surgical intervention rates 2.2% [(0.7-6.7); I2=0%] than others.

Although EC had higher rates of immediate hemostasis while treating lower GI bleeding (LGIB) (87.3% [(55.6-97.4); I2=34%]), HS had better long-term success (84.2% [(59.6-95); 19%]), a lower rebleeding rate (18% [(6.1-42.7); I2=13%]), and a lower IR/surgical intervention rate (8.5% [(1.7-33.7); I2= 0%]). NP did not have enough studies for LGIB.
Conclusion: Nexpowder appears to be the most efficacious for treating UGIB, with the highest rate of immediate hemostasis, long-term success, and lowest incidence of rebleeding. Endoclot appears to be the next best hemostatic powder for managing UGIB, followed by Hemospray. Hemospray appears to be superior in treating LGIB compared to EndoClot. Our study is the first to compare the efficacy of these three hemostatic sprays. This provides important evidence for the use of appropriate hemostatic powder based on the location of GI bleeding.

Dayan Nasr:

INCIDENCE OF GASTROINTESTINAL DISORDERS OR EVENTS IN COVID-19 VERSUS INFLUENZA DURING ACUTE AND DELAYED PHASES OF INFECTION

Authors: Dayana Nasr, Andres Cordova Sanchez, Pujitha Kudaravalli, Vishnu Kumar, Ganesh Aswath, Savio John

Introduction: The acute phase of COVID-19 infection presents with fever, respiratory and gastrointestinal disorders, or no symptoms within 4 weeks of the infection. A subset of patients, whose symptoms persist for months, are diagnosed with long COVID. We aimed to identify the incidence of GI disorders or events in patients with COVID-19 infection compared to influenza during acute and delayed phases of infection.

Methods: We identified patients who were diagnosed with COVID-19 and influenza using the TriNetX research database which provides information from EMRs from several health care institutions primarily based in the US. Patients were divided into 2 cohorts, patients with COVID-19 and those with influenza. Propensity score matching (PSM) was used to equilibrate the cohorts based on past medical history and medications. Acute and delayed GI events were defined as those occurring within 30 days and 90 days respectively from the onset of the respiratory infection. The incidence of acute and delayed GI problems such as ischemic colitis (IC), pancreatitis, elevated liver enzymes, diarrhea, and the need for colonoscopy in the two cohorts were compared.

Results: 124,971 patients were identified in each cohort in the delayed phase of infection. IC was diagnosed more commonly in the COVID-19 cohort than influenza cohort [HR 1.608 (95% CI:1.051-2.460)]. Similarly, elevated liver enzymes [HR 1.424 (95% CI: 1.290-1.573)] and need for colonoscopic exams [HR 1.42 (95% CI: 1.290-1.573)] were more commonly observed in the COVID-19 cohort compared to the influenza cohort. There was no significant difference in the incidence of pancreatitis [HR 1.218 (95% CI: 0.945-1.570)] and diarrhea [HR 2.544 (95% CI: 2.274-2.845)] between the two cohorts.
116,078 patients were identified in each cohort in the acute phase of the infection. Colonoscopic exams were more commonly performed in the COVID-19 cohort compared to the influenza cohort [HR 16.879 (95% CI: 13.863-20.551)]. Similarly, the risk of having diarrhea was also higher in the Covid-19 group compared to the influenza group [HR 1.563 (95% CI: 1.111-2.198)]. There was no significant difference in the incidence of IC [HR 1.722 (95% CI: 0.963-3.078)], pancreatitis [HR 1.473 (95% CI: 0.995-2.179)] or abnormal liver enzymes [HR 0.996 (95% CI: 0.867-1.144)] between the 2 groups.

Conclusion: Our study shows that the incidence of IC, elevated liver enzymes and need for colonoscopic exams were higher in patients with Covid-19 in the delayed phase of illness compared to those with influenza. There was a greater number of colonoscopies performed on patients with COVID-19 and more patients who developed diarrhea in that group in the acute phase compared to those with influenza. Further research will help clarify what the significance of these findings is in patients with long COVID.

	COVID-19	Influenza	Hazard ratio	Confidence interval
Number of patients	124,791	124,791		
Ischemic colitis (percentage)	52 (0.041%)	36 (0.028%)	1.608	(1.051, 2.460)
Pancreatitis	126 (0.10%)	114 (0.091%)	1.218	(0.945, 1.570)
Elevated liver enzymes	904 (0.72%)	692 (0.55%)	1.424	(1.290, 1.573)
Diarrhea	186 (0.15%)	233 (0.18%)	0.878	(0.724, 1.065)
Colonoscopy	987 (0.79%)	443 (0.35%)	2.544	(2.274, 2.845)

Table 1: Incidence of delayed gastrointestinal events in patients with COVID 19 versus influenza occurring at least 90 days after the acute infection

	COVID-19	Influenza	Hazard ratio	Confidence interval
Number of patients	116,078	116,078		
Ischemic colitis (percentage)	31 (0.03%)	18 (0.02%)	1.722	(0.963, 3.078)
Pancreatitis	62 (0.05%)	42 (0.04%)	1.473	(0.995, 2.179)
Elevated liver enzymes	404 (0.37%)	397 (0.37%)	0.996	(0.867, 1.144)
Diarrhea	85 (0.07%)	54 (0.05%)	1.563	(1.111, 2.198)
Colonoscopy	1774 (1.6 %)	105 (0.09%)	16.879	(13.863, 20.551)

Table 2: Incidence of gastrointestinal events in patients with COVID 19 versus influenza occurring within 30 days of the infection

HEMATOLOGY-ONCOLOGY

Alina Basnet:

Bladder Primary Sarcomas (BSar): A Genomic Landscape and Clinical Outcomes Study

A Basnet, J Jacob, R Lemma, R Wong, H Goldberg, D Pavlick, R Huang, D Lin, PE Spiess, R Li, AM Kamat, P Grivas, A Necchi, J Ross, G Bratslavsky

Background: BSar are rare and often present at advanced stage with poor prognosis. Limited data on genomic alterations (GA) exist; we evaluated GA and outcomes in separate cohorts.
Methods: 18 (0.2%) pts with Bsar were identified from 11,193 bladder cancers and underwent hybrid capture-based comprehensive genomic profiling (CGP) using DNA only (6 pts) or DNA and RNA seq (12 pts) to assess GA and other biomarkers. Predominant genetic ancestry was assessed using a SNP-based approach and classified as: African (AFR), European (EUR), Central and South American (AMR), South Asian (SAS), or East Asian (EAS). Assessments of tumor mutational burden (TMB), MSI status, genomic signature (GS), gLOH and prediction of germline status were performed. PD-L1 was determined in 2 pts by IHC (1 DAKO 22C3; 1 Ventana SP142). A separate analysis of 317 patients (pts) with stage I-III BSar using NCBD data (2004-2019) was done.

Results: 18 Bsar (11 male, median age 66) were included: 12 leiomyosarcomas (LMS), 3 rhabdomyosarcomas (RMS),3 high grade undifferentiated sarcomas (HGS). 16 pts of EUR ancestry, 1 AMR, 1EAS. Mean driver GA frequency was 4.8 (1-10); mean TMB 2.9 mutations/Mb (0-9.6), all MS stable; 1 tumor was PD-L1 negative, the other had 1-49% TPS. Mean gLOH 10.4% (1.7-16.9%). APOBEC GS was noted in 1/12 (8.3%) with 11/12 (91.7%) with no dominant GS. Relevant germline mutations were predicted in *RB1* (pt with prior retinoblastoma), *VHL* (pt with radiation-treated prostate cancer), *PTEN* (pt with Cowden Syndrome) and *MUTYH* (pt with intestinal polyposis); 1 pt with prior Wilms tumor had somatic GA only. Most frequently identified GA:*TP53* (78%), *ATRX* (22%), *RB1* (22%), *PTEN* (22%), *CDKN2A* (17%) and *RICTOR*, *MLL2*, *DNMT3A*, *MTAP*, *KDM6A*, *TERT*, *HGF*, *NF1* (each 11%). In the BSar NCDB cohort (LMS only, overall survival was shorter in pts treated with surgery (S) and chemotherapy (CM), S and radiotherapy (RT) vs with S alone, HR 2.73 (95%CI 1.28-5.80), HR 2.24 (95%CI 1.03-4.88) respectively, after adjusting for sociodemographic and health factors. Age and tumor size had prognostic role.

Conclusion: CGP of Bsar revealed several GA relevant for clinical trial design and germline mutations requiring dedicated germline testing. Limitations: retrospective nature and confounding.

Alina Basnet:

RET Fusion Driven (*RET*fus+) Non-Small Cell Lung Cancer (NSCLC): A Comprehensive Genomic Profiling (CGP) Study with Histologic Correlation

Prashanth Ashok Kumar, Basnet Alina, Dean Pavlick, Richard Huang, Douglas Lin, Natalie Danziger, Jeffrey Ross, Steven Graziano

Background: *RET*fus+ status is found in 1-2% of NSCLC in the United States and has emerged as a major subtype that can be treated with both broad and focused targeted therapies using RET inhibitors. Our aim was to describe the genomic alterations (GA) that occurred in *RET*fus+ NSCLC and compare it with *RET*fus- NSCLC.
Methods: Retrospective analysis of 424/57,252 (0.7%) NSCLC *RET*fus+ cases, that were centrally evaluated for predominant histology and underwent hybrid capture based CGP to evaluate all classes of GA was done. PD-L1 expression was determined by IHC (Dako 22C3) with TPS ≥50% = high expression. For statistical comparisons, the false discovery rate was corrected using Benjamini-Hochberg adjustment. Fishers exact and Chi square tests were used.
Results: The RETfus+ cases were younger (64.3 vs 68 years, p<.0001), were more often female (Male sex: 48.1 vs 50%, p=0.601) and featured lower GA/tumor (4.6 vs 6, p<.0001). 21/424 (5.0%) of the *RET*fus+ NSCLC featured activating EGFR SV mutations indicating that the *RET* fusions in these cases are likely acquired resistance mutations. *RET*fus+ had lower chance of having a high genome-wide loss-of-heterozygosity score (gLOH) (17.1 vs27.9%, p=0.002), TMB TMB≥10 mut/Mb (6.4 vs 34.2%, p<.0001) and mean TMB (3 VS 9.1, p<.0001). Tobacco genomic signature was lower (2.9 vs27.2%, p=0.001), but APOBEC signature was higher (38.2 vs 12.9, p=0). MSI-high status was low in both groups (0 vs0.5%, p not significant). High PD-L1 IHC staining was higher in *RET*fus+ cases (42.6 vs 32.2%, p=0.005). Noteworthy GA lower in *RET*fus+ included *BRAF*, *EGFR*, *ERBB2*, *FGFR1*, *KRAS*, *MET, NF1*, *PIK3CA*, *RB1*, *STK11* and *TP53*. 333 RETfus+ NSCLC specimens were histologically sub-classified and consisted of 147 (44%) high grade solid non-acinar, 83 (25%) papillary including micro-papillary variants, 42 acinar (13%), 39 (12%) mucinous/signet ring cell, 11 (3%) squamous, 5 (2%) lepidic, 4 (1%) sarcomatoid and 2 (1%) secretory. There were no significant differences in GA among the histologic subtypes.

Conclusions: *RET*fus+NSCLC differs significantly from *RET*fus-NSCLC and have a unique distribution of histologic subtypes, genomic signatures and biomarker frequencies. When stratified by the histologic subtypes, the *RET*fus+ cohorts were not genetically different, suggesting their tumor biology to be driven by the *RET*fus rather than the histology. With the expanded approval of specific RET inhibitors

(selpercatinib) in the pan-cancer treatment setting, further studies analyzing *RET*fusion+ NSCLC histology and GA/biomarker status is warranted.

NSCLC groups	EAS	EUR	*ARID1A*	*BRAF*	*EGFR*	*ERBB2*	*FGFR1*	*KRAS*	*MET*	*NF1*	*PIK3CA*	*RB1*	*STK11*	*TP53*
***RET*fusion+ (0.74%)**	9.00%	69.40%	3.30%	0.70%	5%	0.90%	0.50%	1.90%	0.50%	1.20%	2.60%	3.50%	1.70%	44.80%
***RET*fusion- (99.26%)**	3.90%	80.40%	6.40%	5.40%	15%	3.80%	4.30%	30.80%	2.50%	7.90%	11.30%	8.40%	13.60%	69.60%
P-value	<.0001	<.0001	0.038	<.0001	<.0001	0.006	<.0001	<.0001	0.041	<.0001	<.0001	0.001	<.0001	<.0001

Dibyendu Dutta

GBT1118, a voxelotor analog, ameliorates sickle hepatopathy

Elio Haroun, Seah H Lim and Dibyendu Dutta

Division of Hematology and Oncology, Department of Medicine, State University of New York Upstate Medical University, Syracuse, New York

Abstract

In sickle cell disease (SCD), hepatopathy is a cumulative consequence of ischemia/reperfusion (I/R) injury from vaso-occlusive crisis, tissue inflammation and iron overload. We hypothesized that GBT1118, a voxelotor analog, may ameliorate sickle hepatopathy. Our results show that GBT1118 treatment exhibited reduced hepatic iron overload and inflammation in the liver of SCD mice. There were significant improvements in liver function, demonstrated by a reduction in liver enzymes, bile acids, and total bilirubin levels. Furthermore, GBT1118 treatment prevented liver injury by limiting apoptosis, necrosis, and fibrosis. SCD mice liver had increased ferroptosis as evident from increased ferroptosis markers, including 4-hydroxynonenal (4-HNE), *malondialdehyde* (MDA) levels and expression of *Slc7a11* mRNA, which significantly reduced after GBT1118 treatment. In addition to I/R injury and inflammation, since iron overload, which occurred in SCD liver, also one of the reasons of ferroptosis, we evaluated markers of iron homeostasis in SCD and GBT1118-treated mice liver. There were increase in the expression of heme oxygenase 1, ferritin, hepcidin, and ferroportin mRNA levels in SCD. These parameters reduced significantly following GBT1118 treatment. Together, our results demonstrate that GBT1118 can prevent sickle hepatopathy by preventing haptic injury in the form of reduced inflammation, fibrosis, apoptosis, iron overload and ferroptosis.

GH Ghelani

HPV-16 Positive Clinically Advanced Squamous Cell Carcinoma of the Urinary Bladder (aBSCC): A Comprehensive Genomic Profiling (CGP) Study

GH Ghelani, M Bou Zerdan, J Jacob, PE Spiess, R Li, A Necchi, P Grivas, A Kamat, N Danziger, D Lin, R Huang, B Decker, ES Sokol, L Cheng, JS Ross, G Bratslavsky, A Basnet

Abstract

Background: Advanced Bladder Squamous Cell Carcinoma (aBSCC) is an uncommon form of urinary bladder malignancy when compared with the much higher urothelial carcinoma incidence. We studied the genomic alteration (GA) landscape in a series of aBSCC based on the association with human papilloma virus -16 (HPV-16) to determine if differences in GA would be observed between the positive and negative groups.

Methods: Using a hybrid capture-based FDA-approved CGP assay, a series of 171 aBSCC were sequenced to evaluate all classes of GA. Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on up to 114 loci. Programmed cell death ligand -1 (PD-L1) expression was determined by IHC (Dako 22C3) with lower expression of positivity set at 1-49% and higher expression set at ≥50% expression.

Results: Overall, 11 (6.4%) of the aBSCC were found to harbor HPV-16 sequences. HPV-16+ status was identified slightly more often in women (NS) and in younger patients (P=.04); 2 female patients with aBSCC had prior history of SCC including 1 anal SCC and 1 vaginal SCC. HPV-16+ aBSCC had fewer GA/tumor (P<.0001), and fewer inactivating GA in CDKN2A (P<.0001), CDKN2B (P=.05), TERT promoter (P=.0004) and TP53 (P<.0001). GA in genes associated with urothelial carcinoma including FGFR2 and FGFR3 were similar in both HPV-16+ and HPV-16- aBSCC groups. *MTAP* loss (homozygous deletion) which has emerged as a biomarker for PRMT5 inhibitor-based clinical trials was not identified in any of the 11 HPV+ aBSCC cases which was significantly lower than the 28% positive frequency of *MTAP* loss in the HPV- aBSCC group (P<.0001). MTOR and PIK3CA pathway GA were not significantly different in the 2 groups. Putative biomarkers associated with immunotherapy (IO) response, including MSI and TMB status, were also similar in the 2 groups. PD-L1 expression data was available for a subset of both HPV+ and HPV- cases and showed high frequencies of positive staining which was not different in the 2 groups.

Conclusions: HPV-16+ aBSCC tends to occur more often in women and younger patients. As reported in other HPV-associated squamous cell carcinomas, HPV-16+ aBSCC demonstrates significantly reduced frequencies of inactivating mutations in cell cycle regulatory genes with similar GA in MTOR and PIK3CA pathways. The implication of HPV in the pathogenesis of bladder cancer remains unknown but warrants further exploration and clinical validation.

Prashanth Ashok Kumar:

A Meta-analysis Studying the Utility of Cryotherapy in the Prevention of Peripheral Neuropathy in Breast Cancer Patients Receiving Paclitaxel and Nab-Paclitaxel.

Prashanth Ashok Kumar, Parth Sampat, Vishnu Charan Suresh Kumar, Abigail Smith, Dongliang Wang, Danning Huang, Abirami Sivapiragasam**.**

Background:

Peripheral Neuropathy (PN) caused by paclitaxel adversely impacts the quality of life in Breast Cancer (BC) patients. Cryotherapy using various cooling devices during taxane infusion is a non-invasive strategy to prevent PN, but its efficacy has not been established.

Methods

A systematic search with controlled vocabulary encompassing breast cancer, and paclitaxel was conducted in PubMed, CINHAL, Embase, Scopus, Web of Science Collections, and CENTRA. 405 records were identified, and duplicates were removed. The remaining 371 records were imported into Covidence, and the titles were screened independently by 2 reviewers. 14 [12 Randomized control studies and 2 retrospective studies] were included for the meta-analysis using R package meta. Only studies that analyzed cryotherapy use in BC patients who received paclitaxel or nab-paclitaxel were included for the final analysis. Relative risk (RR) derived from random effects model with Mantel-Haenszel method was used to compare the occurrence of PN between cryotherapy vs placebo groups.

Results

Pooled incidence of Common Terminology Criteria for Adverse Events (CTCAE) grade ≥ 2 PN was 24.85% (81/326) in the cryotherapy arm and 42.35% (72/170) in the placebo arm. Overall RR for CTCAE grade ≥ 2 PN with cryotherapy compared to placebo was 0.45 [0.27,0.77, p=0.0031]. RR for sensory PN was 0.19 [0.05,0.66, p=0.009] and for motor PN was 0.18 [0.03,0.99, p=0.0491]. RR for Patient Neurotoxicity Questionnaire (PNQ) score ≥ D which connotes severe neuropathy was 0.24 [0.09,0.62, p=0.0035]. Cold intolerance was the predominant adverse effect at 15% (37/247). Fingernail paronychia and skin irritation were reported at 0.8% (2/247) each. 5.1% (15/294) stopped cryotherapy use prior to completion.

Discussion

Use of cryotherapy decreased the occurrence of CTCAE grade ≥ 2 PN by 55%. Cold intolerance was the most frequently reported issue with its use but lead to relatively low discontinuation rates in most studies. Given the lack of any severe adverse effect, cryotherapy use must be encouraged for patients receiving paclitaxel and nab-paclitaxel.

Katja Reuter

Enhancing Survivorship for Adolescent and Young Adults with Cancer Using Mixed-Methods Research

Katja Reuter, PhD; Roberto E. Izquierdo, MD; Rahul Seth, MD; Jody Sima, MD,MS

Background: Research to improve the health, care, and support for Adolescent and Young Adult Cancer Survivors (AYACS) is criKcally needed due to the unique challenges this populaKon faces.

Objective: This presentaKon will highlight ongoing research in the Department of Medicine to improve the survivorship of AYACS. Survivorship describes the health and well-being of a person with cancer from the Kme of diagnosis unKl the end of life, including physical, mental, emoKonal, social, and financial effects of cancer, follow-up care, late effects of treatment, cancer recurrence, second cancers, and quality of life.

Examples of ongoing projects:

1. **Upstate Cancer Center pilot grant 2023**:

Examines the impact of cancer on the health-related quality of life (HRQOL) among AYACS to idenKfy AYACS subgroup-specific intervenKon components. Methods include digital storytelling, surveys, and theoreKcal intervenKon mapping based on the TheoreKcal Domains Framework (TDF).

2. **Department of Medicine pilot grant 2023**: Explores gaps and barriers to care and support services among AYAs with thyroid cancer to inform a mulKlevel intervenKon that increases the uptake of AYA-specific care recommendaKons. Methods include focus groups, surveys, and theoreKcal intervenKon mapping based on the Behavior Change Wheel and COM-B model.

3. **Using paCent-reported data from digital and social media**:

a. **Cross-secConal study** of social media presence among AYACS to inform digital intervenCon research. Part 1 analyzed 300 AYACS across six social media, offering pracKcal guidance for social media-based intervenKons. Part 2 examines the health and care needs expressed by AYACS.

b. **Analysis of risky health behavior expressions** (e.g., vaping, alcohol, cannabis use) among AYACS on social media to inform intervenKons.

Conclusion:

AYACS face unique challenges compared to younger and older cancer paKents. We invite students and residents interested in contribuKng to enhancing the cancer journey for AYACS and parKcipaKng in these or similar AYA cancer research iniKaKves

NEPHROLOGY

Ayorinde I Soipe:

Current Trends in Hospice Care Usage for Dialysis Patients in the USA

Publisher assigned DOI pending online activation: https://doi.org/10.1007/s40620-023-01721-w

Authors: Ayorinde I Soipe, MD, MSc [1,2]; John E Leggat, MD, MPH [1]; Ajibola I Abioye, MD, PhD [3]; Kriti Devkota, MD [1]; Fausat Oke, MD [4]; Kunal Bhuta, MD [1,2]; Moshood O Omotayo, MD, PhD [4]

1. Division of Nephrology, Department of Medicine, Upstate Medical University, 750 East Adams St, Syracuse, New York 13210
2. Department of Medicine, Upstate Medical University, 750 East Adams St, Syracuse, New York 13210
3. Department of Global Health and Population, Harvard TH Chan School of Public Health, 665 Huntington Avenue, Boston, Massachusetts 02115
4. Hospice and Palliative Care Buffalo, 225 Como Park Blvd, Buffalo, New York 14227

Background: This study examined the predictors and latest trends in hospice utilization, adequate duration of hospice care, and dialysis discontinuation without hospice enrollment among patients with end stage renal disease (ESRD).

Methods: Data from the United States Renal Data System (USRDS) for ESRD patients who died between January 1, 2012, and December 31, 2019, were analyzed. Chi-square and logistic regression were used to evaluate associations between outcomes of interest and predictors while Joinpoint regression was used to examine trends.

Results: Among 803,049 patients, the median (IQR) age was 71 (17) years, 57% were male, 27% enrolled in hospice, 8% discontinued dialysis before death without hospice enrollment, and 7% remained in hospice for ≥15 days. Patients who are 65 years and older (adjusted odds ratio [aOR]: 2.75, 95% CI: 2.71-2.79) and white race (aOR: 1.79, 95% CI: 1.77-1.81) were more likely to enroll in hospice. White patients (aOR: 0.75, 95% CI: 0.73-0.76) and those who never received a kidney transplant (aOR: 0.75, 95% CI: 0.73-0.78) were less likely to have adequate duration of hospice care. Hospice enrollment and standardized duration of hospice care increased over time, with an average annual percentage change (AAPC) of 1.1% (95% CI:0.6 – 1.6) and 5% (95% CI:2.6 – 7.4) respectively.

Conclusions: Approximately one in every four ESRD patients who died between 2012 and 2019 had a history of hospice enrollment, while one in every 12 discontinued dialysis before death without hospice enrollment. There was an upward trend in the standardized duration of hospice care. Because a certain proportion of ESRD patients who had discontinued dialysis still did not enroll in hospice, there must be

other factors impeding these patients from enrolling in hospice even after discontinuing dialysis, and this observation necessitates further exploration.

Sara Hashemi

Renal transplant failure by COVID-19 associated collapsing glomerulopathy

Sara Hashemi, MD; Asim Ali, MBBS; Irshad Hussein, MBBS; Brian Gallay, MD

Introduction:

Renal involvement in the form of proteinuria, hematuria and Acute kidney injury (AKI) has been reported with COVID-19 infection. Collapsing glomerulopathy (CG) is also recognized as renal manifestation of COVID-19, especially in African Americans (AA).

Methods:

37-year-old AA female with past medical history of ESRD due to IgA nephropathy s/p decease donor renal transplants (DDRT) times three, biopsy proven antibody-mediated rejection after third DDRT (anti-DQ2 >10,000 MFI) treated with methylprednisolone and plasmapheresis presented with COVID pneumonia. Two months after resolution of pneumonia, the patient presented with AKI (serum creatinine: 5.2 mg/dl) and nephrotic proteinuria (9.81 gm protein urine/24 hours). Transplant renal biopsy revealed acute tubular epithelial injury and focal glomeruli with segmental capillary collapsing consistent with collapsing glomerulopathy. The likely cause of AKI was COVID-19 associated CG. Subsequent genetic testing revealed heterozygous apolipoprotein-L1 (APOL1) high-risk allele. The renal transplant donor was African American with unknown APOL1 genetic status.

Discussion

The mechanisms of COVID-CG are direct viral toxic effects and virus-induced cytokine injury to podocytes. Two APOL1 gene risk variants are predominantly found in AA. These variants are not only recognized as risk factors for COVID-CG but are also associated with worse allograft survival. Genetic susceptibility, particularly presence of high-risk APOL-1 genotypes, likely plays crucial role in pathogenesis of CG among African Americans.

Conclusion

Renal Biopsy is essential for Covid-19 related AKI or ATN to identify collapsing FSGS. Genetic testing for high-risk variants of APOL1 in AA patients is important to prognosticate and guide therapy in the future. DNA testing of donor allograft will be crucial to screen for homozygous high-risk alleles. Further research is required to define characteristics, outcome and treatment of CG in presence of high-risk APOL1 alleles.

Michael Lioudis

Effects of tolvaptan discontinuation in patients with autosomal dominant polycystic kidney disease: a post hoc pooled analysis

Michael Lioudis[1], Xiaolei Zhou[2], Eric Davenport[2], Sasikiran Nunna[3*], Holly B. Krasa[4], Dorothee Oberdhan[3] and

Ancilla W. Fernandes[3]

Background Tolvaptan slows kidney function decline in patients with autosomal dominant polycystic kidney disease (ADPKD) who are at risk of rapid progression. Given that treatment requires commitment to long-term use, we evaluated the effects of tolvaptan discontinuation on the trajectory of ADPKD progression.

Methods This was a post hoc analysis of pooled data from two clinical trials of tolvaptan (TEMPO 2:4 [NCT00413777] and TEMPO 3:4 [NCT00428948]), an extension trial (TEMPO 4:4 [NCT01214421]), and an observational study (OVERTURE [NCT01430494]) that enrolled patients from the other trials. Individual subject data were linked longitudinally across trials to construct analysis cohorts of subjects with a tolvaptan treatment duration > 180 days followed by an off-treatment observation period of > 180 days. For inclusion in Cohort 1, subjects were required have ≥ 2 outcome assessments during the tolvaptan treatment period and ≥ 2 assessments during the follow-up period. For Cohort 2, subjects were required to have ≥ 1 assessment during the tolvaptan treatment period and ≥ 1 assessment during the follow-up period. Outcomes were rates of change in estimated glomerular filtration rate (eGFR) and total kidney volume (TKV). Piecewise-mixed models compared changes in eGFR or TKV in the on-treatment and post-treatment periods.

Results In the Cohort 1 eGFR population (n = 20), the annual rate of eGFR change (in mL/min/1.73 m^2) was -3.18 on treatment and -4.33 post-treatment, a difference that was not significant (P = 0.16), whereas in Cohort 2 (n = 82), the difference between on treatment (-1.89) and post-treatment (-4.94) was significant (P < 0.001). In the Cohort 1 TKV population (n = 11), TKV increased annually by 5.18% on treatment and 11.69% post-treatment (P = 0.06). In Cohort 2 (n = 88), the annual TKV growth rates were 5.15% on treatment and 8.16% post-treatment (P = 0.001).

Conclusions Although limited by small sample sizes, these analyses showed directionally consistent acceleration in measures of ADPKD progression following the discontinuation of tolvaptan.

Keywords Autosomal dominant polycystic kidney disease (ADPKD), Tolvaptan, Glomerular filtration rate, Kidney volume, Clinical trial, Treatment

PULMONARY-CRITICAL CARE

Auyon J. Ghosh[1]

Clinical Features of Genetic Resilience in COPD

Auyon J. Ghosh[1], Matthew Moll[2], Brian D. Hobbs[2], Jonathan Hess[3], Liam Coyne[1], Michael H. Cho[2], Frank A. Middleton[4], Andras Perl[5], Edwin K. Silverman[2], Craig P. Hersh[2]*, Stephen J. Glatt[3]*
[1]Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY, 13210
[2]Department of Medicine, Channing Division of Network Medicine, Division of Pulmonary and Critical Care Medicine, , Brigham and Women's Hospital and Harvard Medical School, 75 Francis Street, Boston, MA, 02115
[3]Department of Psychiatry and Behavioral Sciences, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210
[4]Department of Neuroscience and Physiology, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY, 13210
[5]Department of Medicine, Division of Rheumatology, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210

Jointly supervised this study and are co-senior authors

COPDGene was supported by Award Number U01 HL089897 and Award Number U01 HL089856 from the National Heart, Lung, and Blood Institute. COPDGene is also supported by the COPD Foundation through contributions made to an Industry Advisory Board that has included AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Pfizer, and Sunovion.

Disclosures:

AJG received consulting fee from TDA Research, outside of this study. MM received grant support from Bayer, outside of this study. EKS received grant support from GlaxoSmithKline and Bayer. CPH reports grant support from Boehringer-Ingelheim, Novartis, Bayer and Vertex, outside of this study. MHC has received grant support from GlaxoSmithKline and Bayer, consulting fees from Genentech and AstraZeneca, and speaking fees from Illumina.

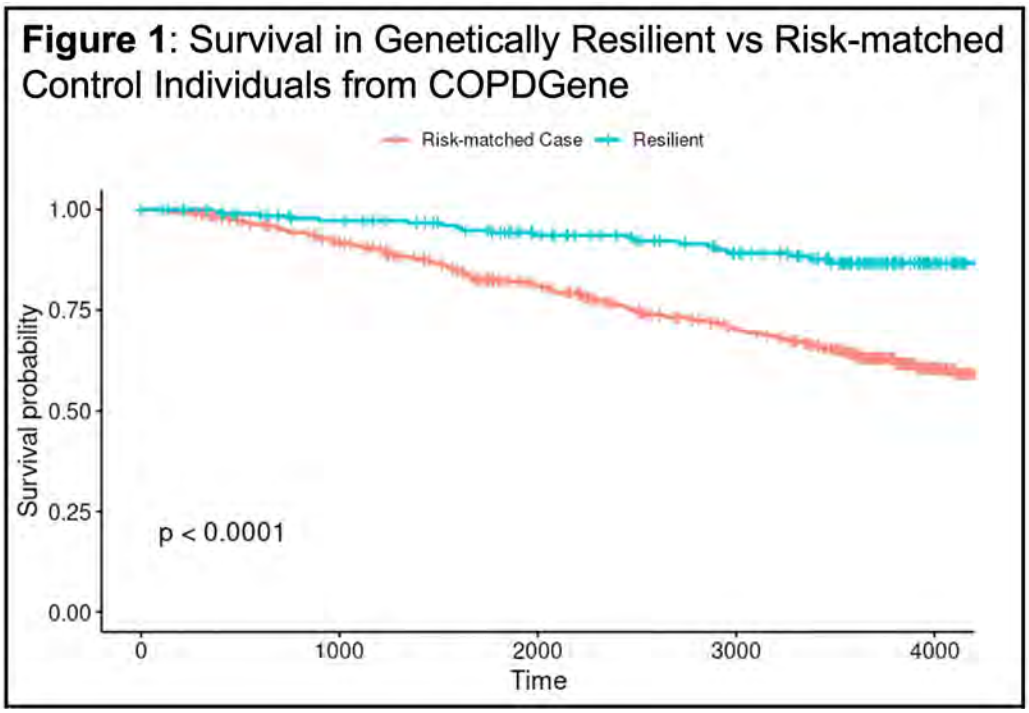
Word count (limit 400): 398

Rationale: In the personalized risk quantification of chronic obstructive pulmonary disease (COPD), genome-wide association studies and polygenic risk scores (PRS), which summarize information from genetic variants across the genome, complement traditional risk factors such as age and cigarette smoking. However, despite being at considerable levels of risk, some individuals do not develop COPD. Research on COPD resilience remains largely unexplored.

Methods: We applied the previously published COPD PRS to whole genome sequencing data from non-Hispanic white (NHW) and African American (AA) individuals in the Genetic Epidemiology of COPD (COPDGene) study. We selected individuals at the highest level of genetic risk, defined as PRS at the 90th percentile or above. Resilient individuals were defined as those at or above the PRS threshold without airflow obstruction ($FEV_1/FVC > 0.70$). We tested for differences in age, gender, current smoking status, smoking pack-years, six-minute walk distance, FEV_1 percent predicted, and percent emphysema on quantitative computed tomography (CT) scans using univariate tests between resilient individuals and genetic risk-matched cases. We tested for differences in FEV_1 and percent emphysema using multivariable models adjusted for age, gender, smoking pack-years, current smoking status, and ancestry. We also performed survival analysis using Kaplan-Meier curves and Cox proportional hazards, adjusted for covariates as above.

Results: We identified 211 resilient individuals without airflow obstruction and 605 genetic risk-matched individuals with COPD from COPDGene. Among both NHW and AA individuals, resilient individuals were more likely to be younger than risk-matched individuals with COPD with higher six-minute walk distance, higher FEV_1 percent predicted, and lower percent emphysema and percent gas trapping. In multivariable analyses, resilient individuals had higher FEV_1 percent predicted (NHW: 41.76%, $p < 0.001$; AA: 39.84%, $p < 0.001$) and lower percent emphysema (NHW: -8.98, $p < 0.001$; AA: -4.52, $p < 0.001$). Survival data were available for all study individuals, who were followed for approximately 10 years. Genetically resilient individuals had a higher survival rate in the unadjusted model (Figure 1). In an adjusted Cox proportional hazard model, the hazard ratio for resilient individuals was 0.35 (95% CI, 0.22 – 0.56; $p < 0.001$).

Conclusion: Genetic resilient individuals, defined by PRS at or above the 90th percentile and unaffected by COPD, have a reduced burden of respiratory symptoms, emphysema and improved survival compared to genetic risk-matched individuals with COPD. Future studies of genetically resilient individuals could lead to biological insights that may be used to prevent and treat COPD.



Rana Prathap Padappayil:

Insurance Status and COVID-19 Outcomes: Observations from the National Inpatient Sample Database

Authors :

1. Rana Prathap Padappayil MBBS, Dishant Shah MBBS, Auyon Ghosh MD MPH

Introduction/Hypothesis:

The COVID-19 pandemic has imposed a significant financial burden on individuals and the US healthcare system. Early estimates have shown that average billing costs for noncomplex COVID-19 hospitalizations vary from $31,339 to $111,213 across the country. This study aims to investigate the influence of insurance status on clinical outcomes in patients hospitalized with COVID-19 infection.

Methods:

Using the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) database for 2020, we identified adult patients hospitalized with COVID-19 infection as the primary admitting diagnosis. Insurance status was categorized into three groups: Medicare, private insurance, and under/uninsured (including Medicaid and self-pay patients). The primary outcome was in-hospital mortality. Secondary outcomes included the need for non-invasive, invasive, and early mechanical ventilation within 24 hours of hospitalization, length of stay, and total hospitalization charges. We performed univariate and multivariable analyses, adjusted for confounding factors such as age, gender, race, median income of the patient's zip code, comorbidity burden, hospital region, size, location, and teaching status. Data analysis was performed using Stata (StataCorp; College Station, TX).

Results:

Compared to patients with Medicare, under/uninsured patients demonstrated higher in-hospital mortality (OR 1.11, 95% CI 1.04-1.18, p-value 0.002). In addition, under/uninsured patients were more likely to undergo intubation and mechanical ventilation, particularly within 24 hours of hospitalization. Patients with private insurance or under/uninsured status also experienced longer lengths of stay and higher average hospitalization charges than patients with Medicare.

Conclusions:

Our study reveals that insurance status significantly impacted clinical outcomes in COVID-19-associated hospitalizations. These findings suggest that cost-related barriers to healthcare access may exist for certain patient populations, particularly the under/uninsured. Equitable access to care is crucial in a pandemic to reduce disease burden. Further investigation is warranted to identify and address these disparities to provide equal access to care for all individuals regardless of insurance status.

Sreechandra Kruthiventi:

Paecilomyces empyema in a renal transplant patient on Carbozantinib.

Sreechandra Kruthiventi MD[1], Carina Hernandez MD PhD[1], SS Prasad Gadula MBBS[1] and Kristopher Paolino MD[2]

[1]Division of Medicine, State University of New York Upstate Medical University, Syracuse, New York; [2]Infectious Disease, State University of New York Upstate Medical University, Syracuse, NY

Introduction. *Paecilomyces* is a common saprobic filamentous fungus and is a member of the Thermoascaceae family, and a rare cause of human infections. The most frequent forms of infections are pulmonary, ophthalmic, sinus and skin infections but can cause disseminated infections in immunocompromised patients. We report a case of *Paecilomyces* empyema in a renal carcinoma patient on Carbozantinib.

Case presentation. We present the case of a male in 60s with a past medical history significant for stage IV left renal cell carcinoma on Carbozantinib initially presented persistent dyspnea and chest pain. Of note, he was treated with antibiotics for pneumonia twice prior to presentation. Infectious workup was negative (sputum and blood culture) at that time, and he was discharged shortly after. During this admission, Computed Tomography demonstrated right sided pneumothorax, consolidation and lung nodules. He was started on broad spectrum antibiotics for pneumonia and underwent right sided chest tube placement. After two days, he developed left sided pneumothorax and had a left sided chest tube placed. Eventually, he became hypoxic, requiring mechanical ventilatory support. His pleural fluid analysis was suggestive of exudate and the cultures initially grew *Pseudomonas* and Zosyn was continued. On D5 pleural fluid grew mold and voriconazole was added for fungal coverage. He was extubated but continued to remain on high flow oxygen and intermittent positive pressure ventilation. He was transitioned to comfort care as per patient's wishes and he passed away the next day. Eventually mold in his pleural fluid was identified as *Paecilomyces* on D11.

Discussion. *Paecilomyces* is a rare fungal infection which causes invasive infections in immunocompromised patients. Tyrosine kinase inhibitors augments risk for invasive fungal infections.This case emphasizes the importance of extended incubation or subcultures to detect fungal infections. Voriconazole has demonstrated good activity and other promising options are ravuconazole and posaconazole.

Sanchit Panda

Impact of Central Line Simulation Training on Improving Confidence of Medical ICU Trainees

Authors: Sanchit Panda, MD; Japjot Chahal, MD; Julia H. Ma; Erin M. Graham, MPH; Auyon Ghosh, MD, MPH; Angela Love, MD

Central venous catheter (CVC) placement is commonly performed in the intensive care unit (ICU) but can be associated with significant adverse events[1]. CVC placement simulation training for learners has been shown to reduce complications[2,3]. We developed a curriculum for simulation training, led by pulmonary and critical care medicine fellows, that focused on performing the 10 core steps of CVC placement, with an emphasis on ultrasound guidance for internal jugular (IJ) vein access. We hypothesized that implementation of our curriculum would lead to an increase in learners' confidence in CVC placement.To evaluate the effectiveness of the simulation training, pre- and post-session survey data was collected from learners over 6 months. The surveys aimed to measure the participants' confidence levels in specific steps of central line placement using a Likert scale. We compared pre- and post-simulation scores using univariate non-parametric paired tests (Wilcoxen signed rank test). A Bonferroni correction was used to set a p value threshold of 0.01 for statistical significance. Statistical analysis was performed using R (version 4.3.1). 36 participants, including 31 (86%) resident physicians, 1 physician assistant student, 1 fellow, and 3 medical students, completed pre- and post-simulation training surveys. We found a significant increase in confidence in IJ CVC placement without supervision (mean change 1.3, $p < 0.001$), confidence in identifying anatomic structure prior to CVC placement (mean change 0.97, $p < 0.001$), confidence in needle maneuvering (mean change 0.89, $p < 0.001$), confidence in guidewire positioning (mean change 1.11, $p <0.001$), and confidence in advancing the catheter (mean change 0.92, $p < 0.001$) across participating learners. These findings demonstrate the effectiveness of dedicated simulation training sessions in enhancing trainees' confidence in various aspects of central line placement. The improvement in confidence levels could lead to improving procedural proficiency and reducing adverse events associated with CVC placement.

References

1. Kornbau C, Lee KC, Hughes GD, Firstenberg MS. Central line complications. *Int J Crit Illn Inj Sci*. 2015;5(3):170-178. doi:10.4103/2229-5151.164940

2. Use of simulation-based mastery learning to improve the quality of central venous catheter placement in a medical intensive care unit - Barsuk - 2009 - Journal of Hospital Medicine - Wiley Online Library. Accessed August 1, 2023. https://shmpublications.onlinelibrary.wiley.com/doi/abs/10.1002/jhm.468

3. Simulation-based mastery learning reduces complications duri... : Critical Care Medicine. Accessed August 1, 2023. https://journals.lww.com/ccmjournal/Abstract/2009/10000/Simulation_based_mastery_learning_reduces.3.aspx

4. Barsuk JH, Cohen ER, McGaghie WC, Wayne DB. Long-Term Retention of Central Venous Catheter Insertion Skills After Simulation-Based Mastery Learning. *Academic Medicine*. 2010;85(10):S9. doi:10.1097/ACM.0b013e3181ed436c

RHEUMATOLOGY-CLINICAL IMMUNOLOGY

Christian Geier[1]

An unorthodox HLA-DR^{hi} 'Hybrid' population in Rheumatoid Arthritis characterized using Spectral Cytometry

Christian Geier[1], Haani Qudsi[2], Jihad BenGabr[1], Robert Winchester[3], Andras Perl[1]

[1] Division of Rheumatology & Clinical Immunology, SUNY Upstate Medical University, Syracuse, NY
[2] Norton College of Medicine, SUNY Upstate Medical University, Syracuse, NY
[3] Division of Rheumatology, Columbia University, New York, NY

Background/Purpose

Many rheumatoid arthritis (RA) patients 'share' a sequence within HLA-DR (DR) expressed on antigen-presenting cells (APC) — suggesting that DR^{hi} APC are important in RA. We wanted to determine whether DR^{hi} immune cells expressing granulocyte-associated molecules contribute to alterations of the DR^{hi} pool in RA.

Methods

We studied individuals with RA and matched healthy donors (n=16 each) by flow cytometry. We isolated blood immune cells by Ficoll gradient centrifugation; we gated on DR^{hi} — excluding lymphocytes and non-viable cells (Fig. 1A) — and quantified the contribution of CD15^{+} cells to the non-lymphoid DR^{hi} pool and their expression (MFI) of co-modulatory molecules. We used t-SNE to clarify the phenotype of the DR^{hi}CD15^{+} population. We used bi-axial gating to validate t-SNE observations and to quantify features of DR^{hi}CD15^{+}. Kruskal-Wallis testing was performed to assess for significant differences.

Results

In RA we found a non-lymphoid DR^{hi}CD15^{+} population that was virtually absent in healthy donors (0.78% vs. 0.13% of non-lymphoid DR^{hi}; p=0.02, Fig. 1B/2B); these cells have near uniform CD16 co-expression (Fig 1A, gated in last plot) yet differ from granulocytes by co-expression of CD303 (plasmacytoid (pDC) marker; Fig. 2A/B; circled). CD123, highly expressed by pDC, was not expressed. Given their shared granulocytic/pDC features we designate them DR^{hi} 'Hybrid' cells. Hybrids formed a separate cluster in RA that co-expressed CD83 and CD275 (ICOS-L) (Fig. 2A, circled population). Lack of CD45RA separated DR^{hi}Hybrids from their apparent *bone fide* pDC counterparts (Fig. 3A/B, p<0.001).

Conclusion

$DR^{hi}CD15^{+}$ cells contribute to the DR^{hi} pool in RA. Because these low-density cells share features with both granulocytes and pDCs we refer to them as DR^{hi}Hybrids; their expression of CD303 challenges the notion that this molecule is pDC-specific. Joint expression of DR^{hi}, CD83, CD275 suggests their potential to pro-inflammatory antigen presentation. These apparently new DR^{hi} Hybrids and other unorthodox DR^{hi} populations are potential treatment targets in RA.

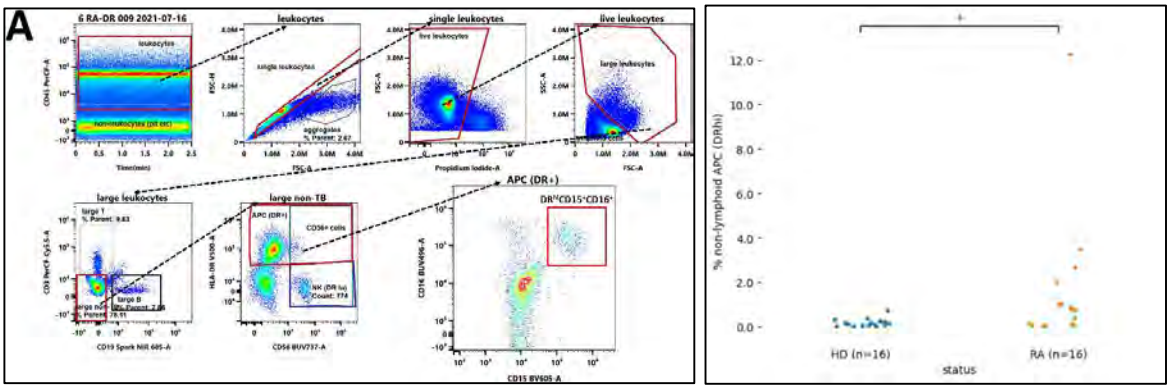


Figure 1. Flow cytometry and quantification of non-lymphoid $DR^{hi}CD15^{+}$ in RA. A) Gating strategy, patient with severe RA shown. B) $DR^{hi}CD15^{+}$ quantification in healthy donors (HD; blue) and RA (orange) and as percentage of non-

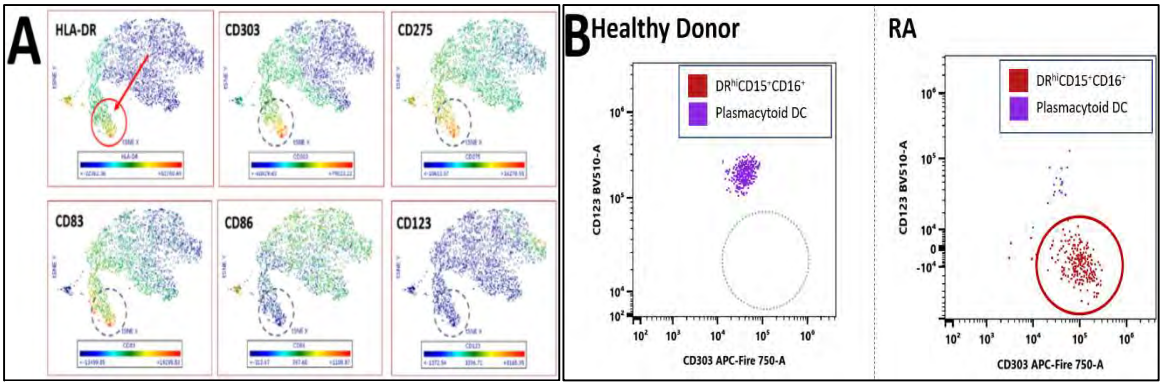


Figure 2. Non-lymphoid $DR^{hi}CD15^{+}CD16^{+}$. A) t-SNE from an RA patient with debilitating polyarthritis population (red circle and arrow) highlighting co-expression of CD303, CD83, CD275; lack of CD123. Red: high expression. Blue: low expression. B) Bi-axial gating of $DR^{hi}CD15^{+}CD16^{+}$ and pDC reference populations. CD303 x-axis, CD123 y-axis. Left

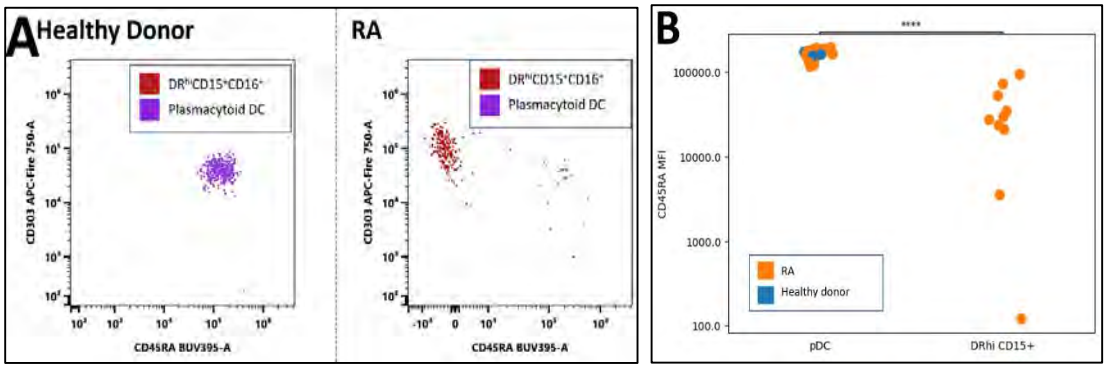


*Figure 3. Comparison of CD303⁺ DR^{hi}Hybrids with CD303⁺ plasmacytoid DC. A) CD45RA and CD303 expression in healthy donor plasmacytoid DC (left; purple) and RA (with presence of DR^{hi} hybrids) B) Quantification of CD45RA MFI of CD303⁺ pDC from RA (orange) and HD (blue) and CD303⁺ DR^{hi} Hybrids. logarithmic scale. Kruskal-Wallis Test **** p= 0.0008324*

Sandy Nasr:

Associations between antiphospholipid antibodies and thromboembolic events in COVID-19 infected and COVID-19 vaccinated patients: a single-center retrospective analysis.

Sandy Nasr[1], Andras Perl[2], [1,2,]SUNY Upstate Medical University, Syracuse, NY.

Introduction/Background: Several months after the introduction of mass COVID-19 vaccination campaign, concerns were raised in regards to possible association between unexpected thromboembolic events and COVID-19 vaccines. Although there were no safety issues that emerged in clinical trials compared to the placebo group, there were some case reports that did describe the development of thrombotic events following these events. It is still unclear how these two are connected, although an immune-mediated mechanism, similar to what happens in antiphospholipid syndrome, could be a possibility. A similar observation was noted in COVID-19 infected patients with occurrence of thromboembolic events during or after the COVID-19 infection. It is hypothesized that the occurrence of thromboembolic events in COVID-19-vaccinated and COVID-19-infected populations might be due to pre-existent antiphospholipid antibodies with these acting as the first trigger in a two hit pathogenetic scenario.

Objective: determine whether there is an association between the presence of antiphospholipid antibodies and the occurrence of thromboembolic events in two populations of patients: COVID-19-vaccinated and COVID-19-infected patients.

Methods: Electronic medical records of SUNY Upstate Medical University Hospital patients who tested positive for COVID-19 and patients who were vaccinated for COVID-19 were reviewed between January 2020 and February 2023. In these two populations, we tracked the levels of cardiolipin IgA, IgM, IgG, beta2 glycoprotein IgA, IgM, IgG, hexagonal phase, platelet neutralization, DRVVT, and antiphophatidylserine IgA, IgM, IgG and we checked whether those patients were diagnosed with any of the following thromboembolic events at any point in time: DVT (deep vein thrombosis), portal vein thrombosis, cerebral vein thrombosis, subclavian vein thrombosis, PE (pulmonary embolism), stroke, miscarriage , MI (myocardial infarction), gangrene and arterial thrombosis. Then we used GraphPad software to calculate the sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio for each blood test and diagnosis.

Results: Results are displayed in tables 1 through 4 below. In total, 42865 COVID-19-vaccinated patients and 6955 COVID-19-infected patients were found. Table 1 shows the numbers of patients with positive and negative blood tests and whether they had or did not have a thrombotic event among patients who were vaccinated for COVID-19. Table 3 shows the numbers of patients with positive and negative blood tests and whether they had or did not have a thrombotic event among patients who were infected with COVID-19. Tables 2 and 4 show the sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio for each of the blood tests and thrombotic events in patients who were vaccinated for COVID-19 and infected with COVID-19 respectively. Missing values are those that cannot be calculated because the denominator of the formula is zero.

The blood tests mentioned below have a specificity and negative predictive value of more than or equal to 90% for each of the following diagnoses (Abbreviations used: cardio for cardiolipin; B2 for Beta-2 glycoprotein):

In COVID-19 Vaccinated patients:

DVT cardio IgA, IgM, IgG; B2 IGM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG.

Portal vein thrombosis: cardio IgA, IgM, IgG; B2 IgM, and IgG; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG

Cerebral vein thrombosis: cardio IgA, IgM, IgG; platelet neutralization, DRVVT; Anti-phosphatidylserine IgA.

Subclavian vein thrombosis: cardio IGA, cardio IgM, cardio IgG; B2 IgM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG.

Pulmonary embolism: cardio IgA, cardio IgM, cardio IgG; B2 IgM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG.

Stroke: cardio IgA, cardio IgM, cardio IgG; B2 IgM; platelet neutralization, DRVVT; Anti-phosphatidylserine IgA and IgG.

Miscarriage: cardio IgA, cardio I GM, cardio IgG; B2 IgM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG

Myocardial infarction: cardio IgA cardio IgM, cardio IgG; B2 IgM; platelet neutralization, DRVVT; Anti-phosphatidylserine IgA and IgG.

Gangrene: cardio IgA, cardio IgM, cardio IgG; B2 IgM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG.

Arterial thrombosis: cardio IgA, cardio IgM, cardio IgG; B2 IgM; platelet neutralization; DRVVT; Anti-phosphatidylserine IgA and IgG.

In COVID-19-infected patients:

DVT: cardio IgA, IgM, IgG; B2 IgA, B2 IgM, B2 IgG; platelet neutralization, Hexagonal phase, and DRVVT; Anti-phosphatidylserine IgA, IgM and IgG.

Portal vein thrombosis: cardio IgA, IgM, IgG; B2 IgA, B2 IgM, B2 IGG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Cerebral vein thrombosis: cardio IGA, IgM, IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA, IgG.

Subclavian vein thrombosis: cardio IgA, cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Pulmonary embolism: cardio IgA, cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Stroke: cardio IgA, cardio IgM, cardio IG; B2 IgA, B2 IgM, B2 IgG specificity and NPPV; DRVVT; Anti-phosphatidylserine IgA and IgG.

Miscarriage: cardio IgA, cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG specificity and NPPV; DRVVT; Anti-phosphatidylserine IgA and IgG.

Myocardial infarction: cardio IgA cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Gangrene: cardio IgA, cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Arterial thrombosis: cardio IgA, cardio IgM, cardio IgG; B2 IgA, B2 IgM, B2 IgG; DRVVT; Anti-phosphatidylserine IgA and IgG.

Conclusion: Many of the antiphospholipid antibodies have an elevated (90% or higher) specificity and negative predictive value for thromboembolic events in both COVID-19-vaccinated and COVID-19-infected patients. Interestingly, none of those blood tests has a high sensitivity nor positive predictive value. However, this study was done over a short period of time following the COVID 19 infection or vaccination. Therefore, it is important to continue following those patients on the long run to determine whether there are additional associations.

Joy Park:

Rab4A controls the depletion of IL-2 in CD4+ T cells via enhanced CD38 expression: Potential involvement in proinflammatory lineage development in systemic lupus erythematosus

Authors: Park, Joy S.; Wang, Xiaojing; Godavarthy, Aparna; Patel, Akshay; Krakko, Daniel; Nolan, Jessica; Chilton, Joanne; Blaker, Bryan; Perl, Andras

Background/Purpose: HRES-1/Rab4 (Rab4A) is a small GTPase that is overexpressed in SLE patient T cells[1,2], mediates the enhanced recycling of CD3 and CD4 cell surface receptors[1,2], and the activation of the mechanistic target of rapamycin (mTOR)[3]. Recently, increased expression of CD38[4], mTOR activation[5], and loss of IL-2 production[6,7] have been implicated in pro-inflammatory T cell development in SLE. In this study, we investigated the impact of Rab4A on the expression of CD38 and the secretion of IL-2 and characterized the impact of CD38 expression on the activation of mTOR in $CD4^+$ T cells.

Methods: To understand the cellular consequences of Rab4A overexpression, our lab has created unique Rab4A-mutant Jurkat cell lines, which contain GFP-expressing vector alone (control), doxycycline-inducible vectors that overexpress Rab4A ($Rab4A^{++}$) or the dominant-negative mutant $Rab4A^{S27N}$ ($Rab4A^{DN}$)[8]. We also CRISPR knocked out (KO) CD38 in these cell lines, leading to six different lines: (1) $Rab4A^{WT}$ $CD38^{WT}$, (2) $Rab4A^{WT}$ $CD38^{KO}$, (3) $Rab4A^{++}$ $CD38^{WT}$, (4) $Rab4A^{++}$ $CD38^{KO}$, (5) $Rab4A^{DN}$ $CD38^{WT}$, and (6) $Rab4A^{DN}$ $CD38^{KO}$. These cells were cultured with doxycycline and co-stimulated with anti-CD3 mAb (OKT3) and phorbol myristate acetate (PMA) to induce cytokine production[9]. Cell surface markers and cytokines were analyzed by flow cytometry and protein levels by western blot. NAD^+ levels were measured by LC-MS/MS. To understand the impact of CD38 expression on mTOR activation, we isolated peripheral blood mononuclear cells from SLE patients (n=21) and age, sex, and race matched healthy controls (n=18). The cells were cultured for 24 hours with and without CD3/CD28 co-stimulation and were analyzed by flow cytometry.

Results: In the $Rab4A^{++}$ cells compared to the control, CD38 expression was upregulated ($p=2.49x10^{-13}$), intracellular production and secretion of IL-2 significantly decreased ($p=1.16x10^{-7}$ and p=0.0401, respectively), NAD^+ concentration decreased (p=0.0039), while pSTAT3 levels increased (p=0.0318). In the $Rab4A^{++}$ $CD38^{KO}$ cells compared to the $Rab4A^{++}$ $CD38^{WT}$ cells, secretion of IL-2 significantly increased (p=0.0145) and pSTAT3 levels decreased. pAkt1 was increased significantly in $CD38^+$ $CD4^+$ T cells compared to $CD38^-$ $CD4^+$ T cells in only the SLE patients (p=0.0004), while p4EBP1 increased significantly in $CD38^+$ $CD4^+$ T cells compared to $CD38^-$ $CD4^+$ T cells for both the SLE patients (p=0.0053) and healthy controls (p=0.0057).

Conclusion: The increased pAkt1 and p4EBP1 in SLE patients' $CD38^+$ $CD4^+$ T cells suggests that CD38 activates mTOR via Akt, coinciding with a recent finding of CD38/PI3K/Akt/mTOR axis in cervical cancer[10]. CD38 is an NAD^+ hydrolase, which regulates Sirtuin-1 activity, a NAD^+-dependent histone deacetylase that suppresses STAT3 activity. STAT3 activation is also known to be regulated by mTOR[11–13]. Elevated pSTAT3 levels may underlie diminished IL-2 production by binding to the promoter of *FoxO1,* which inhibits IL-2 production. The overexpression of Rab4A, increased CD38, pAkt1, p4EBP1, and pSTAT3, and diminished IL-2 production reflect changes observed in SLE patients. Our results suggest that increased expression of Rab4A and CD38 may underlie the diminished secretion of IL-2 in SLE.

Figures:

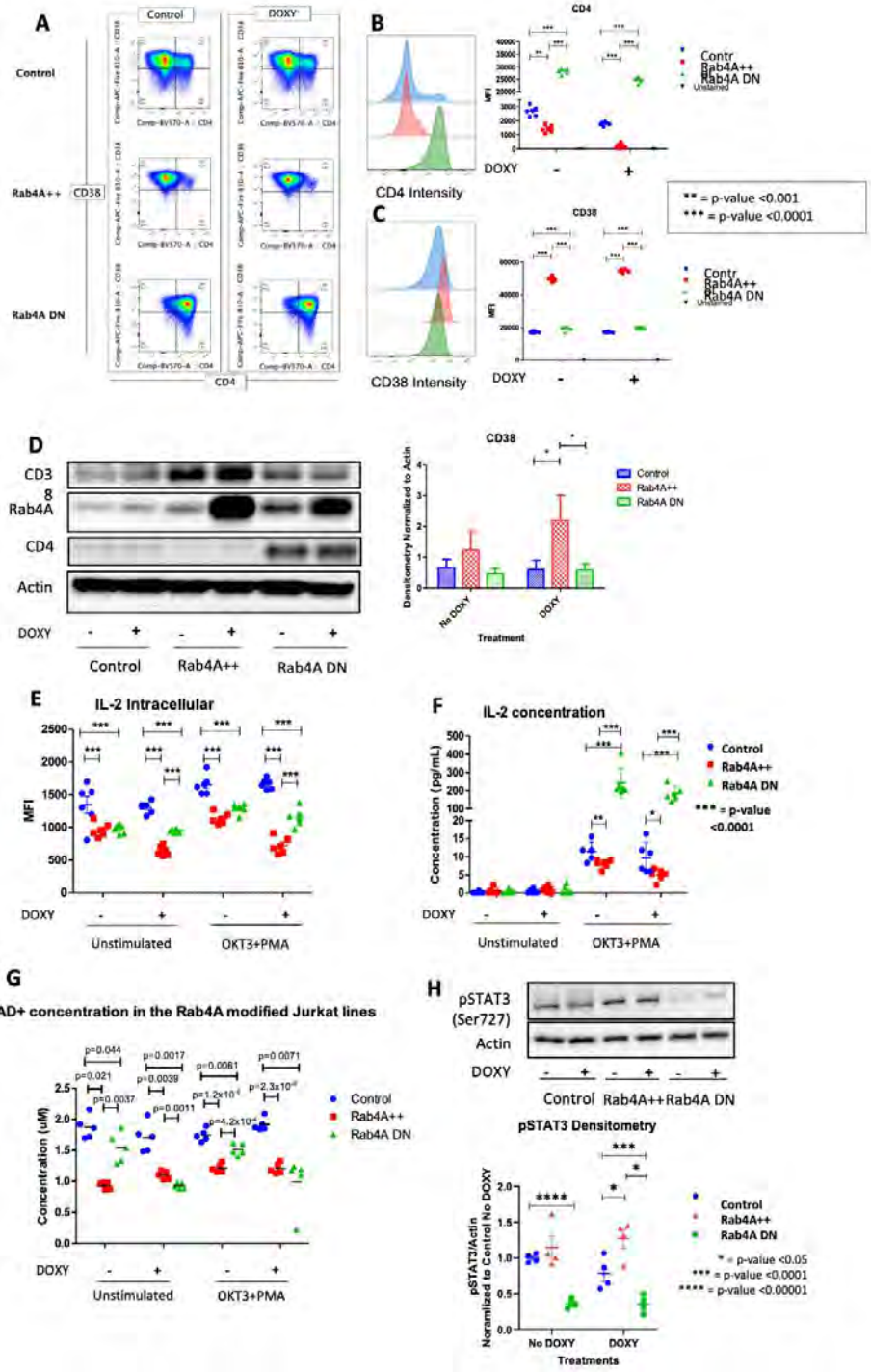


Fig. 1. Rab4A controls the surface expression of CD4 and CD38 in Jurkat cells. **(A)** Flow cytometry and **(D)** Western Blot results show that Rab4A++ cells have increased CD38 expression compared to the control and Rab4A-DN cells. Rab4A effects on CD4 expression is shown for confirmation. Quantified fluorescent intensity of **(B)** CD4 and **(C)** CD38. Rab4A controls the **(E)** intracellular expression and **(F)** production of IL-2, **(G)** NAD^+ levels and **(H)** pSTAT3 (Ser727) levels in Jurkat cells. **(E)** Intracellular production and **(F)** secretion of IL-2 were significantly decreased in the $Rab4A^{++}$ cells (fold change=-0.566, $p=1.16x10^{-7}$ and fold

change=-0.481, p=0.0401, respectively) compared to the control. In the Rab4A^{DN} cells, IL-2 secretion was significantly increased (fold change=18.091, p=7.513x10^{-7}, respectively). **(G)** LC-MS shows NAD^{+} is significantly decreased in in the Rab4A^{++} cells, compared to the control (doxycycline only: fold change=0.647, p=0.0039; doxycycline treated and stimulated: fold change=0.632, p=2.3x10^{-6}). **(H)** In Rab4A^{++} cells, pSTAT3 is increased compared to the control (fold change=2.052, p=0.0318).

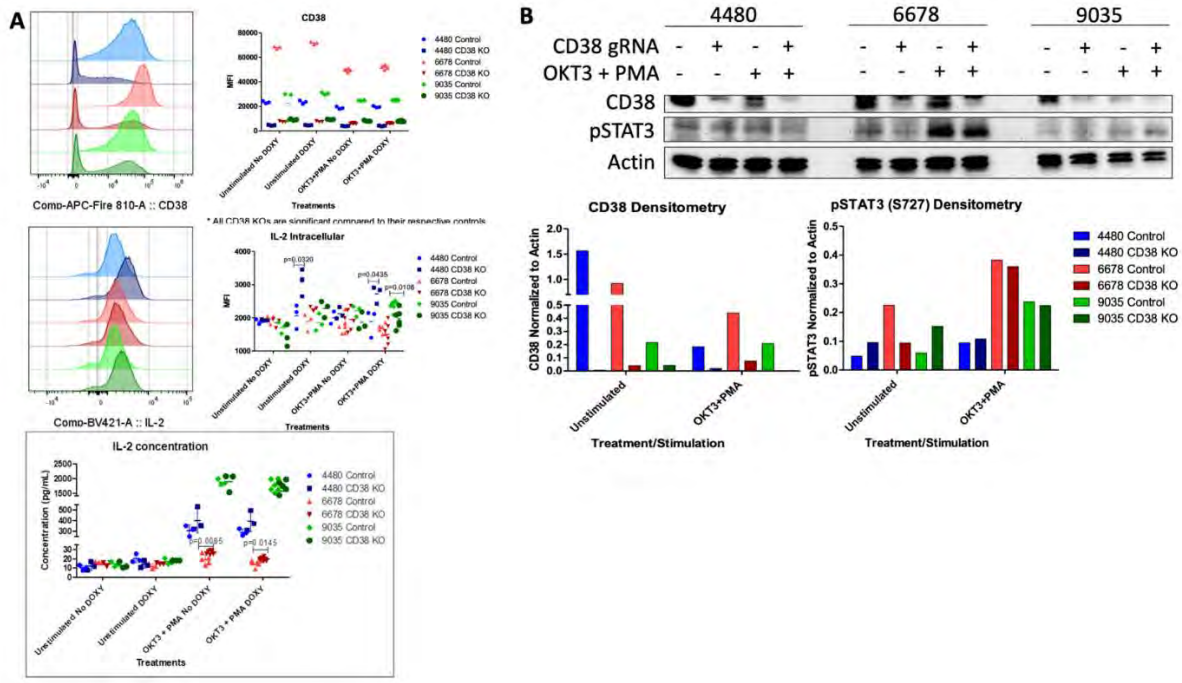


Figure 2. Knocking out CD38 in Rab4A-overexpressed Jurkat cells **(A)** increases IL-2 production (p=0.0145) and **(B)** decreases pSTAT3.

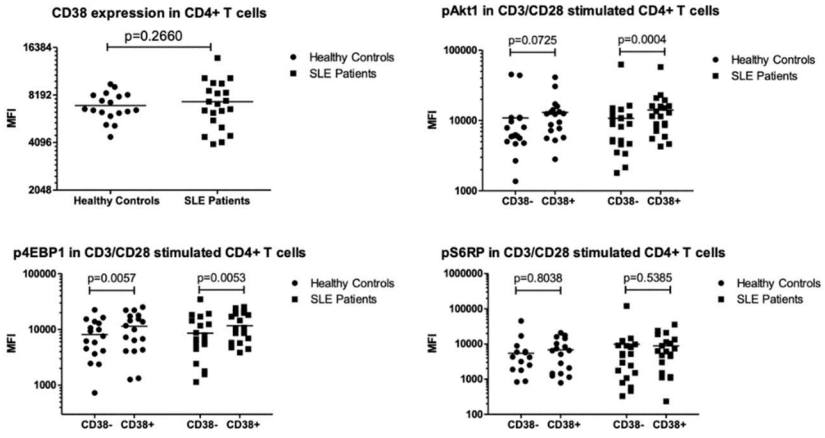


Figure 3. In SLE patients' CD38^{+} CD4^{+} T cells compared to CD38^{-} CD4^{+} T cells, pAkt1 (p=0.0004) and pEBP1 (p=0.0053) are increased.

Works cited:

1. Fernandez DR, Telarico T, Bonilla E, et al. Activation of mTOR controls the loss of TCRζ in lupus T cells through HRES-1/Rab4-regulated lysosomal degradation. *J Immunol*. 2009;182(4):2063-2073. doi:10.4049/jimmunol.0803600
2. Caza TN, Fernandez DR, Talaber G, et al. HRES-1/Rab4-mediated depletion of Drp1 impairs mitochondrial homeostasis and represents a target for treatment in SLE. *Ann Rheum Dis*. 2014;73(10):1888-1897. doi:10.1136/annrheumdis-2013-203794
3. Godavarthy A, Kelly R, Jimah J, et al. Lupus-associated endogenous retroviral LTR polymorphism and epigenetic imprinting promote HRES-1/RAB4 expression and mTOR activation. *JCI Insight*. 2020;5(1):134010. doi:10.1172/jci.insight.134010
4. Chatterjee S, Daenthanasanmak A, Chakraborty P, et al. CD38-NAD+Axis Regulates Immunotherapeutic Anti-Tumor T Cell Response. *Cell Metab*. 2018;27(1):85-100.e8. doi:10.1016/j.cmet.2017.10.006
5. Kurebayashi Y, Nagai S, Ikejiri A, et al. PI3K-Akt-mTORC1-S6K1/2 Axis Controls Th17 Differentiation by Regulating Gfi1 Expression and Nuclear Translocation of RORγ. *Cell Reports*. 2012;1(4):360-373. doi:10.1016/j.celrep.2012.02.007
6. Linker-Israeli M, Bakke AC, Kitridou RC, Gendler S, Gillis S, Horwitz DA. Defective production of interleukin 1 and interleukin 2 in patients with systemic lupus erythematosus (SLE). *Journal of Immunology*. 1983;130(6):2651-2655.
7. Laurence A, Tato CM, Davidson TS, et al. Interleukin-2 signaling via STAT5 constrains T helper 17 cell generation. *Immunity*. 2007;26(3):371-381. doi:10.1016/j.immuni.2007.02.009
8. Nagy G, Ward J, Mosser DD, et al. Regulation of CD4 Expression via Recycling by HRES-1/RAB4 Controls Susceptibility to HIV Infection. *Journal of Biological Chemistry*. 2006;281(45):34574-34591. doi:10.1074/jbc.M606301200
9. Weiss A; W. The role of T3 surface molecules in the activation of human T cells: a two-stimulus requirement for IL-2 production refelcts events occurring at a pre-translational level. *J Immunol*. 1984;133.
10. Liao S, Liang L, Yue C, et al. CD38 is involved in cell energy metabolism via activating the PI3K/AKT/mTOR signaling pathway in cervical cancer cells. *Int J Oncol*. 2020;57(1):338-354. doi:10.3892/ijo.2020.5040
11. Yokogami K, Wakisaka S, Avruch J, Reeves SA. Serine phosphorylation and maximal activation of STAT3 during CNTF signaling is mediated by the rapamycin target mTOR. *Curr Biol*. 2000;10(1):47-50. doi:10.1016/s0960-9822(99)00268-7
12. Dodd KM, Yang J, Shen MH, Sampson JR, Tee AR. mTORC1 drives HIF-1α and VEGF-A signalling via multiple mechanisms involving 4E-BP1, S6K1 and STAT3. *Oncogene*. 2015;34(17):2239-2250. doi:10.1038/onc.2014.164
13. Bezzerri V, Vella A, Calcaterra E, et al. New insights into the Shwachman-Diamond Syndrome-related haematological disorder: hyper-activation of mTOR and STAT3 in leukocytes. *Sci Rep*. 2016;6(1):33165. doi:10.1038/srep33165

Akshay Patel:

T Cell-Specific Deletion of Rab4A Leads to Hepatic mTOR Activation, Liver Inflammation, and Reduction of Regulatory T Cell Expression in Systemic Lupus Erythematosus

Authors: Patel, Akshay[1,2]; Huang, Nick[1,2]; Park, Joy[1,2]; Wyman, Brandon[1,2]; Duarte, Manuel[2]; Lewis, Josh[2]; Banki, Katalin[3]; Perl, Andras[1,2,4]

Departments of Biochemistry and Molecular Biology[1], Medicine[2], Pathology[3], and Microbiology and Immunology[4], SUNY Upstate Medical University

HRES-1/Rab4 (Rab4A) is a GTPase that mediates accumulation of oxidative stress-generating mitochondria[1] and activation of the mechanistic target of rapamycin (mTOR)[2] in T cells of systemic lupus erythematosus (SLE) patients[3] and livers of SLE-prone mice[4]. We investigated the impact of Rab4A on liver disease, mTOR activation, and immunity in SLE-prone mice. Constitutively active Rab4A ($Rab4A^{Q72L}$) and T cell-specific deletion of Rab4A ($Rab4A^{CD4KO}$) were generated on lupus prone *SLE1.2.3. B6*-triple congenic (B6.TC) mice. Rapamycin 3µg/g (or carboxymethylcellulose vehicle control) was administered to 27-week-old B6.TC mice 3 times weekly for 14 weeks. Liver chunks were homogenized for Western Blot analysis or fixed in formalin for histopathology and splenocytes were analyzed by flow cytometry. The number of inflammatory cells, inflammatory foci, and cells/focus were used to measure inflammation and normalized to surface area. Immunohistochemistry was analyzed by Aperio ImageScope. Data are presented as mean±standard error or as percent change. Student's t-test was used to test significance; p values <0.05 were considered significant for hypothesis testing. Among vehicle-treated mice, B6.TC.$Rab4A^{CD4KO}$ livers had more inflammatory foci/mm^2 (0.39±0.092) compared to B6.TC.$Rab4A^{Q72L}$ livers (0.13±0.027; p=0.0498). B6.TC.$Rab4A^{CD4KO}$ livers had elevated p-4EBP1, a target of mTORC1, compared to B6.TC.$Rab4A^{Q72L}$ livers (p=0.0065). B6.TC.$Rab4A^{CD4KO}$ livers had more $CD3^+$ pixels/mm^2 (664126±113298) compared to $B6.TC^{WT}$ (270447±68656; p=0.019) and B6.TC.$Rab4A^{Q72L}$ (135154±10457; p=0.042) and more $B220^+$ Pixels/mm^2 (19837±973) compared to B6.TC.$Rab4A^{Q72L}$ mice (5683±2169; p=0.004). CD3 and B220 clustered together within the inflammatory foci of the B6.TC.$Rab4A^{CD4KO}$ livers. Flow cytometry of B6.TC.$Rab4A^{CD4KO}$ splenocytes showed a 65% decrease in the populations of $FoxP3^+CTLA\text{-}4^+$ $CD4^+$ T cells (p=0.0486) and a 45% decrease in $FoxP3^+Helios^+$ (p=0.033) $CD4^+$ T cells compared to B6.TC.$Rab4A^{Q72L}$ mice. Flow cytometry of B6.TC.$Rab4A^{CD4KO}$ liver-infiltrating lymphocytes showed an 87% decrease in the populations of $FoxP3^+CTLA\text{-}4^+$ $CD4^+$ T cells (p=0.00368) and an 84% decrease in $FoxP3^+Helios^+$ (p<0.001) $CD4^+$ T cells compared to B6.TC.$Rab4A^{Q72L}$ mice. T cell-specific deletion of Rab4A promoted inflammation, mTOR activation, and T and B cell clustering in the livers of lupus-prone B6.TC mice, which may be driven by defects in regulatory T cell populations.

Please Note: "Works Cited" and "Figures" are not part of the abstract; just here for completeness, as the superscripts reference the works cited. The final poster will have a works cited section with all 5 references and figures. Thank You!

Works Cited:

1. Caza TN, Fernandez DR, Talaber G, et al. HRES-1/Rab4-mediated depletion of Drp1 impairs mitochondrial homeostasis and represents a target for treatment in SLE. *Ann Rheum Dis*. Oct 2014;73(10):1888-97. doi:10.1136/annrheumdis-2013-203794

2. Godavarthy A, Kelly R, Jimah J, et al. Lupus-associated endogenous retroviral LTR polymorphism and epigenetic imprinting promote HRES-1/RAB4 expression and mTOR activation. *JCI Insight*. Jan 16 2020;5(1)doi:10.1172/jci.insight.134010
3. Fernandez DR, Telarico T, Bonilla E, et al. Activation of mammalian target of rapamycin controls the loss of TCRzeta in lupus T cells through HRES-1/Rab4-regulated lysosomal degradation. *J Immunol*. 2009;182(4):2063-2073. doi:10.4049/jimmunol.0803600
4. Oaks Z, Winans T, Caza T, et al. Mitochondrial Dysfunction in the Liver and Antiphospholipid Antibody Production Precede Disease Onset and Respond to Rapamycin in Lupus-Prone Mice. *Arthritis Rheumatol*. Nov 2016;68(11):2728-2739. doi:10.1002/art.39791

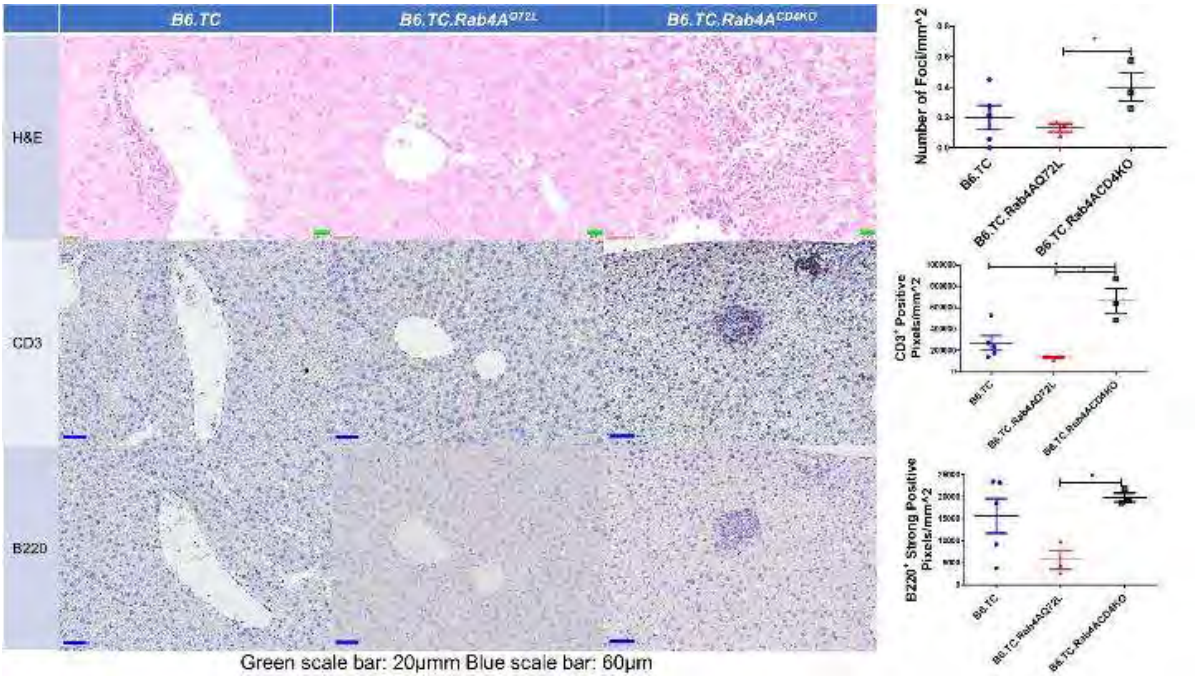


*Figure 2. Representative pathology images showing H&E-, CD3-, and B220-stained liver sections from B6.TC mice show that T cell-specific deletion of Rab4A significantly increases inflammation (inflammatory foci/mm^2) and T and B cell infiltration (IHC Pixels/mm^2) in the livers of B6.TC mice. *: p<0.05; green scale bar: 20µm; blue scale bar: 60µm.*

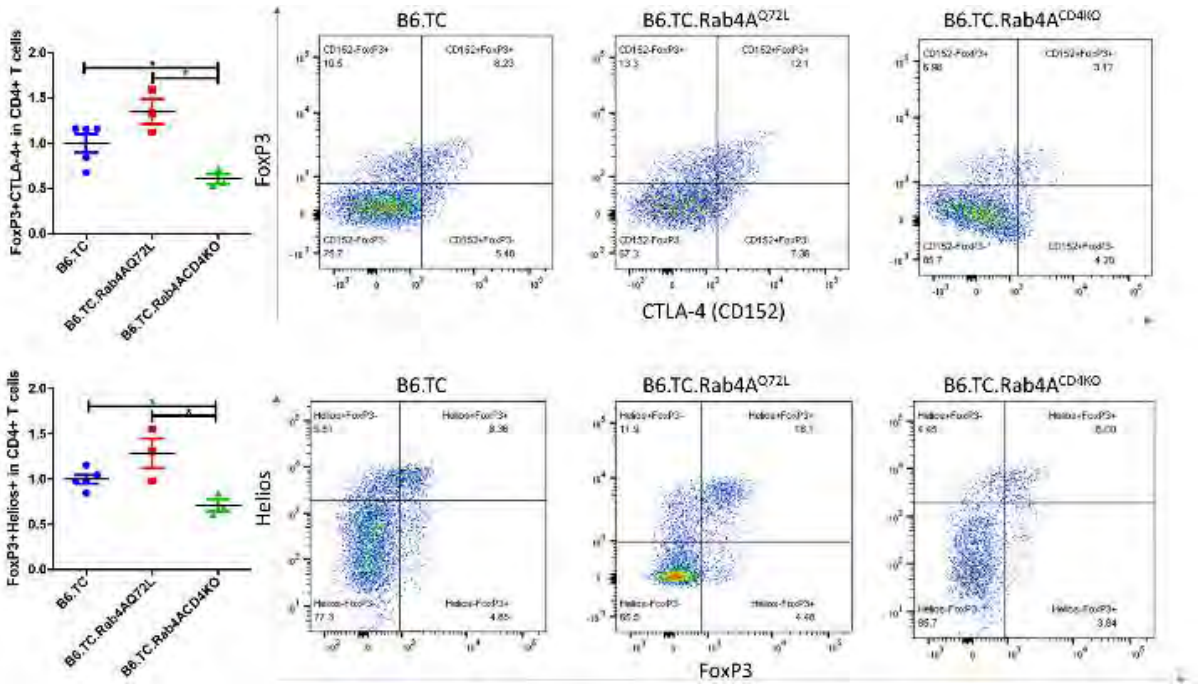


Figure 3. T cell-specific deletion of Rab4A decreases the populations of FoxP3⁺CTLA-4⁺ T cells (top panel) and FoxP3⁺Helios⁺ T cells (bottom panel) among CD4⁺ B6.TC splenocytes. Representative dot plots are shown, along with scatter plots normalized to B6.TC wild type controls.: p<0.05*

Akshay Patel[1]

T Cell-Specific Deletion of Rab4A Causes Steatohepatitis in a Treg- and mTOR-Dependent Manner in a Mouse Model of Systemic Lupus Erythematosus

Akshay Patel[1,2], Nick Huang[1,2], Joy Park[1,2], Thomas Winans[1,2], Xiaojing Wang[1], Daniel Krakko[1], Brandon Wyman[1,2], Zachary Oaks[1,2], Tamas Faludi[1], Manuel Duarte[1], Joshua Lewis[1], Jessica Nolan[1], Frank Middleton[2,3], Karen Gentile[3], Steven Landas[5], Katalin Banki[4], Andras Perl[1,2]

Departments of Medicine[1], Biochemistry and Molecular Biology[2], Neuroscience and Physiology[3], Pathology[4], SUNY Upstate Medical University; St. Joseph's Pathology, St. Joseph's Health[5]

Funding Sources: R01AI072648 and R01AI122176 to Andras Perl, F30DK131849 to Akshay Patel

Abstract:

Systemic Lupus Erythematosus (SLE) is a prototypical autoimmune disease which affects 20-150 out of 100,000 people globally. HRES-1/Rab4 (Rab4A), a GTPase that controls mitochondrial oxidative stress and activation of the mechanistic target of rapamycin (mTOR), is overexpressed in the T cells of SLE patients and drives disease pathogenesis. Liver inflammation is underappreciated in SLE. We examined whether Rab4A activation modulated inflammation and metabolism in the livers of lupus-prone *SLE1.2.3.* triple-congenic (B6.TC) mice using constitutively activated Rab4A ($Rab4A^{Q72L}$) and T cell-specific deletion of Rab4A ($Rab4A^{Q72L\text{-}CD4KO}$) mouse models. B6.TC/$Rab4A^{Q72L\text{-}CD4KO}$ livers showed steatosis and inflammation marked by the invasion of $CD3^+$ cells. Liver-infiltrating T cells exhibited increased mTOR activation and regulatory T cell (T_{reg}) depletion with diminished expression of $CD25^+FoxP3^+$, $Helios^+FoxP3^+$, and $CTLA\text{-}4^+FoxP3^+$ expression and suppressor function by $CD25^+CD4^+$ T_{regs} in the spleen of B6.TC/$Rab4A^{Q72L\text{-}CD4KO}$ mice. T_{reg} depletion resulted in a cytokine storm marked by the accumulation of Eotaxin-1, GM-CSF, IFN-γ, IL-1ß, IL-2, TNF-α, IL-4, IL-5, IL-10, IL-12, MCP-1, MIP-2, and RANTES. Hepatocytes from B6.TC/$Rab4A^{Q72L\text{-}CD4KO}$ mice showed mTORC1 activation and overexpression of sterol regulatory element-binding protein 1 (SREBP-1) and marked steatosis, which was decreased by mTOR blockade with rapamycin and N-acetylcysteine (NAC). These studies suggest that T cell-specific deletion of Rab4A promotes steatohepatitis in B6.TC mice through a cytokine storm downstream of T_{reg} dysfunction and activation of SREBP-1, which are responsive to rapamycin and NAC.

Thomas Winans:

Kynurenine is a proinflammatory metabolite that activates a positive feedback loop of Rab4A-dependent CD98 expression and mTORC1 and mTORC2 activation in SLE

Thomas Winans, Nick Huang, Tamas Faludi, Daniel Krakko, Laurence Morel, Andras Perl

Background/Purpose: The kynurenine (KYN) pathway has been linked to disease pathogenesis in patients with systemic lupus erythematosus (SLE) (https://pubmed.ncbi.nlm.nih.gov/26366134/). Genetically enforced overexpression of Rab4A activates the mechanistic target of rapamycin in SLE patients (https://pubmed.ncbi.nlm.nih.gov/31805010/). The present study was initiated to determine the pro-inflammatory mechanism of action of KYN in lupus-prone SLE1.2.3 triple congenic mice on the C57Bl/6 background (B6.TC) carrying constitutively active Rab4A^{Q72L} alleles (Rab4AKI) or lacking Rab4A in T cells (Rab4AKO).
Methods: KYN levels were measured within T cells and sera of mice carrying wild-type (WT), Rab4AKI and Rab4AKO alleles in female C57Bl/6 (B6) control mice and lupus-prone B6.TC mice using LC/MS. The effects of KYN on expression of its receptor CD98 and activation of mTOR complexes 1 (mTORC1, via pS6RP) and 2 (mTORC2, via pAkt) were studied by flow cytometry. Splenocytes were cultured *in-vitro* for 72 hours with or without KYN along with or without concurrent stimulation with lipopolysaccharide (LPS) or CD3/CD28. Mitochondrial mass and reactive oxygen species (ROS) were measured by flow cytometry using mitotracker Green (MTG) and hydroethidine (HE).
Results: KYN was accumulated in T cells and sera of B6.TC/Rab4A^{Q72L} female mice that exhibited increased expression of CD98 and activation mTORC1 and mTORC2 relative to B6.TC and B6.TC/Rab4A^{KO} controls**.** In C57Bl/6 splenocytes, KYN increased CD98 expression in CD4 and CD8 T cells (CD4 Unstim: FC=1.48, p=0.00012, CD8 Unstim: FC=1.68, p=2.1E-5, CD4 Stim: FC=1.36, p=0.00069, CD8 Stim: FC=1.51, p=0.00058) and significantly increased both mTORC1 (CD4 Unstim: FC=1.13, p=0.0169, CD4 Stim: FC=1.86, p=0.0086 CD8 Unstim: FC=1.24, p=0.0172, CD8 Stim: FC=1.49, p=0.0136) and mTORC2 (CD4 Unstim: FC=1.41, p=0.0003, CD4 Stim: FC=1.91, p=0.0018, CD8 Unstim: FC=1.42, p=0.0005, CD8 Stim: FC=1.55, p=0.0006). KYN increased mitochondrial mass (CD4 Stim: FC=1.25, p=0.0112, CD8 Stim: FC=1.87, p=0.0053) and ROS production (CD4 Stim: FC=2.2, p=0.0008, CD8 Stim: FC=2.34, p=0.0012) in both CD4 and CD8 T cells following KYN and CD3/CD28-stimulation. KYN also expanded CD19+CD11c+ age-related B cells (ABCs) with or without LPS. KYN activated mTORC1 (CD19+: FC=1.15, p=0.012, ABCs: FC=1.97, p=0.0019) and mTORC2 (CD19+: FC=6.289, p=1.21E-5, ABCs: FC=3.70, p=0.00165) and CD98 expression (ABCs: FC=2.06, p=0.0144). Remarkably, the expression of CD138, a plasma cell marker, was also increased by concurrent LPS and KYN treatment (FC=2.76, p=0.001).
Conclusion: This study suggests that KYN accumulation in lupus-prone T cells causes a CD98-KYN-mTOR positive feedback loop which is enhanced by Rab4A activation, conferring secondary KYN-mediated expansion of ABCs and plasma cells. The Rab4A-CD98/mTOR/KYN positive feed-back loop may represent a mechanistic target for therapeutic

Damira Sereda

Assessing the Appropriateness of Imaging Modalities in Primary Care for Low Back Pain and their Impact on Outcomes: A Retrospective Observational Study in a Single Center

Sereda D. , Arcilla C. Arslan K. 3 , Goldsmith D.
1.SUNY Upstate Medical University, Syracuse, NY
2.University of Florida College of Medicine, Jacksonville, FL 3
3Capital Health Regional Medical Center, Trenton, NJ

Background: Low back pain (LBP) is a leading cause of doctor visits and disability. The annual direct expenditures for LBP management exceed $80 billion, not including indirect costs associated with prolonged disability and lost worker productivity. Despite increasing expenses over time, patient outcomes have not improved, which may be due to overutilization of diagnostic imaging, invasive procedures, and unnecessary specialty referrals. Many providers investigate anatomic structures as an underlying etiology for back pain, which can lead to inappropriate, and even harmful low-validity tests. Therefore, evidence-based clinical practice guidelines for optimal utilization of imaging are highly recommended. This study identifies our current practice for utilization of lumbar spine imaging in patients with LBP in our outpatient clinic and outcomes based on imaging findings.
Methods: We used the electronic medical record to generate a patient list, including those 18 years and older who were managed for LBP and referred for lumbar spine imaging between January 1, 2022, and December 31, 2022. Patient demographics, baseline clinical characteristics, and subsequent interventions, such as referrals, counseling, physical therapy, pain management, spinal procedures, opioid prescription, and disability application, were recorded and analyzed using descriptive statistics.
Results: 170 patients were diagnosed with LBP during the study period. Of these, 49% received imaging, with 49% having plain radiography, 9% CT scans, and 40% MRI. 17% of patients had more than one imaging study done, from which 71% had plain radiography followed by MRI. Notably, 82% of those who had plain radiography followed by MRI were done during the chronic course of LBP. Among patients who received imaging, 26% had acute pain, 7% had subacute pain, and 67% had chronic pain. Imaging showed that 43% of the X-ray group had normal or nonspecific results, 73% of the MRI group had degenerative diseases, 44% had herniated discs, and 32% had spinal stenosis. Overall, only 3% of patients had serious diagnoses. Sixty six percent (66%) had lifestyle counseling and referral to physical therapy, 25% of patients were referred to spine specialists, 9% to rheumatologists, and 21% to pain specialists. Half of patients with chronic LBP were treated with muscle relaxants. Only 3% were prescribed opioids and 10% had spinal procedures. Interestingly, 5 patients were referred to rheumatologists for sacroiliac (SI) joint changes.
Conclusion: Majority of LBP in the outpatient setting have an uncomplicated, nonspecific course that require no further diagnostic evaluation. MRI of the lumbar spine is the modality of choice for the majority of patients requiring imaging per ACR appropriateness criteria. Lumbar spine radiographs are of limited utility and are generally only indicated when fracture is a concern. Complete history and careful physical and neurologic examinations are always the cornerstones of LBP management. Our study identifies the current clinical practice for utilization of imaging for patients with LBP among providers in our outpatient clinic. The study recommends further projects to optimize LBP management in our clinic based on evidence-based guidelines.

Marlene Marte:

Effectiveness of Secukinumab and Ixekinumab in patients Psoriatic Arthritis and Systemic Lupus Erythematosus Overlap Syndrome.

BACKGROUND: Th17 cells and IL-17 are elevated in SLE and PsA patients. PsA has increased prevalence in patients with SLE and for some authors, PsA/SLE Overlap Syndrome represents a distinct clinical entity. The role of Il-17 inhibitors has been well established for PsA, but not so for SLE. In lupus-prone mice, IL-17 inhibition improves SLE activity by inhibiting B-cell differentiation into germinal centers and follicular B cells as well as decreased differentiation of T-cells. Therefore, we hypothesize that targeting IL-17 could potentially improve disease activity in patients with PsA/SLE Overlap Syndrome.

OBJECTIVE: Determine if the use of IL-17 inhibitors (secukinumab and ixekizumab) improves SLE clinical disease activity on patients with PsA/SLE Overlap Syndrome.

METHODS: Single center, retrospective chart review. 10 years timeframe (01/01/2012 – 01/01/2022). Performed paired two tailed t test on each group (Secukinumab and Ixekizumab each) to compare SLEDAI scoring results.

RESULTS: A total of 28 patients with PsA/SLE Overlap on secukinumab were studied. 9 of them showed an improvement on SLEDAI scoring, majority being due to arthritis improvement (pvalue 0.0007547). 19 patients did not have a difference in SLEDAI scores. No patient worsened. On the other hand, a total of 11 patients with PsA/SLE Overlap on ixekizumab were studied. A total of 9 patients had statistically significant improvement in SLEDAI scores (p value

0.0000531) all of them due to arthritis resolution. 2 of them did have a change in SLEDAI scores. No one worsened.

CONCLUSION: Our study demonstrates that patients with PsA/SLE Overlap Syndrome treated with IL-17 inhibitors such as secukinumab and ixekizumab have an statistically significant improvement in SLEDAI scores on average by 4 points.

	Pre-Secukinumab	*Post-Secukinumab*	*Comments*
Patient 1	9	2	Pre-SLEDAI 9 points based on arthritis, oral ulcers, Low C3 (5), thrombocytopenia (127). Secukinumab started December 2017 -> arthritis, oral ulcers and thrombocytopenia resolved. C3 remained low (5).
Patient 2	6	2	Arthritis resolved but painless oral ulcers remained unchanged.
Patient 3	4	0	Secukinumab initially improved, but lost effect in 18 weeks.
Patient 4	4	0	Secukinumab effective for 3 years.

Table 1. Comparison of SLEDAI Scores in some of the patients studied prior to starting secukinumab and at least 3 months after starting secukinumab. Comments pertaining each patient discussed in the table.

	Pre-Ixekizumab	*Post-Ixekizumab*	*Comments*
Patient 1	6	2	Arthritis resolved, hair loss did not improve.
Patient 2	4	0	Arthritis resolved. Had been taking Ixekizumab for 1 year. Stopped due to positive QuantiFERON.
Patient 3	4	0	Arthritis resolved. Has been on Ixekizumab for 4 months with excellent response.
Patient 4	4	0	Arthritis resolved. Ixekizumab effective for 6 years.

Table 2. Comparison of SLEDAI Scores in some of the patients studied prior to starting ixekizumab and at least 3 months after starting ixekizumab. Comments pertaining each patient discussed in the table.

1) Koga, T., Ichinose, K., Kawakami, A., & Tsokos, G. C. (2019). *The role of IL-17 in systemic lupus erythematosus and its potential as a therapeutic target. Expert Review of Clinical Immunology.*doi:10.1080/1744666x.2019.1593141
2) Lee, Sy., Lee, S.H., Seo, HB. *et al.* Inhibition of IL-17 ameliorates systemic lupus erythematosus in Roquin$^{san/san}$ mice through regulating the balance of TFH cells, GC B cells, Treg and Breg. *Sci Rep* **9**, 5227 (2019). https://doi.org/10.1038/s41598-019-415341
3) Bonilla E (2016) Association of psoriasis and psoriatic arthritis with systemic lupus erythematosus. Rheumatol Orthop Med: DOI: 10.15761/ROM.1000105.

UPSTATE
MEDICAL UNIVERSITY

Department of Medicine

Department of Medicine Research Mission Statement

The Department of Medicine conducts cutting edge research in 12 academic divisions. Our faculty has made paradigm-shifting discoveries during the last decade which are described in the research pages of each division. The Department is home to basic and translational research laboratories and investigator-initiated clinical trials supported by the National Institutes of Health, Research Foundations, and Pharmaceutical Organizations.

www.upstate.edu