Global Thrombosis Forum

High School Scholars' Day

Friday, July 19th, 2024

12:00pm – 6:00pm CST

CTRE Building of Loyola University, Health Science

4th Floor Atrium, Room 428

2160 S 1st Ave, Maywood, IL60153

AGENDA

Poster Presentations
12:00 pm – 1:00 pm
Posters in the 4th floor atrium

EKOS catheter
Presenters: Arya Karmarkar
Mentor: Anterpreet Dua, MD

Race and VTE
Presenters: Srishti Sawant
Mentor: Atul Laddu, MD

Stress, Thrombosis, and cardiac arrest
Presenters: Sahithi Rajuladevi, Aditya Patankar
Mentor: Girish Pore, MD

Welcome Addresses
1:00 pm - 1:30 pm
Provost Dr. Margaret Callahan
Atul Laddu, MD
Jawed Fareed, PhD
1:30 pm - 1:45 pm - Recorded Keynote lecture by Trent Reed, MD

Internship Research Presentations
1:45 pm ***Hypercoagulable state in thalassemia patients***
Presenters: Aarushi Dua
Mentor: Neha Thomas, MD

2:00 pm ***Thrombogenesis in Sickle Cell Anemia***
Presenters: Krish Punyarthi, Preston Reed
Mentor: Neha Thomas, MD

2:15 pm ***Cancer and thrombosis***
Presenters: Arushi Garud
Mentor: Fakiha Siddiqui, MD

2:30 **pm** ***International registry for cancer and thrombosis - RIETE trial***
Presenters: Priyanka Kavdikar
Mentor: Fakiha Siddiqui, MD

Medical Student Presentation:
2:45 pm ***The relevance of thrombo-inflammatory, cardiac, and kidney injury biomarkers and cellular indices in cardiorenal syndrome.***
Presenters: Katherine Konczak

3:00 pm ***Analysis of thrombo inflammatory and oxidative stress-biomarkers in patients with end-stage renal disease relative to presence of atrial fibrillation***
Presenters: Ella Kaufmann

PowerPoint Presentations
3:15 pm ***Chronic Immune TT***
Presenters**:** Abhinav Paknikar, Siddharth Suresh
Mentor**:** Rashmi Kulkarni, MD

3:25 pm ***Heparin Resistance***
Presenters: Arav Raghunathan
Mentor: Sagar Garud, MD

3:35 pm Benefit ***Risk Ratio***
Presenters: Ayan Raghunathan and Surabhi Fadnavis
Mentor: Atul Laddu, MD

High School Student Presentations
3:50 pm Comparison of aggregation of CRP-A to standard agonists
Presenters: Yash Gupta

4:05 pm The Comparison of the Aggregation of Porcine and Bovine Heparin in Heparin Induced Thrombocytopenia Antibodies
Presenters: Gia Kapur

Closing Remarks
4:20 pm - 4:35 pm Remarks by the mentors Neha Thomas, MD and Fakiha Siddiqui, MD
4:35pm - 4:50 pm Closing Remarks by Joseph Caprini, MD and Atul Laddu, MD

ABSTRACTS

Poster Presentations:

EKOS catheter

Presenters: Arya Karmarkar
Mentor: Anterpreet Dua, MD
The EKOS catheter, a minimally invasive way of treating patients suffering from DVT and PE, is used to treat blood clots. The EKOS catheter uses ultrasound-accelerated thrombolysis technology involving high-frequency sound waves. It consists of an infusion catheter, an ultrasound core wire, and a control unit. The ultrasound accelerates the fibrinolytic process, allowing administered drugs to penetrate deeper into the clot and decreasing treatment time and the total dose of thrombolytic agent needed. EKOS catheter causes rapid improvement, reducing clot size and restoring RV function. The EKOS catheter is safe in the hands of experienced physicians.

Race and VTE

Presenters: Srishti Sawant
Mentor: Atul Laddu, MD
VTE stands as the third leading cause of cardiovascular deaths. The research aimed to assess the risk of VTE across diverse racial and ethnic groups, including Black Hispanics, White Hispanics, non-Hispanics, Caucasians, Native Americans, Asians, Pacific Islanders, and other races and ethnicities. Our findings reveal a heightened risk of VTE among Black Hispanics compared to other demographic groups. Furthermore, non-Hispanic Black patients exhibited the highest likelihood of VTE compared to non-Hispanic White patients. Additionally, the risk of arterial thromboembolic events was notably higher in men and non-Hispanic Black patients compared to other racial cohorts. These insights underscore the importance of tailored interventions and heightened all contribute to the increased hypercoagulability in addition to decreased levels of natural anticoagulants (protein C, protein S, antithrombin III). This has indeed caused a major burden for affected patients and clinicians. Even though this high risk of thrombotic complications in patients with intravascular hemolysis is broadly accepted, the exact mechanisms that are responsible for this hypercoagulable states remain under-established and unknown. Thus, it is crucial to illuminate the main mechanisms of thrombosis in thalassemia patients to help determine a better diagnosis and optimal therapeutic approach to prevent such events.

Stress, Thrombosis, and cardiac arrest

Presenters: Naga Sahithi Rajuladevi, Aditya Patankar
Mentor: Girish Pore, MD
In the 20th Century, there appears to be a high incidence of stress that results in thrombosis and cardiac arrest. Stress is the body's response to threats or challenges. Stress greatly impacts the cardiovascular system, contributing to thrombosis and cardiac arrest through mechanisms

involving the coagulation cascade. Understanding the connection between stress and cardiovascular events can help develop prevention and treatment strategies. Managing stress is crucial for reducing the risk of thrombosis and cardiac arrest.

Internship Research Presentations:

Hypercoagulable State in Thalassemia Patients

Presenter: Aarushi Dua
Mentor: Neha Thomas, MD

Thalassemia is one of the most common hereditary hemolytic anemias and is a fatal disease. It is a condition that affects the production of hemoglobin, causing defective alpha or beta globin chains, resulting in either alpha or beta thalassemia. The condition typically occurs in people of Southeast Asian, Mediterranean, and African American descent with an incidence of one in every one hundred thousand people. Over the last decade, life expectancy of thalassaemia sufferers has markedly improved due to regular blood transfusion treatments, iron chelation therapies, and others. However, some complexities such as thalassaemia-associated thrombosis have been identified in patients presenting with thrombotic complications. Complications in thalassemia result in a constant hypercoagulable state, increasing the risk of venous thromboembolism (VTE) in these patients. Increased platelet activation, expression of P-selectin and CD63, increased levels of endothelial adhesion proteins, and hemolysis of red blood cells all contribute to the increased hypercoagulability in addition to decreased levels of natural anticoagulants (protein C, protein S, antithrombin III). This has indeed caused a major burden for affected patients and clinicians. Even though this high risk of thrombotic complications in patients with intravascular haemolysis is broadly accepted, the exact mechanisms that are responsible for this hypercoagulable states remain under established and unknown. Thus, it is crucial to illuminate the main mechanisms of thrombosis in thalassaemia patients to help determine a better diagnosis and optimal therapeutic approach and prevent such events.

Thrombogenesis in Sickle Cell Anemia

Presenters: Krish Punyarthi, Preston Reed
Mentor: Neha Thomas, MD

Sickle cell anemia (SCA) is an inherited disorder characterized by hemoglobin S. In addition to the well-known hemolytic as well as vaso-occlusive complications, SCA sufferers have been identified to carry a high risk of thrombotic complications. Several thrombotic complications occurring in these patients have been reported. Thrombogenesis in SCA represents a complex and multifaceted pathological process contributing to the disease's morbidity and mortality. One of the key mechanisms involved is hemolysis, which releases free hemoglobin and heme, depleting nitric oxide (NO) and inducing oxidative stress, thereby triggering endothelial activation and dysfunction. This is evidenced by increased circulating microparticles, abnormal platelet function, and altered coagulation pathways. SCA patients often exhibit impaired fibrinolysis, alterations in thrombin generation markers, and decreased levels of natural anticoagulants such as Protein C and Protein S. Additionally, activated platelets, dysfunctional

endothelial cells, elevated circulating microparticles, and elevated levels of TNF R1, a receptor for tumor necrosis factor, are linked with increased inflammation and thrombotic risk in SCA. These factors foster an environment with the expression of adhesion molecules and tissue factor, increasing thrombus formation risk. Despite this wealth of information, the precise molecular and cellular mechanisms leading to hypercoagulable state in sickle cell patients remains largely unknown. Understanding the intricate mechanisms of thrombogenesis in SCA is crucial for developing targeted therapeutic strategies.
This comprehensive review of current literature aims to delineate this disease's complex pathophysiology, highlighting potential biomarkers and therapeutic drugs to guide future research and improve patient outcomes.

Cancer and Thrombosis

Presenters: Arushi Garud
Mentor: Fakiha Siddiqui, MD

The cancer-associated thrombosis (CAT) relationship was explained by Armand Trousseau in 1865 and is called Trousseau Syndrome. Cancer patients are at a 4 to 6.5-fold higher risk of developing thrombotic events. The patient-related risk factors of CAT include age, gender, race, and comorbidities. In contrast, the cancer-related risk factors include the site and stage of cancer, histology of cancer, and time of diagnosis. Cancer treatment-related risk factors include surgery and hospitalization, chemotherapy, and the use of central venous catheters. Pathophysiology of CAT involves the direct or indirect activation of coagulation cascade either by the release of tumor-derived procoagulant factors (microparticles, tissue factors, cancer procoagulants, and platelet agonist), expression of thrombi-inflammatory mediators (TNF-α, IL6, and IL-1β) and adhesion molecules, tumor-associated inhibition of fibrinolysis, endothelial damage either by chemotherapy, tumor itself or angiogenic factors (VEGF), hemodynamic changes due to immobility, surgery or chemotherapy. Besides these, cancer-associated neutrophil extracellular traps (NETs) and damage-associated molecular patterns (DAMPs) are also associated with CAT. CAT treatment options include using anticoagulants such as unfractionated heparin, low molecular weight heparin, direct-oral anticoagulants, indirect factor-Xa inhibitors, and vitamin K agonists. With effective prevention and treatment for CAT, morbidity can be reduced, and mortality may decrease.

International registry for cancer and thrombosis - RIETE trial

Presenters: Priyanka Kavdikar
Mentor: Fakiha Siddiqui, MD

VTE is a condition that presents itself as DVT or PE and affects approximately 10 million people every year. Extensive data has been generated through research on various patient populations worldwide to improve treatment and better understand the factors influencing VTE. The International Registry for Cancer and Thrombosis (RIETE) registry is an ongoing registry that began in Spain in 2001 and has expanded to 26 countries with 124,602 patients in its database. Valuable data was collected on the various risk factors and types of cancer and surgery for VTE in their patient population, which included those of different demographics. The goal of the

RIETE registry was to gather information in one database that would consist of subgroups excluded from previous trials and learn about the history of VTE.

Medical Student Presentation:

The relevance of thrombo-inflammatory, cardiac, and kidney injury biomarkers and cellular indices in cardiorenal syndrome.

Presenters: Katherine Konczak

Cardiovascular disease (CVD) is highly prevalent in patients with end stage renal disease (ESRD) on maintenance hemodialysis. Cardiorenal syndrome (CRS) describes heart and kidney disorders in which dysfunction in one organ perpetuates damage to the other organ. As a result of the linkage between heart and kidney physiology, CRS pathophysiology, diagnosis, and risk stratification is poorly understood. Previous research has demonstrated that elevated levels of thrombo-inflammatory, renal, and cardiac biomarkers are associated with CVD and chronic kidney disease (CKD) progression. Additionally, CBC-derived cellular indices, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), hemoglobin-to-platelet ratio (HPR), mean platelet volume (MPV), and systemic-immune-inflammation-index (SII) have shown potential in predicting morbidity and mortality in CVD and CKD. Plasma samples from 70 patients in the 2023 ESRD study cohort were collected under an approved IRB protocol at LUMC. Normal human plasma control samples were obtained from a commercial blood bank source. Biomarkers were quantified using ELISA and analyzed using non-parametric statistical tests. Cellular indices were calculated using patient CBC results from EPIC. Investigating these biomarkers along with cellular indices will lead to a greater understanding of the pathophysiology of CRS, can be used to risk stratify patients with ESRD undergoing maintenance hemodialysis, and can serve as valuable diagnostic and prognostic tools for CRS.

Analysis of thrombo inflammatory and oxidative stress-biomarkers in patients with end-stage renal disease relative to presence of atrial fibrillation

Presenters: Ella Kaufmann

Atrial fibrillation (AF) is a frequent comorbid condition in patients with end-stage renal disease (ESRD). Due to its high prevalence, there is considerable interest in investigating the different pathologies driving AF. Its mechanism is varied and dependent on which segment of coagulation cascade is affected. The study determines the differences between thrombo-inflammatory and oxidative stress related biomarkers in ESRD patients with and without comorbid AF. Endothelial dysregulation may contribute to molecular and cellular imbalance involved in AF and may become exacerbated in the comorbid disease states of ESRD and AF, illustrated by increased levels of circulating endothelial, inflammatory, and oxidative stress related biomarkers. Plasma samples banked from the clinical study on ESRD were identified to select patients with AF.

Controls are commercially available normal plasma from 10 individuals. Validated ELISA and appropriate statistical methods were used to profile the biomarkers and clinical correlates. From initial analysis, there is statistically significant difference in some biomarker levels in ESRD patients with and without AF, as well as some moderate correlations between various biomarkers. The studies will be useful in assessing the pathophysiology and risk stratification by using biomarkers in patients with ESRD with or without AF.

PowerPoint Presentations

Chronic Immune TT

Presenters: Abhinav Paknikar, Siddharth Suresh

Mentor: Rashmi Kulkarni, MD

Immune Thrombocytopenia (ITP) is a condition characterized by an abnormally low platelet count due to auto-antibodies attacking platelet antigens. We discuss the epidemiology, pathogenesis, and clinical presentation of ITP, highlighting its impact on bleeding and thrombotic risks. The diagnosis is based on exclusion, given the necessity of multiple laboratory tests, while treatment involves corticosteroids, immunosuppressive agents, and supportive care. Importantly, despite its association with bleeding, ITP also increases the risk of thrombosis, necessitating careful management to balance thrombotic and bleeding complications.

Heparin Resistance

Presenters: Arav Raghunathan

Mentor: Sagar Garud, MD

Heparin is a widely used anticoagulant used to treat VTE. Heparin is a negatively charged polysaccharide developed from the porcine intestine. Heparin resistance refers to the inadequate response received from patients when a sufficient dose of heparin has been administered. More than 20% of cardiac surgery patients suffer from heparin resistance, along with those with severe respiratory and circulatory complications such as COVID-19. Heparin resistance is diagnosed through assays such as aPTT that measure the amount of time it takes for blood to clot when treatment is administered. Treatments such as direct thrombin inhibitors can be provided for those suffering from conditions such as thrombocytopenia.

Benefit Risk Ratio

Presenters: Ayan Raghunathan and Surabhi Fadnavis

Mentor: Atul Laddu, MD

All drugs produce a range of effects, both therapeutic and adverse. A risk-benefit ratio (or benefit-risk ratio) is the ratio of the risk of an action to its potential benefits. Risk-benefit

analysis (or benefit-risk analysis) is the analysis that seeks to quantify the risks and benefits and hence their ratio. The risk-benefit ratio is a crucial concept that weighs the estimated harm (adverse effects, cost, inconvenience) against the expected benefits (symptom relief, cure, reduced complications). A drug should only be prescribed when the benefits outweigh the risks. However, this ratio is difficult to quantify precisely for each patient due to variables like the nature and duration of harm and individual patient values. Therefore, clinicians often rely on large-scale data (pharmacoepidemiology) and personal experience.

High School Student Presentations

Comparison of aggregation of CRP-A to standard agonists

Presenters: Yash Gupta

Agonists have been a valuable tool in helping patients, physicians, and scientists diagnose platelet-related disorders and determine bleeding tendencies, monitor homeostasis and platelet response during surgery, or the administration of anticoagulants. CRP-A is a synthetic agonist formed by collagen, which can be used in these platelet function tests to replace standard agonists. Its maximum aggregation, primary slope, and onset time of aggregation with different concentrations were compared to standard agonists such as arachidonic acid, ADP, and collagen to evaluate its ability as an agonist. The results demonstrated that CRP-A with a concentration of 10 ug/mL could compare to the aggregation of other agonists; in contrast, 1, .1, and .01 ug/mLwere not comparable to these common agonists. When the collagen solutions were diluted to the same concentrations as the CRP-A, they aggregated significantly less than their synthetic counterparts, demonstrating the efficiency of the agonist. The data indicated that collagen becomes slightly weaker over time compared to CRP-A. Our data supports the introduction of CRP-A as a commonly used synthetic agonist due to its high aggregation, low concentration requirement compared to collagen, and slightly longer shelf life. vigilance in addressing thromboembolic risks across diverse populations.

The Comparison of the Aggregation of Porcine and Bovine Heparin in Heparin Induced Thrombocytopenia Antibodies

Presenters: Gia Kapur

Heparin stops the formation of clots in the blood. However, 3-5% of patients develop a potentially fatal condition called Heparin-induced thrombocytopenia (HIT), in which blood coagulates in the presence of heparin due to the presence of platelet factor 4 complexes. Currently, porcine heparin is the main source of this drug. However, due to an outbreak of African swine flu in pig herds, the US has been unable to attain enough batches of this drug as the herds are dying. So, the FDA is currently looking into alternatives, such as bovine heparin, to

be tested and approved. The present experiment compares the level of aggregation that porcine and bovine heparin induce at different concentrations in HIT plasma to discover the safety of bovine heparin. The experiment was run on PAP8 machines, which used light transmission aggregometry to detect the level of aggregation in each sample. This experiment showed that bovine heparin behaves similarly to porcine heparin at concentrations 10, 1, and 0 ugm/L but not at 0.1 ugm/L concentration. This suggests that bovine heparin is an acceptable candidate for FDA approval and can be used as a substitute for heparin in HIT patients because there is no added risk from using bovine over porcine heparin.