Vascular Health Innovation Summit
Precision Medicine and Patient-Centric Vascular Health: Present and Future State
Friday, September 22, 2023

Overview

The 2023 Innovation Summit investigated ways that precision medicine approaches can improve the patient experience in the intersectional space between risk identification, treatment, and outcomes. Participants, all experts representing vascular surgery, clinical care, industry, and patient and caregiver experience, collaborated to identify innovative research approaches that would improve patient outcomes, with particular attention to addressing disparities and ensuring representation and diversity. The role of data-derived phenotyping, artificial intelligence, and omics across vascular disease areas was examined, including peripheral artery disease, venous thrombosis, aortic aneurysms and dissections, and carotid artery disease. The Summit concluded with a mapping out of potential collaborative high-impact projects that address the identified issues and prioritize the patient experience, incorporating patient and caregiver perspectives of how vascular health problems can be directly addressed by the research topic in light of health disparities and quality of life priorities. Co-Chairs of the Summit were Dr. Michael Conte, Chief of Vascular Surgery at UCSF and Manesh Patel, Chief of Cardiology at Duke University, and the Summit management team was led by Foundation to Advance Vascular Cures, CEO Isabel Bjork, and Lisa Huntzinger, Program Manager.

Introduction: Dr. Michael Conte, Chief of Vascular Surgery, UCSF; CMO, Foundation to Advance Vascular Cures; Isabel Bjork, CEO Foundation to Advance Vascular Cures

Dr. Conte kicked off the summit with an overview of precision medicine in vascular health, highlighting the importance of answering how can we: (1) more accurately define clinical and molecular subtypes to improve care?; (2) use 'big data' and AI to identify at-risk populations for prevention/early interventions?; and (3) maintain a patient-centric approach rather than an actuarial one? Isabel Bjork set forth the day's agenda, and the Summit goal to arrive at emphasized the possibilities of big data computational analysis for improving vascular health outcomes and addressing health inequities. While now almost mainstream in cancer research, precision medicine is barely

Presentation: Bringing Precision Medicine to Vascular Disease Investigations: Challenges and Opportunities: *Scott Damrauer*, MD, Associate Professor of Surgery, Associate Professor of Genetics, University of Pennsylvania.

Defining precision medicine as "the use of information about an individual's genome, environment and lifestyle to provide a more precise approach for the prevention, diagnosis and treatment of disease," Dr. Damrauer discussed how the use of precision medicine can inform

risk prediction of incident disease and disease progression as well as the selection of therapies. He concluded that the future includes developing polygenic risk scores for diverse populations, identifying novel biomarkers, and using precision medicine approaches to inform therapeutic selection.

Panel: Precision Medicine as a Path to Improved Prevention and Care

Precision Medicine: the Patient Perspective: *Katie Wright*, VEDS Patient Advocate; Podcaster, Staying Connected, Translucent One LLC; VEDS Research Project Coordinator, Division of Vascular and Endovascular Surgery, Oregon Health and Sciences University.

Bringing the patient perspective to the Summit, Katie Wright highlighted the importance of early genetic investigation and integration of precision medicine approaches to personalize care in partnership with the patient. She urged researchers and clinicians to work closely with the patient at multiple time points during the care and research continuum and to prioritize patient input regarding conditions, experiences and preferences to truly arrive at innovative solutions.

Genetic Predisposition to Disease: Using Genetic Data to Identify Aortic Dissection Risk: *Dianna Milewicz*, MD PhD, Chair of Cardiovascular Medicine, Director of the Division of Medical Genetics, Vice-Chair Department of Internal Medicine, UTHealth McGovern Medical School.

Presenting on genetic predisposition to disease, Dr. Milewicz highlighted the challenges of using genetic data to identify aortic dissection, including how to translate gene- and variant-based management data into clinical care and how clinical trials of thoracic aortic disease may be impacted by the genetic information of the participants. Other challenges are finding ways to identify individuals at risk for acute aortic dissections and determining which therapeutics prevent aneurysm growth and acute aortic dissections.

Serum Biomarkers for Atherosclerosis: How Do We Scale for Primary Prevention?: Mohamed Zayed, MD PhD MBA, Associate Professor of Surgery, Radiology, Molecular Cell Biology, & Biomedical Engineering, Washington University.

Posing the question, “Are there more sensitive methods for screening & diagnosis PAD?” Dr. Mohamed Zayed highlighted that atheroprogression in PAD is likely a different disease process and as a consequence, traditional lipid biomarkers are not reliable for primary screening/prevention for PAD. Surgeon-Physician-Scientists should leverage existing biobanks and trials for specimens and there is a need for a synergistic scaling strategy to progress new discoveries.

Panel: Using Genetic and Electronic Data to Personalize Treatment Approaches

Introduction and Panel Facilitation by Manesh Patel, MD, Chief of Cardiology, Duke University; Advisory Board Member and Research Committee Member, Foundation to Advance Vascular Cures. Dr. Patel introduced the panel and provided an overview of how “omics” can improve the patient experience and outcomes.

Phenotypic Expressions and Their Relation to Gene Discovery Approaches: The Potential of AI and Biobanks/Consortia-Based Discovery: Santhi Ganesh, MD, Professor of Cardiology, Professor of Internal Medicine and Human Genetics, University of Michigan.

Dr. Santhi Ganesh spoke on gene discovery principles and strategies to maximize discovery for cardiovascular diseases, including methodologic approaches, phenotype considerations, and current gene discovery topics including multisite consortia, biobanks, electronic health records, and applications of AI.

Machine Learning–Based Risk Stratification Scheme for CLTI, Kate McGinigle, MD MPH, Associate Professor of Surgery, University of North Carolina.

Dr. Kate McGinigle discussed her work on using machine learning to develop possible treatment algorithms for patients with PAD. The goal is to develop a fully realized precision medicine algorithm that matches patients to their best treatment. To realize the potential of precision medicine, research efforts need to be directed toward characterizing how combinations of medical and surgical treatment affect disease progression over time, evaluating the social complexities and healthcare priorities and constraints that impact treatment possibilities, and using diagnostic evaluation to prospectively test different treatment regimes.

Molecular Genetic Evaluation of Pediatric Renovascular Hypertension to Enable a Personalized Treatment Approach: The Value of a Consortia Model: Dawn Coleman, MD, Chief, Division of Vascular and Endovascular Surgery, Duke University.

Dr. Dawn Coleman shared the work she is doing with the International pRVH PCOR Collaborative for children with Renovascular Hypertension (pRVH). Stakeholders have shared that early diagnosis and treatment along with multidisciplinary/specialty care optimizes the care of pediatric pRVH. She emphasized the value of deep phenotyping and genotyping to drive an individualized surgical decision making/treatment plan for pRVH patients.

Presentation: Clinical Practicalities Using Pharmacogenomics in Thrombosis:

Marc Bonaca, MD MPH, Executive Director, CPC Clinical Research, University of Colorado.

Presenting on pharmacogenomics, the branch of genetics concerned with the way in which an individual's genetic attributes affect the likely response to drug therapies, Dr. Bonaca explored ways that precision medicine can contribute to therapeutic efficacy. . He discussed ways that genetics can contribute to therapeutic efficacy, including promising use of genetics to identify a specific target/mediator of risk for treatment, such as with Factor XI and lipoprotein (a), and promising (but potentially slower adoption) of genetics to identify higher risk of an outcome. For example, the PAD genetic risk score is a strong independent predictor of PAD in patients with cardiometabolic disease, and it also predicts risk of limb and cardiac events, supporting overlapping biological mechanisms for atherosclerosis across vascular beds.

Panel: Opportunities and Challenges of AI and Imaging for Precision Medicine:

Introduction and Panel Facilitation by Oliver Aalami, MD, Clinical Professor, Surgery - Vascular Surgery, Stanford University.

Dr. Aalami and the panel brought their expertise on precision medicine and patient-centric vascular care to the afternoon session.

Carotid Plaque Analysis / AAA Registry Development for Risk Prevention and Identification: Bobby Chang, MD, Assistant Chair of Vascular Surgery, Northern CA, The Permanente Medical Group.

Dr. Bobby Chang talked about his work to leverage AI-enabled image analysis and large disease datasets to enhance patient-focused risk prediction. He is working on developing a more precise predictor of stroke for each patient with carotid stenosis to better determine the need for intervention. For patients with abdominal aortic aneurysms, the goal is to use artificial intelligence-assisted image analysis for automated disease detection and enhanced surveillance recommendations.

Multi-Modal AAA Progression Model Development: Sharon Kiang, MD, Chief, Vascular Surgery, Associate Professor of Surgery, Loma Linda VA Healthcare System.

Dr. Sharon Kiang provided an overview of AI, Machine Learning and Deep Learning. Imaging based AI utilizes neural networks, a form of deep learning. Dr. Kiang described her work with convolutional neural networks (CNN) to process CT scan images to better detect abdominal aortic aneurysms. The goal is to use CNNs along with other clinical, laboratory and genomics data to develop prediction models for personalized medicine for each surgical patient.

Video Understanding for Risk and Resilience Screening: Integration of Computer Vision, Phenotype, and Clinical Data: Matthew Corriere, MD, Frankel Professor of Cardiovascular Surgery, Associate Professor, Vascular Surgery, University of Michigan.

Dr. Matthew Correire described his work to find a smarter way to evaluate preoperative risk for patients. He has developed a technique that uses a six second smartphone video to do an automated analysis to determine if a patient is frail or resilient. The process detects how well the patient can transfer from chair to table and uses phenotype, clinical, demographic and measured data in the determination process. Surgeons can use this tool to help with their preoperative risk analysis.

The Future of Generative AI & Multi-Modal AI in Health Care

Akshay Chaudhari, PhD, Assistant Professor, Integrative Biomedical Imaging Informatics, Stanford University.

Presenting work he is doing on precision diagnostics with large scale medical imaging and deep learning, Dr. Akshay Chaudhari discussed the role of open source software in enabling innovation. He and his team are developing open source software and looking for ways to integrate their work with clinical use.

The Power of a "Human-in-The-Loop" - Cognitive Behavioral Therapy to Personalize SET Programs: Oliver Aalami, MD, Clinical Professor, Surgery - Vascular Surgery, Stanford University.

Dr. Oliver Aalami spoke about the work he has done to create a home-based, mobile phone delivered exercise therapy program. The app is designed to be a universally accessible approach to remote therapy for high need populations and uses coaching techniques, both automated and live, for maximum engagement. These cognitive behavior techniques (having a

“Human-in-The-Loop”) provide an effective patient-centric approach to engage patients with PAD and claudication to help them achieve their goals.

Break-out Sessions

Prior to attendees gathering in their respective breakout sessions, Jim Tietjens, a former professional soccer player, championed support for research that has direct patient impact. He challenged the Summit participants with this question: “What will this do for me and for others like me with PAD?” Jim knows what he’s talking about since he has undergone a kidney transplant, beaten Stage 4 nonHodgkin’s lymphoma, tongue and throat cancer, and now, he is fighting PAD. He wondered aloud about why PAD gets less attention than these diseases, and why there seems to be less progress. “We need to fix this.”

Three afternoon brainstorming sessions provided the opportunity for participants to discuss innovative strategies to accelerate collaborative solutions around specific areas of interest. Participants were divided into the following groups: (1) Innovative Approaches in Atherosclerosis; (2) Using AI and Imaging to Advance Vascular Disease Investigation; and (3) Genetics and Omic Approaches for Prevention and Care. Following the Summit, an RFA was issued for pilot research funding for collaborations focused on the following project areas, based on priorities identified collaboratively by participants at the Summit.

RFA

A call for proposals for a 16 month pilot project was issued. Calls asked proposals to focus on the following areas:

- Disease risk prediction and progression models, applying precision medicine approaches. Examples include quantitative assessment of vascular calcification from CT imaging to predict intervention outcomes, or investigation of historical vascular lab data to identify at-risk patients and model disease progression.
- Identification of novel vascular disease phenotypes based on clinical trajectory, morphology, or responses to treatment
- Insights into mechanisms underlying disparities in vascular disease, identifying data and/or methods for obtaining such data, and analytical approaches to assess disparities in treatment and/or outcomes.
- Exploration of new (or new interpretations of) biomarkers of vascular disease.
- Medical management best practices, including timing and frequency of screening, scans, genetic testing, based on computer modeling and deep learning. Examples include assessing viability of ultrasounds and CT scans as clinical decision support tools for dialysis readiness, viability of supervised exercise therapy, and pharmacological responses.
- Translation of risk prediction metrics to providers and patients, including assessing requirement for uptake, validation studies, and patient preferences. This covers studies that focus on lifestyle and behavioral changes.