AUC
Association of
University Cardiologists

PROGRAM
AND
ABSTRACTS

Association of University Cardiologists
Sixty-First Annual Meeting
Virtual Meeting

January 19-21, 2022

2022

2022 AUC Annual Meeting Program
All times are PACIFIC STANDARD TIME

Wednesday, January 19, 2022

9:00 AM – 12:00 PM PST	**Council Meeting** Location: via Zoom (Executive Committee Members only)

Thursday, January 20, 2022
Presidential Session:
Achieving Global Health Equity in Academic Medicine and Healthcare

7:45 AM – 8:10 AM PST	**President's Welcome and Address** Michelle A. Albert, MD MPH *Disrupting and Transforming: Overcoming Inequities in Academic Medicine/Cardiology*
8:10 – 8:25 AM PST	**Nanette K Wenger Honorary Lecture** Paula Johnson, MD MPH *Creating Novel Solutions to Address Structural Barriers for Trainees Across the Academic Lifecourse: Lessons from A College President*
8:25 – 8:30 AM PST	*Q&A* *Moderator: Michelle A. Albert, MD MPH*
8:30 – 8:50 AM PST	**The 32nd Annual George Burch Memorial Lecture** Gary Gibbons, MD PhD *Moving from Statistics to Solutions for Addressing Structural Discrimination in Research*
8:50 – 9:00 AM PST	*Q&A* *Moderator: Michelle A. Albert, MD MPH*
9:00 – 9:20 AM PST	**Presidential Lecture** Victor Dzau, MD PhD *The Role of the NAM in Fostering Solutions to Achieve Health Equity Globally*
9:20 – 9:30 AM PST	*Q&A* *Moderator: Michelle A. Albert, MD MPH*
9:30 – 9:45 AM PST	**BREAK**

9:45 – 9:55 AM PST **Introduction of New Members in Attendance**

Michelle A. Albert, MD MPH

Raymond L Benza, MD	*Anekwe E Onwuanyi, MD*
Kristina I Boström, MD	*Kristen K Patton, MD*
Biykem Bozkurt, MD PhD	*Subha V Raman, MD*
Quinn Capers IV, MD	*Carlos J Rodriguez, MD*
Paul Friedman, MD	*Svati H Shah, MD MHS*
Isabella Grumbach, MD PhD	*Jil Tardiff, MD PhD*
Naomi Hamburg, MD	*Kim A. Williams Sr, MD*
Tzung Hsiai, MD PhD	*Marlene S Williams, MD*
JoAnn Lindenfeld, MD	

Scientific Session Day 1, Part 1

9:55 – 10:10 AM PST **The Universal Definition and Classification of Heart Failure**

Biykem Bozkurt, MD PhD

Moderator: Barry London, MD

10:10 – 10:15 AM PST *Q&A*

10:15 – 10:30 AM PST **Light at the End of SARS-CoV-2 Pandemic: Integration of Light-Sheet and Light-Field to Uncover Cardiac Morphogenesis**

Tzung Hsiai, MD PhD

Moderator: Barry London, MD

10:30 – 10:35 AM PST *Q&A*

10:35 – 10:50 AM PST **Standards for clinical practice guidelines**

Kristen Patton, MD

Moderator: Barry London, MD

10:50 – 10:55 AM PST *Q&A*

10:55 – 11:10 AM PST	**BREAK**
11:10 – 11:25 AM PST	**Impact of Health Equity Intervention Measures on Outcomes in Heart Failure Management** Anekwe Onwanyi, MD *Moderator: Karol Watson, MD PhD*
11:25 – 11:30 AM PST	*Q&A*
11:30 – 11:45 AM PST	**Cardiovascular Health Effects of Pod-Based Electronic Cigarettes** Naomi Hamburg, MD *Moderator: Karol Watson, MD PhD*
11:45 – 11:50 AM PST	*Q&A*
11:50 AM – 12:05 PM PST	**Towards a Better Understanding of Cholesterol in Hispanics/Latinos** Carlos Rodriguez, MD *Moderator: Karol Watson, MD PhD*
12:05 – 12:10 PM PST	*Q&A*
12:10 – 12:30 PM PST	**BREAK**
12:30 – 12:45 PM PST	**Follow Up platelet functional changes in Depression and Heart disease** Marlene Williams, MD *Moderator: Susan Smyth, MD PhD*
12:45 – 12:50 PM PST	*Q&A*
12:50 – 1:05 PM PST	**Predictors of Cardioprotective Medication Prescription versus Mortality in Patients Hospitalized with Acute Myocarditis** Subha Raman, MD *Moderator: Susan Symth, MD PhD*

1:05 – 1:10 PM PST	*Q&A*	
1:10 – 1:25 PM PST	**Dysregulation of Ca2+ Homeostasis in Hypertrophic Cardiomyopathy** Jill Tardiff, MD PhD *Moderator: Susan Symth, MD PhD*	
1:25 – 1:30 PM PST	*Q&A*	

Business Meeting

1:30 – 2:20 PM PST	**Honoring Longstanding Members**	Michelle A. Albert, MD MPH
	Memorials	
	Election of New Officers	
	New Business	
	AUC Finances	Charles Lowenstein, MD
	Discussion	Michelle A. Albert, MD MPH
	Passing the Gavel	

Scientific Session – Day 1, Part 2

2:20 – 2:30 PM PST	**BREAK**
2:30 – 2:45 PM PST	**Devices for patients with heart failure** JoAnn Lindenfeld, MD *Moderator: Charlie Lowenstein, MD*
2:45 – 2:50 PM PST	*Q&A*
2:50 – 3:05 PM PST	**Dueling the Dual Pandemics: Nutrition and the Microbiome** Kim Allan Williams Sr, MD *Moderator: Charlie Lowenstein, MD*

3:05 – 3:10 PM PST	*Q&A*
3:10 – 3:20 PM PST	**Comments and Adjourn** Sumeet Chugh, MD

Friday, January 21, 2022

Emeritus Program

8:00 – 8:05 AM PST	**Introduction** Sumeet Chugh, MD
8:00 AM – 8:15 AM PST	**Emeritus Program** Moderators: *Nanette Wenger* *RoseMarie Robertson* *Michael Cain*
8:15 – 8:45 AM PST	**Featured Lecture** Eugene Braunwald, MD Distinguished Hersey Professor of Medicine at Harvard Medical School Founding Chair, Thrombolysis in Myocardial Infarction Study Group, Brigham and Women's Hospital ***Directions for Cardiology for the Next Decade***
8:45 – 8:55 AM PST	*Q&A*

8:55 – 9:25 AM PST	**Featured Lecture** Dr. Ileana Piña MD, MPH, FAHA, FACC, FHFSA Clinical Professor of Medicine, Central Michigan University College of Medicine Adjunct Professor of Epidemiology and Biostats, Case Western University, Population & Quantitative Health Sciences Senior Staff Fellow, Medical Officer FDA, CDRH ***The Hispanics and Heart Disease: A True Hispanic's Perspective***
9:25 – 9:35 AM PST	*Q&A*

Scientific Session – Day 2

9:35 – 9:50 AM PST	**Shaping Waves of Bone Morphogenetic Protein Inhibition during Vascular Growth** Kristina Boström, MD *Moderator: Jane Freedman, MD*
9:50 – 9:55 AM PST	*Q&A*
9:55 – 10:10 AM PST	**Bayesian network modeling coupled with genetic feature selection as a mortality model for PAH** Raymond Benza, MD *Moderator: Jane Freedman, MD*
10:10 – 10:15 AM PST	*Q&A*
10:15 – 10:30 AM PST	**Heart Failure Omics: Cardiac Metabolism and Beyond** Svati Shah, MD MHS *Moderator: Sumeet Chugh, MD*
10:30 – 10:35 AM PST	*Q&A*

10:35 – 10:50 AM PST	**Protecting mitochondrial function to prevent cardiovascular toxicity of cancer therapies** Isabella Grumbach, MD PhD *Moderator: Sumeet Chugh, MD*
10:50 – 10:55 AM PST	*Q&A*
10:55 – 11:10 AM PST	**Practical Strategies to Enhance Diversity in Cardiology** Quinn Capers IV, MD *Moderator: Sumeet Chugh, MD*
11:10 – 11:15 AM PST	*Q&A*
11:15 – 11:25 AM PST	**Closing Comments** **Meeting Adjourns** Sumeet Chugh, MD

Emeritus Program Featured Lecture

Directions for Cardiology for the Next Decade

Dr. Eugene Braunwald

Distinguished Hersey Professor of Medicine at Harvard Medical School

Founding Chair, Thrombolysis in Myocardial Infarction Study Group, Brigham and Women's Hospital

EUGENE BRAUNWALD, M.D. is the Distinguished Hersey Professor of Medicine at Harvard Medical School and the founding Chair of the Thrombolysis in Myocardial Infarction Study Group at the Brigham and Women's Hospital.

Dr. Braunwald trained at New York University School of Medicine and his medical housestaff training was at Mount Sinai Hospital and Johns Hopkins Hospital. He served as Chief of Cardiology and as Clinical Director of the National Heart, Lung and Blood Institute, and then as founding Chair of Medicine at the University of California, San Diego. From 1972 to 1996 he was Chair of the Department of Medicine at the Brigham and Women's Hospital, Harvard Medical School. From 1980 to 1989 he served simultaneously as Chair of Medicine at Boston's Beth Israel Hospital. He was a founding trustee and Chief Academic Officer of Partners HealthCare System. Since 2003 he has devoted himself full time to cardiology research.

Dr. Braunwald's first cardiology paper was published in Circulation Research in 1954, and he has been a major force and has contributed continuously to many areas of cardiology in a career now spanning over two thirds of a century. His early work focused on the control and assessment of ventricular function, and he was the first to measure both left ventricular ejection fraction and left ventricular dp/dt in patients. His group described the first neurohumoral defect in human heart failure, defined the pathophysiology of hypertrophic cardiomyopathy and demonstrated salvage of ischemic myocardium. This improved clinical outcomes in patients with myocardial infarction whose occluded arteries were opened, leading to the widely accepted "open artery concept." His group was also the first to show improved survival of such patients with ACE inhibition treatment.

In 1984 Dr. Braunwald became the Founding Chair of the TIMI Study Group, an Academic Research Organization that thus far has conducted 70 clinical trials involving 350,000 patients worldwide. In the PROVE-IT TIMI 22 Trial, published in 2004, they demonstrated the benefit of intensive reduction of LDL cholesterol in high risk coronary disease patients, which changed practice guidelines and favorably affected many lives. Science Watch listed Dr. Braunwald as the most frequently cited author in Cardiology with an h index of 229.

Dr. Braunwald served as an editor of Harrison's Principles of Internal Medicine for 12 editions, and is the founding editor of Heart Disease, now in its 12th Edition; these two textbooks are considered to be the most influential in their respective fields.

Dr. Braunwald has received numerous awards and honors, including the Distinguished Scientist Awards of the American College of Cardiology, the American Heart Association, and the European Society of Cardiology. He has received the Kober Medal of the Association of American Physicians, as well as Lifetime Achievement Awards from the Heart Failure Society of America, the American Association for Thoracic Surgery, and the American College of Cardiology. He has served as the President of the American Society for Clinical Investigation as well as the Society of Chairs of Medicine.

The Brigham and Women’s Hospital named its major bed tower and a research center in his honor.

Dr. Braunwald received an honorary Doctor of Science degree from the University of Oxford and is the recipient of honorary doctorates from twenty-three other distinguished universities on three continents. Harvard University established the Eugene Braunwald endowed Chair in Medicine. He was the first adult cardiologist elected to the National Academy of Sciences of the U.S. The American College of Cardiology and the Heart Failure Association of the European Society of Cardiology have established annual lectures in his name. The living Nobel Prize winners in medicine voted Dr. Braunwald as “the person who has contributed the most to cardiology in recent years.”

Emeritus Program Featured Lecture

The Hispanics and Heart Disease: A True Hispanic's Perspective

Dr. Ileana Piña

MD, MPH, FAHA, FACC, FHFSA
Clinical Professor of Medicine, Central Michigan University College of Medicine Adjunct Professor of Epidemiology and Biostats, Case Western University, Population & Quantitative Health Sciences Senior Staff Fellow, Medical Officer FDA, CDRH

ILEANA L. PIña, MD, MPH, is a Clinical Professor at Central Michigan University and Adjunct Professor of Biostats and Epidemiology from Case Western University. Dr. Piña also serves as Senior Fellow and Medical Officer to the Food and Drug Administrations' Center for Devices and Radiological Health.

Dr. Piña earned her undergraduate degree in chemistry from the University of Miami in Florida. She completed her medical degree and cardiology fellowship at the University of Miami School of Medicine; an internal medicine residency at the University of South Florida Tampa, where she was Chief Resident; and fulfilled a surgery internship at the University of Miami Hospitals and Clinics. She earned a master's degree in public health from Case Western Reserve University School of Medicine in Cleveland, Ohio while pursuing a VA Quality Fellowship.

Dr.Piña's research interests include transition of care in heart failure patients, quality improvement and the role of natriuretic peptide–guided management for patients hospitalized for heart failure, biomarkers of myocardial stress and fibrosis in chronic heart failure, and heart failure differences by sex. She has been actively involved in gender, racial and ethnic issues in the health care delivery and written on the intersection of race/ethnicity and heart failure. Along with Dr. Pam Douglas, Dr. Piña led the Diversity section of the new Ethics and Professionalism paper. She is the author/co-author of more than 300 publications. She is currently the past Chair of the FIT committee of the AHA and currently on the Board of Directors National AHA.

In 2017, Dr Piña received the Wenger Award for Excellence in Research, which honours those who make extraordinary contributions to the advancement of women's heart health in underserved communities. In 2020, she received the Laennec Master Clinician Award from the American Heart Association. She is the

author/co-author of more than 300 publications. In 2021, Dr. Piña will receive the Distinguished Service Award from the American Heart Association, Council on Clinical Cardiology.

Nanette K Wenger Honorary Lecture

Creating Novel Solutions to Address Structural Barriers for Trainees Across the Academic Lifecourse: Lessons from A College President

Dr. Paula Johnson
MD MPH

President, Wellesley College
Grayce A. Young Family Professor of Medicine in the Field of Women's Health, Harvard Medical School
Professor of Epidemiology, Harvard T.H. Chan School of Public Health
Physician, Brigham and Women's Hospital

PAULA A. JOHNSON, M.D., M.P.H. is the 14th president of Wellesley College. Throughout a groundbreaking career in academic medicine, public health, and higher education, President Paula Johnson has focused on creating the conditions that allow women to thrive.

Since joining Wellesley in 2016, she has put the College at the forefront of STEM education for women and has led the creation of its bold new strategic plan, which places inclusive excellence at the heart of the Wellesley experience.

President Johnson strongly believes that health and wellness are crucial to academic and personal success, and is reimagining how a college promotes resilience, resolve, and balance in its students at a time when this is needed most. Under her leadership, the College is leading a collaboration that is funded by the Carnegie Corporation to inform the development of a more equitable economy for women as we emerge from the Covid-19 pandemic.

As a physician-scientist, President Johnson has improved health outcomes for women around the globe by revealing and addressing gender biases in both clinical care and medical research. The founder of the Connors Center for Women’s Health and Gender Biology at Brigham and Women’s Hospital, she shifted paradigms by recognizing that disease presentation is often influenced by sex, a biological factor, intersecting with the social determinants of health, including race.

President Johnson developed the center's efforts to both undertake cutting-edge research and translate it into outstanding clinical care for women, and she oversaw the center's work to utilize its research and care models to better educate the next generation of physicians and scientists. Her vision for achieving sustainable improvement in women's health is reflected in the Connors Center's unique approach to all aspects of health throughout the lifespan.

A cardiologist, President Johnson was also the Grayce A. Young Family Professor of Medicine in Women's Health at Harvard Medical School, a professorship named in honor of her mother, and a professor of epidemiology at the Harvard T.H. Chan School of Public Health.

Her research and the research, health care models, and training programs of the Connors Center have had an impact on women across the country by helping to shape health care and health policy reforms. Her work has also influenced and educated emerging leaders beyond the borders of the United States who seek to improve the health of women globally. In 2018, President Johnson co-chaired the landmark report of the National Academies of Sciences, Engineering and Medicine, titled Sexual Harassment of Women: Climate, Culture and Consequences in Academic Sciences, Engineering and Medicine.

In 2020, as the COVID-19 pandemic shut down schools and college campuses across the country, President Johnson joined Massachusetts Governor Baker's 14-member Higher Education Working Group (HEWG) to develop a framework to safely reopen campuses. She also chairs the Massachusetts Higher Education Testing Group. Her 2021 essay, "Learning the lessons of Covid, in order to teach them," was published by the Global Institute for Women's Leadership.

President Johnson is a member of the National Academy of Medicine and the American Academy of Arts and Sciences. She has been recognized as a national leader in medicine by the National Library of Medicine and has received several honorary degrees and numerous awards for her contributions to science, medicine, and public health. Her most recent honors include the Alma Dea Morani Renaissance Woman Award from the Women in Medicine Legacy Foundation and the Stephen Smith Medal for Distinguished Contributions in Public Health from the New York Academy of Medicine. In 2021, she was awarded the Harvard T.H. Chan School of Public Health Alumni Award of Merit.

She earned international acclaim for her 2013 TED Talk, "His and hers...healthcare," which continues to raise awareness of the crucial need to understand sex differences in treating disease.

Her vision, research, and ability to lead at the intersection of education, health care, and public health have earned President Johnson key leadership roles in

organizations around the world. She chaired the board of the Boston Public Health Commission and was a member of the National Institutes of Health Advisory Committee on Research on Women's Health. She has served on numerous national and international boards, and currently serves on the board of directors of the Rockefeller University and is an independent director at Abiomed.

President Johnson attended Harvard and Radcliffe colleges, received her A.B., M.D., and M.P.H. degrees from Harvard, and trained in internal medicine and cardiovascular medicine at Brigham and Women's Hospital. She was born and raised in Brooklyn, New York.

The 32nd Annual George Burch Memorial Lecture

Moving from Statistics to Solutions for Addressing Structural Discrimination in Research

Dr. Gary H. Gibbons

MD PhD

Director, National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health (NIH)

ctor of the National Heart, Lung, and Blood
ıtes of Health (NIH), where he oversees the
n annual budget of approximately $3 billion
oloyees, contractors, and volunteers. NHLBI
rch, training, and education programs to
ıt of heart, lung, and blood diseases and
that they can live longer and more fulfilling

HLBI, Dr. Gibbons has enhanced the NHLBI
science, steadily increasing the payline and
arly stage investigators. His commitment to nurturing the next generation of scientists is manifest in expanded funding for career development and loan repayment awards as well as initiatives to facilitate the transition to independent research awards.

Dr. Gibbons provides leadership to advance several NIH initiatives and has made many scientific contributions in the fields of vascular biology, genomic medicine, and the pathogenesis of vascular diseases. His research focuses on investigating the relationships between clinical phenotypes, behavior, molecular interactions, and social determinants on gene expression and their contribution to cardiovascular disease. Dr. Gibbons has received several patents for innovations derived from his research in the fields of vascular biology and the pathogenesis of vascular diseases.

Dr. Gibbons earned his undergraduate degree from Princeton University in Princeton, N.J., and graduated magna cum laude from Harvard Medical School in Boston. He completed his residency and cardiology fellowship at the Harvard-affiliated Brigham and Women's Hospital in Boston. Dr. Gibbons was a member of the faculty at Stanford University in Stanford, CA, from 1990-1996, and at Harvard Medical School from 1996-1999. He joined the Morehouse School of Medicine in 1999, where he served as the founding director of the Cardiovascular Research Institute, chairperson of the Department of Physiology, and professor of physiology and medicine at the Morehouse School of Medicine, in Atlanta. While at Morehouse

School of Medicine, Dr. Gibbons served as a member of the National Heart, Lung, and Blood Advisory Council from 2009-2012.

Throughout his career, Dr. Gibbons has received numerous honors, including election to the Institute of Medicine of the National Academies of Sciences; selection as a Robert Wood Johnson Foundation Minority Faculty Development Awardee; selection as a Pew Foundation Biomedical Scholar; and recognition as an Established Investigator of the American Heart Association (AHA).

Presidential Lecture

The Role of the NAM in Fostering Solutions to Achieve Health Equity Globally

Victor Dzau

MD PhD

President, US National Academy of Medicine (NAM)
Vice Chair, of the US National Research Council
Chancellor Emeritus, Duke University
James B. Duke Distinguished Professor of Medicine at Duke University

nt of the US National Academy of Medicine
onal Research Council. He is Chancellor
guished Professor of Medicine at Duke
Professor of Medicine at Harvard Medical
Medicine at Brigham and Women's Hospital
Chairman of Department of Medicine at
lliam Irwin Professor and Chief of the
ardiovascular Research Center at Stanford.

r and physician scientist who has made a significant impact through his seminal research in cardiovascular medicine and genetics. His important work on the renin angiotensin system laid the foundation for the development of the class of lifesaving drugs used globally to treat hypertension and heart. He pioneered research in vascular gene therapy and was the first to introduce DNA decoy molecules in humans in vivo. His pioneering research in cardiac regeneration led to the Paracrine Hypothesis of stem cell action and his recent strategy of direct cardiac reprogramming using microRNA. He maintains an active NIH-funded research laboratory.

At the NAM, Dr. Dzau has led important initiatives such as the Global Health Risk Framework for the Future, the Human Genome Editing Initiative, the Grand Challenge in Healthy Longevity, and the Grand Challenge in Climate Change and Human Health. As a global health leader, he has engaged actively with the US and global responses to COVD-19 as a member of the Global Preparedness Monitoring Board, co-chair of the G20 Scientific Expert Panel on Global Health Security, Advisor to the G20 High Level Independent Panel on Financing and a principal of the ACT-Accelerator which includes COVAX, the global collaboration for accelerating the development, manufacture and equitable distribution of COVID19 vaccines.

Dr Dzau has served on the Advisory Committee to the NIH Director and as former chair of the Cardiovascular Disease Advisory Committee and the NHLBI Progenitor

Cell Biology Consortium. Currently, he chairs the NHLBI Progenitor Cell Translational Consortium, the Scientific Boards of Qatar Precision Medicine Institute, the Peter Munk Cardiac Center, University of Toronto and Institute of Cardiovascular and Medical Sciences, University of Glasgow. He co-chairs the Healthy Brain Global Initiative. He is a member of the Health and Biomedical Sciences Advisory Council of Singapore, as well as a board member of the Imperial College Health Partners, UK and the Gairdner Foundation.

Among his many honors and recognitions are the American Heart Association Research Achievement Award, the Max Delbruck Medal from Germany, Gustav Nylin Medal from the Swedish Royal College of Medicine, the Ellis Island Medal of Honor, the Poulzer Prize of the European Academy of Sciences and Arts, and the Henry Freisen International Prize. In 2019, he was named an Honorary Citizen of Singapore- the highest level of honor bestowed to a foreign citizen conferred by the President of Singapore. He has been elected to the National Academy of Medicine, the American Academy of Arts and Sciences, the European Academy of Sciences and Arts, UK Academy of Medical Sciences, the Japan Academy, Mexican Academy of Medicine, Chinese Academy of Engineering and Academia Sinica. He has received 16 honorary doctorates.

The Universal Definition and Classification of Heart Failure

Biykem Bozkurt, MD PhD
Baylor University

Background: Historically available definitions of heart failure (HF) are ambiguous and lack standardization. Some definitions have focused on the diagnostic features of the clinical syndrome, whereas other definitions approach the definition as a characterization of the hemodynamic and physiological aspects. There is significant variation in different platforms, and a growing need for standardization of the definition of HF.

Methods: On August 20, 2020, in response to the necessity for consensus for definition of HF, the Heart Failure Society of America (HFSA), Heart Failure Association of the European Society of Cardiology (HFA) and the Japanese Heart Failure Society convened a virtual consensus conference to develop a universal definition of heart failure with participation from fourteen different countries and six continents. The proceedings of the workgroups were then assembled, resulting in the universal definition chaired by Dr. Bozkurt. The 2020 Universal Definition of HF was reviewed by official reviewers nominated by the HFSA, HFA and JHFS and published jointly in *Journal of Cardiac Failure* and *European Journal of Heart Failure in March 2021*.

Results: The Universal Definition of HF is summarized as " HF is a clinical syndrome with current or prior symptoms and or signs caused by a structural and/or functional cardiac abnormality and corroborated by at least one of the following: Elevated natriuretic peptide levels, objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities such as imaging or hemodynamic measurement at rest or with provocation will be reviewed. Revised stages of HF are: At-risk for HF (Stage A), Pre-heart failure (Stage B), Symptomatic HF (Stage C) and Advanced HF (Stage D). Finally, a new and revised classification of HF according to left ventricular ejection fraction (LVEF) include HF with reduced ejection fraction (HFrEF): symptomatic HF with LVEF ≤40%; HF with mildly reduced ejection fraction (HFmrEF): symptomatic HF with LVEF 41–49%; HF with preserved ejection fraction (HFpEF): symptomatic HF with LVEF ≥50%; and HF with improved ejection fraction (HFimpEF): symptomatic HF with a baseline LVEF ≤40%, a ≥10 point increase from baseline LVEF,and a second measurement of LVEF >40%. Additionally, revised definitions according to trajectories of HF are provided.

Conclusion: The Universal Definition of HF that is clinically relevant, simple but conceptually comprehensive, with the ability to sub-classify and to encompass stages within, with universal applicability globally, and with prognostic and therapeutic validity and acceptable sensitivity and specificity. We envision the proposed universal definition and classifications to be used in a standardized fashion across scientific societies and guidelines, employed by clinicians and used in research studies.

Light at the End of SARS-CoV-2 Pandemic: Integration of Light-Sheet and Light-Field to Uncover Cardiac Morphogenesis

Tzung Hsiai, MD PhD
University of California at Los Angeles

During cardiac development, peristaltic contraction of the embryonic heart tube produces time-varying hemodynamic forces and pressure gradients across the atrioventricular canal. However, the relative importance of myocardial contraction and hemodynamic force to modulate cardiac morphogenesis remain poorly understood. By using dual illumination and dual detection light-sheet system, we recapitulate flow-mediated Notch1b-Nrg1-ErbB2 signaling underlying the initiation of endocardial trabeculation for contractile function. We demonstrate myocardial contractile force-mediated Notch1b-endothealial mesenchymal transition underlying valvulogenesis in the ventricular outflow tract. Overall, we integrate advanced optics with zebrafish genetics to provide biomechanical insights into cardiac development with translational implications to congenital heart disease.

Standards for clinical practice guidelines

Kristen Patton, MD
University of Washington

Clinical practice guidelines are documents intending to establish standards of care supported by scientific evidence. Recommendations within guidelines are informed by an evidence review and an assessment of the benefits and harms of alternative care options. Guideline development is fraught with challenge, yet there is widespread general agreement regarding basic elements of methodology. In 2011, the IOM's Clinical Practice Guidelines We Can Trust, proposed 8 standards for developing high-quality, methodologically rigorous documents, designed to reliably translate complex scientific research into practical, relevant, and individualizable recommendations for patient care. These standards emphasize transparency of the development process and funding, management of conflict of interest, assembling a multidisciplinary and balanced writing group, using quality systematic reviews, establishing the evidence base and rating the strength of recommendation, communicating recommendations, external review, and updating. Despite this and other similar published standards, there is no universally accepted method for guideline development. Multiple instruments to evaluate guideline quality have likewise been developed, and similar to published standards, different tools share many commonalties. The AGREE II tool, one of the most frequently used, measures 6 domains: explicit scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. Neither standards, nor quality evaluation tools, offer guidance to developers in constructing the detailed processes necessary to successful document creation. In this session, we will discuss focused areas of guideline development, including constructing the writing committee, managing relationships with industry, and evaluating the evidence to enable assessment of the strengths and limitations of current standards.

Impact of Health Equity Intervention Measures on Outcomes in Heart Failure Management.

Anekwe Onwuanyi, MD
Morehouse School of Medicine

Background: Disparities in clinical outcomes for cardiovascular diseases, including heart failure are well documented. African Americans and other socioeconomically disadvantaged groups have a higher burden of morbidity and mortality compared to Whites. Social determinants of health (SDOH) have been identified as important contributors to the gap in outcomes. Consequently, identifying key domains of SDOH and health equity interventions to reduce or eliminate the gap is critically needed.

Methods: This study was performed in a safety net hospital with an electronic medical records system (EPIC) that has a population health tool (Healthy Planet), allowing for the collection of comprehensive social and behavioral details of patients. After identifying the key SDOH variables, using a quasi-experimental mixed methods analysis we evaluated how specific interventions in addition to guideline directed medical therapy impacted clinical outcomes. Qualitative data was obtained from patient and staff interviews.

Statistical Analysis: All statistical analyses were performed in Stata (version 13; Stata Corp LLC, College station, Texas). Categorical and continuous variables were summarized using frequency distributions and means with standard deviations (SD) respectively. Wilcoxon sign-rank test was used for the group comparison. $P< 0.05$ was considered statistically significant difference. Each patient was used as its own control for analysis on readmission and hospital length of stay.

Results: Study cohort was 92% African American with majority male (60.2%) and mean age of 60 years, range 23-99 years. Majority of patients were in NYHA class III. 23.5% of our study cohort reported being homeless in the past year. The financial barrier represented by the inability to purchase medication was the most frequent SDOH (33.3%). Among all health equity interventions to mitigate identified social barriers provision of 30-day supply of medications at discharge incurred the highest cost. Participants receiving health equity interventions were less likely to be readmitted in 30 days and had shorter stay in hospital.

Conclusion: Strategies to alleviate or resolve SDOH barriers were effective in improving clinical outcomes for heart failure patients. Large prospective studies with rigorous financial evaluation are needed to validate our findings.

Cardiovascular Health Effects of Pod-Based Electronic Cigarettes

Naomi M. Hamburg, MD, MS
Boston University

Objectives: Robust evidence links combustible cigarette use to chronic cardiovascular disease potentially mediated by endothelial toxicity. Pod-based electronic cigarettes such as JUUL are particularly popular in young adults and deliver high levels of nicotine.

Methods and Results: We measured several axes of cardiovascular health and urinary volatile organic compounds (VOCs) in 133 healthy adults (age 18-45) including pod-based electronic cigarette users, combustible cigarette users before and after a structured product use session. Pod-based electronic cigarette use led to increases in systolic blood pressure (6±8mmHg P=0.00001 vs non-use) and heart rate (4.4±7bpm, P=0.00001) to a similar degree as combustible cigarette use (P=NS). Similarly, we observed reductions in vasodilator function measured by brachial artery flow-mediated dilation (-3.2%±2.7%) and heart rate variability (SDNN -5.9±3.3ms) with by pod-based electronic cigarette use to a greater degree than non-use (P<0.001) and similar to combustible cigarette use (P=NS). The effects of pod-based electronic cigarettes persisted in models adjusted for age, race, and sex. The vascular effects were similar across groups of pod-based users including JUUL compared to non-JUUL pods, dual compared to sole electronic cigarette use, never combustible cigarette users compared to former, and across the flavor categories. Urinary cotinine and nicotine levels were higher in cigarette and pod-based users following acute exposure. The product use induced changes in blood pressure, heart rate variability and flow-mediated dilation but not heart rate related to the urinary levels of acrolein metabolites. In endothelial cells isolated from pod-based electronic cigarette users, we observed impaired activation of endothelial nitric oxide synthase suggesting a potential cellular based mechanisms for the observed differences in vasodilator function. Consistent with the human findings, several pod-based electronic cigarette liquids impaired stimulated nitric oxide bioavailability.

Conclusions: Our results indicate that pod-based electronic cigarette use decreases endothelial function, raises blood pressure, and reduces heart rate variability to a degree comparable to the use of combustible cigarettes. The acute impact is present in young adults who have never used combustible cigarettes. Exposure to selected metabolites of key harmful elements including acrolein may relate to vascular toxicity. At the level of the endothelial cells, there is impaired nitric oxide activation relevant to the observed impact on vasodilator function. Overall our findings suggest that pod-based electronic cigarette use has adverse cardiovascular impact in healthy young adults. Further studies are ongoing to evaluate the longitudinal impact of electronic cigarette use on vascular health.

Towards a Better Understanding of Cholesterol in Hispanics/Latinos

Carlos Rodriguez, MD MPH
Albert Einstein College of Medicine

Hispanics make up ~18% of the United States (US) population and by 2050 the Hispanic population aged ≥65 years is projected to increase six-fold, making Hispanics the fastest-growing aging population. Hispanics are a diverse a heterogeneous group without a race/ethnicity- specific risk equation for atherosclerotic cardiovascular disease (ASCVD). We evaluated the impact of genetic ancestry (African and European) on ASCVD risk prediction on Multi-Ethnic Study of Atherosclerosis (MESA) Hispanic participants.

Methods: Our proposed study will evaluate the impact of Hispanic ethnic group and genetic ancestry on the performance of the Pooled Cohort Equation (PCE) on Predicted ASCVD risk among Hispanic participants of the using both NH-White and NH-Black PCE. Observed ASCVD Events and predicted ACSVD risk discrimination performance of NH-White and NH-Black PCE in Hispanics were stratified by three groups of Hispanic background [consisting of Caribbean-Hispanics (Dominicans, Cubans, Puerto Ricans), Mexicans and Central/South-Americans (Other Hispanic)] and by European and African ancestry.

Results: There were 955 MESA Hispanics included stratified into the following ethnic groups: Mexican (n=517), Caribbean (n=287), Other Hispanic (n=151). When comparing predicted to observed ASCVD events at 10-years using the NH-White and the NH-Black equation there is a general trend towards risk overestimation for all MESA participants. After stratifying by Hispanic ethnic group, we observed a trend towards risk underestimation among Mexicans particularly in the clinically significant categories of 5-7.5% and 7.5-20% risk using both the NH-Black and NH-White PCE. Among Caribbean-Hispanics, there was a general trend towards risk underestimation in the 7.5-20% risk category using the NH-Black and NH-White PCE. In the Other Hispanic group, there was a trend towards risk underestimation in the 5-7.5 and 7.5-20% with the NH-White equation and risk underestimation in the 7.5-20% with the NH-Black equation. In groups with greater than average African or European ancestry, there was risk overestimation across ASCVD categories using the NH-White or NH-Black equation.

Conclusions: Our study looked at the role of Hispanic ethnic subgroup and European or African ancestry on risk estimation of ASCVD risk. Overall, there was no significant difference in using the NH-Black vs NH-White PCE to predict ASCVD risk. However, when stratifying by ASCVD risk categories, both the NH-White and NH-Black PCE seemed to underestimate risk among Hispanic background groups in the clinically relevant 5-7.5% and 7.5-20% risk categories. Given the importance of the PCE for blood cholesterol as well as blood pressure treatment in the current guidelines, our results can have important implications for a large segment of the US population.

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Follow Up platelet functional changes in Depression and Heart disease

Marlene Williams, MD
Johns Hopkins University

Comorbid depression in patients with cardiovascular disease carries higher rates of morbidity and mortality as has been previously documented. As such, several mechanisms have been proposed to account for this increased risk. We have examined whether platelet activation and in particular platelet serotonin signaling can play a part of this increased morbidity. Of particular importance is the timing of biological assessments in depression and heart disease. Many studies have assessed platelet function and other biological factors several months after the initial cardiac event. We have assessed platelet function in a cohort of both stable coronary artery disease and acute coronary syndrome patients (ACS) with and without depression within 72 hours after presentation with a repeat assessment at a one-month follow up period. We hypothesize that depressed ACS patients but not depressed stable CAD patients would have persistently increased platelet activation after a one month follow up period.

Methods: A total of 300 patients with CAD were enrolled (145 with acute coronary syndrome and 155 with stable coronary artery disease). Of these 262 returned for a second visit at a one-month follow up period. Symptoms of depression were assessed by the Beck Depression Inventory – II scale (BDI-II) and major depression was assessed using the Structured Clinical Interview for DSM III-R (SCID) at both visits. Platelet activation was measured by PAC1 expression. Platelet serotonin response was measured by serotonin augmented aggregation and direct platelet serotonin activation.

Results: ACS patients had a reduction in the rate for depressive symptoms (BDI ≥ 10) from 48% to 33.6%, p=0.0017 compared to the stable CAD group who had no significant reduction in the rate of depressive symptoms, 24.5% at first visit compared to 20.5% at follow up visit, p=0.18. The overall level of MDD did not change at the one month follow up in the overall group which was 14% in the entire group on the first visit and at the one month follow up it was 11.4%, p=0.13. Of note ACS patients had no difference in their level of MDD which was 18.7% on presentation and 17.6% at follow up. Depressed ACS (N=53) and depressed stable CAD (N=37) (BDI ≥ 10) patients have decreased platelet activation as measured by change in PAC1 and serotonin response from visit 1 to visit 2: PAC 1 change: -10.82%, p=0.0006 for ACS, -5.59%, p=0.03 stable CAD, Serotonin (0.03-30uM) change: -6.68 to -9.05%, p=0.001-0.01 for ACS, -4.71 to -7.15%, p=0.01-0.15 for stable CAD. Non-depressed (BDI<10) ACS patients had no difference in PAC 1 platelet activation p=0.06 but had decreased platelet serotonin response from visit 1 to visit 2: Serotonin (0.03-30uM) change: -4.97 to -6.83% p=0.01-0.03. Non-depressed stable CAD patients had no significant change in PAC-1 or platelet serotonin response (p=NS).
Conclusion: Persistent platelet activatio

n is not evident by assessment of platelet response to serotonin in depressed patients with either stable or unstable CAD.

Additional platelet functional assessment may be warranted in comorbid depression and cardiovascular disease.

Predictors of Cardioprotective Medication Prescription versus Mortality in Patients Hospitalized with Acute Myocarditis

Subha Raman, MD
Indiana University

Importance: High-sensitivity blood biomarkers and cardiovascular magnetic resonance (CMR) have increased recognition of myocarditis in acutely symptomatic patients. Cardioprotective medications (CPM) such as renin-angiotensin-aldosterone system (RAAS) inhibitors and betablockers have proven mortality benefit across other cardiac conditions, yet their benefit in acute myocarditis remains uncertain.

Objectives: We sought to test the hypothesis that CPM prescription is driven by low LV ejection fraction (EF), whereas myocardial injury burden drives mortality.

Methods: We retrospectively analyzed electronic health records of patients hospitalized for a first episode of acute myocarditis at two quaternary referral centers. Logistic regression and survival analysis were used to evaluate the association between clinical parameters, treatment, and all cause mortality.

Results: Of 362 patients identified with acute myocarditis, 177 (48.9%) were prescribed at least 1 new CPM at discharge; as expected, such therapy was more frequent with LV dysfunction (56% of patients with reduced LVEF vs 17% with preserved LVEF, $p<0.001$). In a multivariable model, myocardial injury by CMR portended greater all-cause mortality (OR=1.81, 95% CI 1.26-2.61, p=0.001), which persisted after accounting for segmental wall motion abnormality (WMA; OR=1.4. 95% CI 1.02-1.92, p=0.04). While LVEF best accounted for CPM prescription, CPM prescription after adjustment for injury burden was not associated with improved outcomes.

Conclusions: All-cause mortality in patients hospitalized with acute myocarditis is predicted by myocardial injury burden by LGE-CMR after accounting for segmental WMA, and not overcome by CPM prescription per current LVEF-guided practice. Myocardial injury itself as a treatment target warrants investigation to reduce mortality after acute myocarditis events.

Dysregulation of Ca2+ Homeostasis in Hypertrophic Cardiomyopathy

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University of Arizona

Hypertrophic Cardiomyopathy (HCM) is the most common genetic cardiomyopathy, and its clinical manifestations are near protean, vastly complicating clinical management and the development of new therapeutics. One of the few common findings is varying degrees of impairment of cardiac relaxation, though the etiologies are likely complex, given that symptoms are not always directly related to the degree of LV hypertrophy, an observation that suggests a primary myocellular mechanism. Moreover, decreased ventricular compliance contributes to an increase in LV filling pressures that can promote adverse left atrial remodeling and increases the risk of atrial fibrillation and stroke, poor prognostic indicators in patients with HCM. Our group focuses on the structure, biology and pathobiology of the cardiac thin filament (CTF). Given the primary role of the CTF as the transducer of oscillatory myocellular [Ca2+] into mechanical work (sarcomeric contraction), our primary hypothesis is that HCM-linked CTF mutations disrupt the kinetics of Ca2+ association and dissociation at the myofibrillar Ca2+ “axis” and lead to complex downstream alterations in Ca2+ signaling that contribute to progressive pathogenic remodeling and eventually impaired relaxation in HCM. We have developed an integrated in silico – in vitro – in vivo approach that facilitates coupling between molecular level biophysical mechanisms and whole heart function via transgenic mouse models. Building on our original myocyte-level observations that revealed mutation-specific differences in Ca2+ homeostasis in CTF mutant mice and a potential nodal role for CaMKII (the latter recently validated in human samples), more recently we have focused on using our all-atom computational model of the CTF to predict the mechanisms whereby mutation-specific allosteric modulation of Ca2+ association and dissociation kinetics at Site II of cTnC potentially alters the local [Ca2+] domain, leading to the auto-activation of CaMKII. We propose that this modulation is regulated by a mutation-driven disruption of the physical orientation of the N- terminus of cTnI that physically alters the efficiency of Ca2+ association/release from cTnC Site II. Of note, this region of cTnI contains the PKA-mediated substrate site that coupled CTF function to beta-adrenergic signaling. The complexity of this proposed mechanism likely contributes to the phenotypic variability observed in patients and provides a potential target for therapeutic modulation that may have broader applicability.

Devices for patients with heart failure

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Despite substantial advances in medical therapy for heart failure with reduced ejection fraction (HFr EF) and more recent advances in the medical therapy of heart failure with preserved EF (HFpEF),heart failure remains a progressive medical condition. A number of devices have been developed and approved for the treatment of heart failure with both the number and diversity of targets these devices address increasing rapidly. Despite improved morbidity and mortality in both HFpEF and particularly HFrEF,both morbidity and mortality remain high. Furthermore, medical therapy requires constant patient compliance, titration of beneficial medical therapies is often limited by hypotension, and the patient's tolerance for taking additional medications may also be limited. In addition there are a number of manifestations of heart failure and/or targets for heart failure that medical therapy alone cannot completely address. These include treating ventricular tachycardia or fibrillation, synchronizing cardiac contraction, improving cardiac contractility, reducing severe secondary mitral regurgitation, improving autonomic imbalance characteristic of heart failure monitoring pulmonary artery pressures to recognize and prevent exacerbation of heart failure. In addition to FDA approved devices for heart failure the use of devices to shunt blood from the left atrium to the right atrium and reduce pulmonary pressures during exercise in order to reduce exercise dyspnea is an exciting new potential device therapy. Some devices may be beneficial but have important effects that could be addressed to improve outcomes. I will review the ongoing benefits of the following devices: Implantable cardiac defibrillator (ICD's), cardiac resynchronization therapy, transcatheter edge-to-edge repair for severe secondary mitral valve replacement, devices to monitor pulmonary artery pressures allowing therapeutic management, devices that improve autonomic imbalance and more recently intra-atrial shunts. I will also review the vascular remodeling that occurs with left ventricular assist devices that may be a target for improving outcomes with these devices.

Dueling the Dual Pandemic: Nutrition, COVID-19 and Cardiovascular Mortality

Kim A Williams Sr, MD
Rush University

Heart disease, kidney disease and stroke mortality are increasing, driven by diet, exercise and lifestyle choices, mediated by risk conferred by the microbiome. The microbiome accounts for the majority of the cell count in humans, i.e., humans are only about 43% human. A dysbiotic microbiome is associated with a variety of degenerative and autoimmune disorders. Risk factors for mortality are promoted by nutrition that results in dysbiosis, while being reduced by nutritional factors that have been associated with improved outcomes, as recommended in the 2019 ACC/AHA Primary Prevention Guidelines' nutrition section:

- *A diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish is recommended to decrease ASCVD risk factors.*
- *Replacement of saturated fat with dietary monounsaturated and polyunsaturated fats can be beneficial to reduce ASCVD risk.*
- *A diet containing reduced amounts of cholesterol and sodium can be beneficial to decrease ASCVD risk.*
- *As a part of a healthy diet, it is reasonable to minimize the intake of processed meats, refined carbohydrates, and sweetened beverages to reduce ASCVD risk.*
- *As a part of a healthy diet, the intake of trans fats should be avoided to reduce ASCVD risk.*

Plant-based diets, are associated with lower rates of obesity, and diabetes, high quality of life and longer life-expectancy, as well as less hypertension, dyslipidemia, peripheral artery disease, coronary disease, myocardial infarction, erectile dysfunction, heart failure, chronic kidney disease, stroke and death, much of which is mediated by the microbiome.

In our dual pandemic of cardiovascular and COVID-19, we need to advocate for risk factor reduction, whenever and wherever possible by improving our microbiome to reduce mortality associated with nutrition-related illnesses.

Shaping Waves of Bone Morphogenetic Protein Inhibition during Vascular Growth

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Rationale: The bone morphogenetic proteins (BMPs) are essential morphogens in angiogenesis and vascular development. Disruption of BMP signaling can trigger cardiovascular disease such as arteriovenous malformations.

Objective: A computational model predicted that BMP4 and BMP9 and their inhibitors matrix Gla protein (MGP) and Crossveinless-2 (CV2) would form a regulatory system consisting of negative feedback loops with time delays, and that BMP9 would trigger oscillatory expression of the two inhibitors. The goal was to investigate this regulatory system in endothelial differentiation and vascular growth.

Methods and Results: Oscillations in the expression of MGP and CV2 were detected in endothelial cells (ECs) in vitro, using qPCR and immunoblotting. These organized temporally downstream BMP-related activities including expression of stalk cell markers and cell proliferation, consistent with an integral role of BMP9 in vessel maturation. In vivo, the inhibitors were located in distinct zones in relation to the front of the expanding retinal network, as determined by immunofluorescence. Time-dependent changes of the CV2 location in the retina, and the existence of an endothelial population with signs of oscillatory MGP expression in developing vasculature supported the in vitro findings. Loss of MGP or its BMP4-binding capacity disrupted the retinal vasculature, resulting in poorly formed networks, especially in the venous drainage areas, and arteriovenous malformations as determined by increased cell coverage and functional testing.

Conclusions: Our results suggest a previously unknown mechanism of temporal orchestration of BMP4 and BMP9 activities that utilizes the tandem actions of the extracellular antagonists MGP and CV2. Disruption of this mechanism may contribute to vascular malformations and disease.

Bayesian network modeling coupled with genetic feature selection as a mortality model for PAH

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Ohio State University

Background: Pulmonary arterial hypertension (PAH) is a fatal and difficult to treat disease due to patient inter-variability. Accurate patient risk stratification is necessary for guiding treatment, but no PAH risk calculator has been able to achieve an excellent performance in receiver-operator area under the curve (AUC > 0.8). New cutting-edge techniques with Bayesian network modeling for risk stratification have been published recently, show promising results (Pulmonary Hypertension Outcomes Risk Assessment or PHORA 1.0). Early studies of a newly derived Bayesian Network model (PHORA 2.0) demonstrated feasibility of improving PHORA 1.0 accuracy with an expanded feature set and new network structure. In this study, a finalized PHORA 2.0 model was developed that balances the number of variables required with model accuracy.

Methods: Patient-level data had been previously aggregated and harmonized across six contemporary PAH clinical trials (AMBITION, PATENT-1/2, GRIPHON, SERAPHIN, FREEDOM-EV, ARIES-1/2); all patients were assessed at baseline (for cross-over placebo patients from PATENT and ARIES, baseline was start of extension). Forty-one clinical variables were initially considered, based on their p-value ranking from previous meta-analyses, availability across trials, and expert opinion. A correlation heatmap was used to aggressively remove variables with moderate-to-strong correlation (R > 0.6), with priority given to the most significant variables in the meta-analysis. Training data was created by random sampling of 80% of the harmonized dataset, dropping early censored patients (N = 2531), leaving 20% of the data as a validation set (N = 626). Continuous variables were discretized through univariate supervised decision trees using 10-fold cross-validation that maximized Brier score. A novel method of genetic search optimization determined candidate groups of features that maximized ranked correlation with the outcome (Kendall's tau for one-year survival) and reduced redundant features, with increasing penalty for redundancy. This method established four feature combinations that were evaluated in Augmented Naïve Bayesian Network classifiers, and the best model was selected by multiple rounds of 10-fold cross-validation on training data. Final performance is reported as performance on the validation set.

Results: The best final model as determined from genetic search of feature combinations maintained a high cross-validation (Average AUC 0.82) using 16 out of 19 possible variables (see Figure 1). Final performance on the test set using this model was an AUC = 0.85. The final model outperformed all other published risk calculators at test time (Figure 1).

Conclusion: Bayesian network modeling coupled with genetic feature selection has discovered, for the first time, a mortality model for PAH with excellent performance (AUC > 0.8).

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Heart Failure Omics: Cardiac Metabolism and Beyond

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Duke University

Heart failure (HF) is a major public health problem and while HF and its related risk factors portend poor prognosis, there is marked heterogeneity in development of, and survival from, HF. As such there is a need for more personalized approaches to risk models, prevention and therapies for HF. Advances in molecular profiling technologies have facilitated identification of potentially clinically relevant in parallel with highlighting potential novel molecular mechanisms of disease. Given the central role of metabolism to the normal and failing heart, metabolomic profiling holds great promise for such a personalized approach. Our laboratory studies genetic and metabolic biomarkers and pathways in cardiometabolic diseases including obesity and HF. Our work has elucidated the role of dysregulated mitochondrial branched chain amino acid (BCAA) metabolism and related circulating biomarkers in obesity, functional impairment in HF and in HF with reduced ejection fraction. We have also identified circulating metabolites reflecting impaired mitochondrial fatty acid oxidation in HF with reduced and preserved ejection fraction. Finally, we have expanded our work in the molecular epidemiology of HF most recently with identification of protein biomarkers and pathways for HFpEF and post-heart transplant outcomes.

Protecting mitochondrial function to prevent cardiovascular toxicity of cancer therapies

Isabella Grumbach, MD PhD
University of Iowa

Background: Approximately 18 million cancer survivors currently live in the U.S. These individuals represent more than 5.0% of the U.S. population. With improving therapies, the number of cancer survivors is projected to increase to > 25 million by 2040. At least 40% of this population received radiation therapy (RT) as part of their cancer treatment.

A major concern related to these predictions is that, despite dramatic improvements in techniques that target RT to malignant tissue, some radiation is always dispensed to normal tissue. Despite a well-documented high incidence of heart failure, premature valvular and occlusive vascular diseases, the mechanisms of radiation injury to the heart, large arteries and are not completely understood. Endothelial damage within the microvasculature, also termed “radiation endotheliopathy” is believed to be the major driver of radiation-induced injury to normal tissue in all organs, including acute gastrointestinal syndrome, lung and skin fibrosis, and heart failure. One striking understudied example of such syndrome is radiation-induced cognitive impairment. Radiation-induced cognitive impairment occurs in up to 90% of adult survivors of brain tumors after RT.

Methods and Results: Our studies *in vivo* and *in vitro* in endothelial cells from different vascular beds confirm that mitochondria are particularly susceptible to damage by RT. In our studies, we established the concept that the repair of mitochondrial DNA after RT is rudimentary, leaving DNA only partially repaired and altering the expression and activity of electron transport chain complexes.

These events cause a chronic increase in the production of mitochondrial oxidative stress and ultimately leads to cell senescence and further epigenetic changes that are propagated upon cell division. We also demonstrate that mitochondrial Ca^{2+} uptake is augmented in irradiated cells because of an increase in the mitochondrial membrane potential. Influx of Ca^{2+} into mitochondria via the mitochondrial Ca^{2+} uniporter (MCU) leads to increases in the activity of the Krebs cycle as well as of the electron transport chain, thereby promoting generation of oxidative stress. RT-induced oxidative stress can be blocked by inhibiting mitochondrial Ca^{2+} uptake. These findings suggest that either scavenging mitochondrial oxidative stress or reducing mitochondrial Ca^{2+} overload might prevent radiation endotheliopathy, potentially by promoting efficient repair of mitochondrial DNA. Indeed, blocking either event prevents endothelial dysfunction in vivo in larger arteries after RT as well as blood brain barrier dysfunction.

We also tested the effects of statins in our models given that incidental use of statins has been reported to decrease the progression of macrovascular disease after RT. Surprisingly, we found differential effects of statins on mitochondrial function and vascular reactivity *in vivo* after RT.

Conclusions: Despite the growing number of cancer survivors that have been treated with to RT, there are no proven mitigators that prevent RT-induced cardiovascular dysfunction. Our research program has identified mitochondrial pathways that drive endothelial dysfunction after RT and may be druggable. Lastly, our data point towards differential effects of statins in experimental models that require urgent validation in humans.

Practical Strategies to Enhance Diversity in Cardiology

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Racial diversity in medicine and cardiology will result in the following: enhanced patient satisfaction and communication with an increasingly diverse patient population; enhanced cultural competence of all physicians and providers; expanded access to and utilization of health services for minority and disadvantaged patients; and enhanced breadth, scope, and impact of biomedical research with a broader range of racial/ethnic perspectives. This will clearly result in lives saved and enhanced quality of life for many. Yet, despite decades of major healthcare organizations calling for an increase in the diversity of the healthcare workforce, individuals from Black, Hispanic, Native American, and other Indigenous groups remain severely underrepresented in cardiology. Ultimately, inequities in the social determinants of health and academic success will need to be eliminated before all demographic groups have an equal opportunity to become physicians. In the meantime, several strategies have proven to have limited success in diversifying medicine and cardiology.

When discussing practical strategies to enhance diversity it is useful to consider the following framework to focus efforts:

1. The Deep Pipeline: Reaching out to children in the early grades to inspire them to pursue careers in medicine and keep them motivated through the early years when many obstacles discourage them from envisioning themselves as physicians.
2. The Intermediate Pipeline: Reaching out to college, medical students, and internal medicine residents to demystify the processes for successfully preparing for and applying to medical school, residency, and cardiology training.
3. The “End-Game” Processes: Dismantling racism, bias, and other forms of injustice in the selection processes from medical school to cardiology subspecialty fellowships and faculty.

In this presentation the speaker will review strategies that academic medical centers and individuals can develop and actualize to accelerate attempts to enhance diversity in medicine and cardiology. Emphasis will be on practical strategies that have proven successful and can be deployed immediately.

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