AUC
Association of University Cardiologists

PROGRAM AND ABSTRACTS

Association of University Cardiologists
Sixty-Second Annual Meeting
Hybrid Meeting

January 18-20, 2023

2023

AUC
Association of
University Cardiologists

PROGRAM

2023

2023 AUC Annual Meeting Program
All times are PACIFIC STANDARD TIME

Wednesday, January 18, 2023

9:00 AM – 12:00 PM PST	**Council Meeting** *Location:* The Think Tank (AUC Council Members only)
Emeritus Session	3:00 PM – 5:00 PM PST *Location:* Oak Room and Oak Courtyard
3:00 – 4:00 PM PST	Speaker: Martha Gulati, MD MS *Chest Pain*
4:00 – 5:00 PM PST	Speaker: Michael E. Cain, MD *Evolution of Nonpharmacologic Therapy for VT*
5:00 PM PST	**ADJOURN**
6:00 – 8:00 PM PST	**AUC Welcome Reception** *Location:* Oak Room / Courtyard

2023

2023 AUC Annual Meeting Program
All times are PACIFIC STANDARD TIME

Thursday, January 19, 2023

7:30 AM – 8:30 AM PST	**Continental Breakfast** *Location:* Redwood Terrace
Presidential Session	8:30 – 11:15 AM *Location:* Redwood Room
8:30 – 8:40 AM PST	**President's Welcome and Address** Sumeet S. Chugh, MD
8:40 – 9:25 AM PST	**Nanette K Wenger Honorary Lecture** Dianna M. Milewicz, MD PhD *Deploying Cardiovascular Genomic Findings in Clinical Care* *Moderator: Sumeet Chugh, MD*
9:25 – 10:10 AM PST	**George Burch Memorial Lecture** Eric Topol, MD *Artificial Intelligence in Cardiovascular Medicine* *Moderator: Sumeet Chugh, MD*
10:10 – 10:30 AM PST	**BREAK** *Location:* The Gallery
10:30 – 11:15 AM PST	**Presidential Lecture** Sumeet S. Chugh, MD *Prevention of Sudden Cardiac Death: Challenging Our Assumptions* *Moderator: Barry London, MD PhD*
11:15 – 11:20 AM PST	**Introduction of New Members in Attendance** Sumeet S. Chugh, MD

Emma Birks, MD PhD	*Andrea Russo, MD*
Gregory Marcus, MD MAS	*Win Shen, MD*
Dennis McNamara, MD	*Kalyanam Shivkumar, MD PhD*
Frederick Ruberg, MD	*Frederick Welt, MD*

12:00 – 1:00 PM PST	**LUNCH** *Location:* Redwoods Terrace

2023

Scientific Session 1	1:15 – 3:25 PM *Location:* Redwood Room
1:15 – 1:35 PM PST	**Scientific Talk 1** Emma Birks, MD PhD *Moderator: Karol Watson, MD PhD*
1:35 – 1:55 PM PST	**Scientific Talk 2** Frederick Welt, MD *Moderator: Karol Watson, MD PhD*
1:55 – 2:15 PM PST	**Scientific Talk 3** Gregory Marcus, MD MAS *Moderator: Jane E. Freedman, MD*
2:15 – 2:45 PM PST	**BREAK**
2:45 – 3:05 PM PST	**Scientific Talk 4** Dennis McNamara, MD *Moderator: Jane E. Freedman, MD*
3:05 – 3:25 PM PST	**Scientific Talk 5** Frederick Ruberg, MD *Moderator: Charles J. Lowenstein, MD*
3:25 PM PST	**ADJOURN**
6:00 – 7:00 PM PST	**Reception** *Location:* Golf Clubhouse Patio
7:00 – 10:00 PM PST	**Formal Dinner** (black-tie) *Location:* Golf Clubhouse

2023

2023 AUC Annual Meeting Program
All times are PACIFIC STANDARD TIME

Friday, January 20, 2023

7:00 AM – 8:00 AM PST	**Continental Breakfast** *Location:* Redwood Terrace
Business Meeting	8:00 – 9:00 AM *Location:* Redwood Room

AGENDA

Memorials	
Election	
AUC Finances	Charles J. Lowenstein, MD
Discussion	Sumeet S. Chugh, MD
Passing the Gavel	Sumeet S. Chugh, MD Barry London, MD PhD
Scientific Session 2	9:00 – 10:30 AM *Location:* Redwood Terrace
9:00 – 9:20 AM PST	**Scientific Talk 6** Andrea M. Russo, MD *Moderator: Barry London, MD PhD*
9:20 – 9:40 AM PST	**Break**
9:40 – 10:00 AM PST	**Scientific Talk 7** Win Shen, MD *Moderator: Joseph Wu, MD PhD*
10:00 – 10:20 AM PST	**Scientific Talk 8** Kalyanam Shivkumar, MD PhD *Moderator: Joseph Wu, MD PhD*
10:20 – 10:40 PM PST	**Closing Comments** Barry London, MD PhD
10:40 AM PST	**ADJOURN**

2023

AUC
Association of
University Cardiologists

INVITED SPEAKERS

2023

Emeritus Program Featured Lecture
Chest Pain

Martha Gulati
MD MS

Anita Dann Friedman Professor of Cardiology,
Director of CVD Prevention
Associate Director, Barbra Streisand Women's Heart Center
Cedars-Sinai Health System., Los Angeles

MARTHA GULATI, MD, MS, FACC, FAHA, FASPC, FESC is the President of the American Society for Preventive Cardiology. She was a Professor of Medicine and the inaugural Chief of Cardiology at the University of Arizona. She is the author of the best-seller, "Saving Women's Hearts". She served as the chair of the national chest pain guidelines that were released in late 2021. She recently joined the Cedars-Sinai Heart Institute as a professor of cardiology and is the director of prevention, the associate director of the *Barbra Streisand Women's Heart Center and holds the* Anita Dann Friedman Endowed Chair in Women's Cardiovascular Medicine and Research.

Dr Gulati has won her numerous awards and distinctions, including being named by *Crain's Chicago Business* as one of Chicago's Top 40 under 40. In 2019, she received the 2019 American College of Cardiology's Bernadine Healy Award for her leadership and accomplishment in the field of cardiovascular disease in women. She is the principal investigator of the St. James Women Take Heart Project and a co-investigator on the Women Ischemic Syndrome Evaluation (WISE) and previously served as a co-investigator on the Women's Health Initiative (WHI). She has published articles in peer-reviewed publications, including *The New England Journal of Medicine, Circulation,* and *Journal of the American Medical Association* (*JAMA*). She has also been featured on *Oprah*.

Emeritus Program Featured Lecture
Evolution of Nonpharmacologic Therapy for VT

Michael Cain
MD

Professor of Medicine and Biomedical Engineering
Vice President (Emeritus) for Health Sciences
Dean (Emeritus), Jacobs School of Medicine and Biomedical Sciences

MICHAEL CAIN, M.D., is a specialist in abnormal heart rhythms. He is board-certified in internal medicine, cardiovascular diseases and clinical cardiac electrophysiology and pacing. He is a fellow of the American College of Cardiology, the American Heart Association and the Heart Rhythm Society.

A former associate editor of Circulation, Cain is a member of the editorial boards of the American Journal of Cardiology, the Journal of Cardiovascular Electrophysiology, Nature Clinical Practice Cardiovascular Medicine and Heart Rhythm.

His NIH-supported research has focused on determining the mechanisms of life-threatening heart rhythm abnormalities that occur in heart attacks and other conditions that damage heart muscle cells. This information is being used to better characterize and more accurately localize the abnormal heart tissue responsible for these abnormal heart rhythms and to improve the identification of patients at increased risk for sudden cardiac death.

Nanette K Wenger Honorary Lecture

Deploying Cardiovascular Genomic Findings in Clinical Care

Dianna Milewicz MD PhD

President George H.W. Bush Chair of Cardiovascular Medicine
Vice-Chair, Department of Internal Medicine
Director, Medical Genetics Division
Professor of Medicine
University of Texas Health Science Center at Houston (UTHealth) McGovern Medical School

DIANNA M. MILEWICZ, M.D. Ph.D, is the President George H.W. Bush Chair of Cardiovascular Medicine, Director of the Division of Medical Genetics and Vice-Chair of the Department of Internal Medicine at the University of Texas Health Science Center at Houston (UTHealth) McGovern Medical School. She completed her postgraduate training in internal medicine, specialized further in medical genetics, and forged a career in translational studies focused on genetic predisposition to vascular diseases. She has received numerous honors and awards for her research, including the Antoine Marfan Award, the Doris Duke Distinguished Clinical Scientist Award, and the University of Texas Presidential Scholars Award for Excellence in Research. She has been inducted into the American Society of Clinical Investigation and the Association of American Physicians. Dr. Milewicz has been the Director of the M.D./Ph.D. Program offered jointly between the University of Texas Health Science Center at Houston and MD Anderson Cancer Center institutions for over 10 years and is Chair of the GREAT MD/PhD Section Committee.

The 33rd Annual George Burch Memorial Lecture
Artificial Intelligence in Cardiovascular Medicine

Dr. Eric Topol MD

Founder & Director, Scripps Research Translational Institute
Executive Vice President, Scripps Research
Gary and Mary West Endowed Chair of Innovative Medicine, Scripps Research
Editor-in-Chief, Medscape and theheart.org

ERIC J. TOPOL, M.D., is the Founder and Director of the Scripps Research Translational Institute, Professor of Molecular Medicine, Executive Vice-President, and Gary and Mary West Endowed Chair of Innovative Medicine at Scripps Research. Dr. Topol is also Editor-in-Chief of Medscape. He has published over 1300 peer-reviewed articles, with more than 300,000 citations, elected to the National Academy of Medicine, and is one of the top 10 most cited researchers in medicine. His principal scientific focus has been on the use of genomic and digital data, along with artificial intelligence, to individualize medicine. He is a practicing cardiologist.

Dr. Topol earned his medical degree from the University of Rochester and, after additional training at the University of California, San Francisco and Johns Hopkins University, went to the University of Michigan, where he became a tenured professor, and then was appointed chief of cardiovascular medicine at Cleveland Clinic. He was elected to the National Academy of Medicine in 2004. Three years later, he founded the Scripps Research Translational Institute, which joined Scripps Research in 2017.

In 2016, Topol was awarded a $207 M grant from the NIH to lead a significant part of the Precision Medicine (All of Us) Initiative. He is principal investigator for a $35 M NIH CTSA grant to promote innovation in medicine.

Presidential Lecture

Prevention of Sudden Cardiac Death: Challenging Our Assumptions

Sumeet S. Chugh MD

Pauline and Harold Price Professor of Cardiac Electrophysiology
Director, Heart Rhythm Center
Associate Director, Smidt Heart Institute
Director, Division of Artificial Intelligence, Dept of Medicine
Cedars-Sinai Health System, Los Angeles

Dr. Chugh is a clinical cardiac electrophysiologist and his research efforts have focused on improving prediction and prevention of sudden cardiac arrest. In the last two decades, he has founded and led a research cooperative of emergency medical services, hospitals and the medical examiner network in Oregon and California that studies a total population of 1.8 million residents. This effort resulted in a data repository of sudden cardiac arrest patients linked to a biobank that has been mined for mechanisms and predictors of this condition, now in its 21st year. His group has recently published a novel clinical risk prediction score as well as unique plasma and genomic biomarkers that are being explored as tools to enhance management and prevention of sudden cardiac death. Dr Chugh is a member of the American Society for Clinical Investigation and has received the Howard Morgan Award for distinguished achievements in cardiovascular research, the Simon Dack Award from the American College of Cardiology and the Douglas P Zipes lectureship award from the Heart Rhythm Society. He is the current President of the Association of University Cardiologists, and immediate Past-President of the Cardiac Electrophysiology Society. Dr. Chugh is funded by the National Heart Lung and Blood Institute and has published over 240 peer-reviewed scientific papers (citations >80,000, Dec 2022).

AUC
Association of
University Cardiologists

ABSTRACTS

2023

Myocardial Recovery Using Left Ventricular Assist Device (LVAD)s

Emma Birks, MD PhD BSc MBBS
University of Kentucky

Background: Advanced heart failure (HF) is generally considered largely irreversible once severe or present for a long time. However, LVAD support, which provides near-total unloading of the ventricle, can promote near-normalization of the structural abnormalities of the myocardium, or "reverse remodeling" in patients with chronic advanced HF. This is often associated with significant recovery of the underlying cardiac function sufficient to allow LVAD removal (myocardial recovery or "remission" of end-stage HF). However, the rate at which this occurs is generally reported at only 1-2%.

Methods and Results: I will present my work studying the use of LVADs as a platform to induce myocardial recovery using a strategy of optimizing LVAD speed for optimal hemodynamic unloading combined with aggressive pharmacologic therapy, specifically designed to enhance reverse remodeling, along with regular testing of underlying myocardial function. Using this approach in an initial prospective study of 20 patients with chronic advanced HF receiving a pulsatile HeartMate XVE LVAD, 73% of those receiving this protocol reached pre-determined explant criteria and were explanted, with 1 and 4 years survival after explantation of 90.9% and 81.8%. Initially it was thought likely only pulsatile devices were effective at mechanical unloading but in a second prospective study of 20 patients with chronic HF due to non-ischemic cardiomyopathy (NICM) supported with an axial Heartmate II continuous flow pump, 12 (60%) were explanted. The cumulative freedom from death and recurrence of HF in the explanted patients was 83.3% at 30 days, 1 and 3 years. A prospective multicenter non-randomized study (RESTAGE-HF) then investigated whether such an approach could be reproducible across multiple centers, 40 NICM patients requiring Heartmate II LVAD implantation were enrolled from 6 centers. Overall 19 patients were explanted (19/36, 52.3% of those receiving the protocol) and 40% of all enrolled (16/40) achieved the primary endpoint ($p<0.0001$) of explantation within 18 months with sustained remission from HF (freedom from transplant/VAD/death) at 12 months. Post-explantation survival free from LVAD or transplantation was 90% at 1-year and 74% at 3 and 5 years. Hence this strategy resulted in a high rate of LVAD explantation and was feasible and reproducible with explants occurring in all six participating sites.

Long-term a significant percentage of these LVAD explanted patients achieve cardiac and physical functional capacities that are within the normal range of healthy controls, and these patients have a good quality of life. A longer-term

comparison of LVAD patients explanted for myocardial recovery with those transplanted from LVAD support found similar survival in the explanted and transplanted groups at 1, 5, and 7 years, respectively with creatinine significantly better in the explanted group. Furthermore, myocardium obtained during LVAD implantation and at transplant (non-recovered) or explant can be correlated with clinical and hemodynamic changes during recovery providing a unique model of the reversal of human heart failure.

Conclusion: This approach, now shown to be reproducible amongst centers and with different devices, is likely to dramatically increase the rate of myocardial recovery/explantation seen and parallel molecular research might lead to new therapeutic targets for HF.

Acute Exposures and Arrythmia Outcomes

Gregory Marcus, MD MAS
University of California, San Francisco

Background: While risk factors for arrhythmias, predominately atrial fibrillation (AF), have been well-established, these tend to be chronic, are generally immutable, and largely portend the eventual diagnosis of the disease. However, arrhythmia patients have communicated a particular interest in acute exposures that might influence discrete arrhythmia episodes. Understanding these more immediate phenomena may provide clinically useful insights into both primary and secondary prevention of arrhythmias.

Methods: We have conducted several analyses utilizing case-crossover, N-of-1, and instrumental variable analyses to examine relationships between acute exposures and discrete arrhythmia episodes, including: 1. Fitting paroxysmal AF patients with continuously recording ECG monitors to assess for AF while wearing continuous alcohol sensors 2. Assessing patterns of use of Bluetooth-enabled breathalyzer devices to infer nationally recognized events as instrumental variables reflecting enhanced alcohol consumption; then comparing those events to emergency department visits for atrial fibrillation 3. Utilizing a smartphone-based mobile application to conduct N-of-1 randomized trials of patient-selected triggers of acute AF episodes and 4. Randomly assigning volunteers to avoid versus consume coffee on a daily basis to assess relationships with wearable ECG-based ectopy counts, as well as other activities relevant to cardiovascular health, including sleep and step counts measured by wearable accelerometers.

Results: Our case-crossover analyses revealed that consuming one drink of alcohol was associated with a greater than two-fold greater odds of a discrete AF event within four hours. The amount of alcohol consumed per the wearable alcohol sensor predicted a near-term AF event. In our instrumental variable analysis, events associated with more alcohol consumption were associated with a substantial increase in emergency department visits for AF over a 10-year period in California. In our N-of-1 studies: although caffeine was the trigger most commonly selected for testing, its consumption exhibited no relationship with acute AF; in contrast, in per-protocol analyses, consumption of alcohol was associated with a greater risk of self-reported AF. In our randomized trial, coffee consumption was not associated with any changes in premature atrial contraction counts but was associated with more premature ventricular contractions. Days randomly assigned to consume (versus avoid) coffee were also associated with substantially less sleep that evening, but significantly more steps taken during that day.

Conclusions: Alcohol appears to increase the risk that a discrete AF episode will occur, resulting in enhanced healthcare utilization for AF. In contrast, caffeine does not appear to acutely increase the risk of either AF or one of the most relevant harbingers of AF, premature atrial contractions. Acute caffeine consumption also appears to increase premature ventricular contractions, reduces sleep, and is associated with more physical activity. Understanding real-time relationships between acute exposures and arrhythmias may provide clinically relevant information to empower patients. These data may also inform clinicians regarding immediately modifiable risk factors that have meaningful effects on cardiovascular health.

Pathogenesis and Therapy of Peripartum Cardiomyopathy: Results from IPAC and plans for the REBIRTH Trial

Dennis McNamara, MD
University of Pittsburgh Medical Center

Peripartum cardiomyopathy (PPCM) remains a major cause of maternal morbidity and mortality. While improvements in myocardial function occur in more than half of women, those who do not recover are left with chronic cardiomyopathy and 5-10% of women die or require cardiac transplantation or LVAD support during the first year postpartum. Black women are at greater risk for this disorder, present with more severe LV dysfunction and have poorer outcomes. The pathogenesis remains unknown but vascular, genetic and inflammatory etiologies have been postulated. The Investigation of Pregnancy Associated Cardiomyopathy (IPAC) study enrolled 100 women with PPCM at 30 centers and evaluated LV recovery and event free survival to determine the impact of genetic background as well as vascular and inflammatory mediators on subsequent recovery and outcomes. As with other forms of nonischemic cardiomyopathy, a significant subset of women with PPCM have truncation mutations in sarcomere proteins. These appear to impact the risk of the disorder but not subsequent recovery. In terms of vascular mediators, soluble sFlt1 (circulating VEGF receptor) was associated in IPAC with more severe disease and poorer outcomes.

A 16kD N terminal fragment of prolactin appears to be pathogenic in murine models of PPCM. This role of prolactin in pathogenesis has led to the investigation of the dopaminergic agonist bromocriptine which inhibits prolactin release as a potential therapy. Previous studies in Africa and Europe have suggested improved outcomes with bromocriptine therapy for PPCM, but these studies have not been definitive. No well controlled randomized trial comparing standard guideline directed medical therapy to standard therapy plus bromocriptine has been performed in a diverse multi-racial cohort, and as a result bromocriptine therapy is rarely used to treat PPCM in the United States. The recently initiated REBIRTH trial (Randomized Evaluation of Bromocriptine In myocardial Recovery THerapy for peripartum cardiomyopathy) will randomize 200 women to bromocriptine or placebo at 50 centers across North America to determine the role of bromocriptine in the treatment of this disorder.

By inhibiting prolactin release bromocriptine prevents breastfeeding, and women who wish to continue breastfeeding are excluded from the randomized trial. The potential therapeutic impact of bromocriptine has led to suggestions that raising prolactin levels by breastfeeding may worsen recovery. Small studies of breastfeeding women with PPCM have not suggested a hazard but are limited in number. A recommendation against breastfeeding would have significant

impact on infant survival in developing countries where PPCM is more prevalent. The impact of breastfeeding on recovery requires more investigation and will be examined in REBIRTH by the recruitment of an additional cohort of 50 women excluded from the randomized trial due to an intent to continue breastfeeding.

The REBIRTH trial will determine whether the addition of bromocriptine to standard heart failure therapy improves myocardial recovery and clinical outcomes for women with PPCM and will also clarify the impact of breastfeeding on myocardial recovery.

Hereditary Val122Ile transthyretin (ATTR) cardiac amyloidosis: an under-recognized cause of heart failure in older Black Americans

Frederick Ruberg, MD
Boston University School of Medicine

Introduction/Rationale: Cardiac amyloidosis (CA) is a protein folding disorder wherein misfolded precursor proteins aggregate as amyloid fibrils and deposit within the cardiac interstitium causing heart failure (HF) and death. While over 30 different precursor proteins can misfold into amyloid fibrils, over 95% of cardiac amyloidosis cases are caused by misfolding of either immunoglobulin light-chain (AL) or transthyretin (ATTR) protein. ATTR-CA, in specific, has recently emerged as an important, increasingly common, and treatable cause of HF. Previously held to be rare and only diagnosable by invasive cardiac biopsy, ATTR-CA is a commonly encountered but often missed diagnosis that is now a treatable disease affecting up to 10% of older patients with HF and increased left ventricular wall thickness. ATTR-CA can be diagnosed by nuclear imaging in combination with blood testing that excludes AL amyloidosis. ATTR-CA is classified by the genetics of the TTR gene as either wild-type (ATTRwt) or variant (ATTRv). Importantly, ATTRv-CA most commonly results from the TTR variant pV142I (Val122Ile or V122I) observed in 3.4% of self-identified Black individuals, or 1.5 million people, in the US. While the phenotypic penetrance of this allele is unknown, studies suggest that carriers are at increased risk for HF over age 70y. Missed diagnoses of ATTRv-CA Val122Ile perpetuates inequities in care.

Methods: Using different cohorts of older, self-identified Black patients with heart failure identified both prospectively from Boston Medical Center and retrospectively from the Boston University Amyloidosis Center, different studies were designed to evaluate the clinical features, prevalence, and clinical penetrance of Val122Ile, as well as test novel diagnostic strategies to facilitate recognition.

Results: The multi-center TRACS (TRansthyretin Amyloidosis Cardiac Study) study first described the survival of ATTR-CA Val122Ile in comparison to ATTRwt prior to the advent of effective therapy. Median survival was only 26 months vs. 43 months ($p< 0.05$). We recognized that patients in TRACS were identified with advanced ATTR-CA disease. Next, data demonstrated that patients who are variant carriers of Val122Ile can have evidence of abnormal nuclear imaging indicative of early ATTR-CA even in the context of normal cardiac biomarkers, suggesting a more sensitive means to identify disease. Accordingly, data from the ongoing SCAN-MP study (Screening for Cardiac Amyloidosis with Nuclear Imaging) reproduced prior evidence that the Val122Ile allele is more frequent in older Black patients with HF (6.7%) but showed that only approximately 40% have clinically evident ATTR-CA by

imaging. Finally, a point-of-care risk calculator was developed that utilized the endogenous TTR ligand retinol binding protein 4 (RBP-4) as well as standard ECG and echocardiographic measures afforded a high degree of accuracy (AUC 0.9) for ATTR-CA identification.

Conclusions: ATTR-CA Val122Ile is an important cause of HF in older Black Americans that can be identified by sensitive nuclear imaging as well as a novel point-of-care risk calculator that may facilitate earlier recognition. Data also suggest that genotype assessment alone is insufficient to infer ATTR-CA as the cause of HF in older allele carriers owing to incomplete penetrance.

Sex Differences in Atrial Fibrillation

Andrea Russo, MD
Cooper Medical School of Rowan University

Introduction: Sex differences in atrial fibrillation (AF) epidemiology and treatment have been previously described. Women are underrepresented in clinical AF trials and less likely to receive rhythm control therapies, including catheter ablation, for unclear reasons. In addition, rhythm control therapy for AF may be delayed that may impact on outcomes. We examined sex differences in a large population with mobile telemetry monitoring in real life practice.

Hypothesis: We hypothesized that presentation of AF differs in women and men with respect to rate, duration, and symptoms.

Methods: We examined 27,512 patients (42% men) with up to 30-day ECGs recorded using PocketECG (MediLynx), which transmits a three-lead ambulatory ECG, labels every heartbeat and detects AF using an algorithm based on heart rhythm and beat morphology. AF was defined if duration was at least 30 seconds. The Chi2 and Spearmans rho test, with Bonferroni correction, was used to compare women to men for arrhythmia characteristics, symptoms, AF burden, and age.

Results: Fewer women than men had AF (13.7% vs. 19.0%, $p<0.001$) and women were older at diagnosis (median 76 vs. 73 years, $p<0.001$). Heart rate was faster during AF in women than in men (104.7 +26.0 vs. 96.7 +26.7, $p<0.001$, Figure 1). Median AF duration was shorter in women (2.9 minutes vs. 10.8 minutes, $p<0.001$). Report of symptoms during AF was similar (46.5% in women vs. 43.7% in men, $p=0.062$). Women presented with AF at an earlier stage or lower AF burden than men (Figure 2). Mean AF burden was lower in women than man aged between 60-90 years (all $p<0.01$), and equivalent in men and women by age 90-100 (Figure 2).

: AF was detected at an older age but earlier stage on ambulatory 30-day monitoring in women, and women experienced symptoms during AF at least as often as men. Reasons for previously reported sex differences in therapy cannot be explained by differences in symptoms or delayed detection. Therefore, further study is needed to identify reasons for sex differences in arrhythmia therapies.

Is Syncope an Independent Predictor of Mortality in Heart Failure Patients?

Win Shen, MD
Mayo Clinic College of Medicine

Background: Syncope is a common presentation in heart failure (HF) patients. However, the associations between syncope and prognosis in HF patients have not been well defined. In the section on Evidence Gaps and Future Direction of the 2017 AHA/ACC/HRS Syncope Guideline, it was stated that investigations are needed to determine whether syncope is an independent predictor of fatal and non-fatal outcomes in selected populations. The goal of this study is to examine the association between syncope and all-cause mortality in a large cohort of HF patients with syncope.

Methods: A retrospective cohort of patients with HF and syncope at Mayo Clinic between 2010 and 2015 were identified, and 1:1 propensity-matched with a control group of HF patients without syncope. Follow-up was completed in January 2022. A chart review was conducted to decipher the etiology of syncope. The multivariate Cox regression model was applied to estimate the association between syncope and the all-cause mortality.

Results: 3,449 HF patients with syncope (mean age 72.8±14.5 years, 41.5% women, follow-up 62.13±40.0 months) were compared to the propensity-matched controls (n=3,449, mean age 72.8±14.3 years, 42.5% women, 51.64±42.0 months). Cardiovascular syncope was the most common etiology (31.5%), followed by orthostatic (28.5%), unexplained (25.7%), and vasovagal (12.7%). Syncope is not an independent risk of all-cause mortality in the overall HF (hazard ratio [HR]=0.95, 95% confidence interval [CI]: 0.89-1.01, p=0.526), HF with preserved ejection fraction (EF) (HR=0.94, 95%CI: 0.87-1.01, p=0.529), HF with mid-range EF (HR=1.01, 95%CI: 0.83-1.242, p=0.489), or HF with reduced EF (HR=0.95, 95%CI: 0.86-1.06, p=0.525). In subgroup analysis, cardiovascular syncope was not an independent risk of all-cause mortality in the overall HF (HR=0.99, 95%CI: 0.91-1.08, p=0.529), as well as orthostatic (hazard ratio=0.97, 95%CI: 0.89-1.07, p=0.557), and unexplained syncope (HR=0.97, 95%CI: 0.88-1.07, p=0.524). Interestingly, vasovagal syncope was an independent predictor of lower all-cause mortality in HF patients (HR=0.81, 95%CI: 0.72-0.93, p=0.002).

Conclusion: Cardiovascular and orthostatic syncope were common in the HF population. Syncope is not an independent risk of all-cause mortality in HF patients. Additional investigation is warranted to determine the plausible mechanism of lower mortality in HF patients with vasovagal syncope.

Heart Disease Treatment from Cardiac Interventions to Neurointerventions

Kalyanam Shivkumar, MD PhD
University of California, Los Angeles

Interoceptive neurotransmission from the heart and cardiovascular system is vital for maintaining blood circulation in all mammals. The timescales of the neural circuits that control the heart and circulation operate in the millisecond time scale and finely regulate the heart from one beat to next. Afferent signals from the myocardium and the blood vessels originating in and taking blood back to the heart are 'processed' at various levels of the neuraxis [intrinsic cardiac neurons (the 'little brain' on the heart), extracardiac-intrathoracic ganglia (stellate ganglia), spinal cord, brain stem, and higher centers], and are required for the fine efferent cardiomotor control via the sympathetic and parasympathetic nerves. The nervous system modulates almost all the known physiological aspects of cardiac physiology (chronotropy, dromotropy, lusitropy, inotropy and response to injury). These reflex feedback loops (cardio-cardiac and cardio-extracardiac) provide precise regulation of sympathetic–parasympathetic balance in the heart under normal conditions and during periods of increased physiological demands for a higher cardiac output.

Following cardiac injury, the alterations in this system (sympatho-excitation and parasympathetic withdrawal) is responsible for progression of heart disease (heart failure and arrhythmias that lead to sudden cardiac death affecting 12 million deaths per year in the world today!). The sequence of disease starts when short term adaptations seen after cardiac injury become seriously maladaptive in the intermediate and long term resulting in adverse outcomes (neuroendocrine activation e.g. after a myocardial infarction). In recent times we (and others have established); (i) There is structural and functional remodeling of the neural structures that control the heart following cardiac injury (ii) There are multiple avenues for cardiac neuromodulation (most of them powerfully modulate cardiac afferent neurotransmission) and some of these approaches show great promise for saving lives (e.g. surgical stellate ganglionectomy), (iii) Several recent advances in scientific methods have improved our understanding the cellular and molecular processes involved in innervation and the functional control of the myocardium in health and disease. This explosion of knowledge is now setting the mechanistic framework to develop targeted neuraxial therapies for preventing cardiac disease progression and sudden cardiac death. This staggering death toll of 22 deaths per minute can be prevented by low cost globally applicable therapies that are highly likely to result from a deeper understanding of cardiac neural control. Diseases ranging from atrial & ventricular fibrillation, heart failure, 'tako-tsubo' cardiomyopathy and sleep apnea have an important neural link and

therapies that can target the nervous system. I will summarize some key insights from 15 years of research to entice our colleagues to think more holistically about this promising area of science and help save millions of lives!

Mechanical unloading of the left ventricle and infarct size after acute myocardial infarction

Frederick Welt, MD
University of Utah Health

Introduction: In their landmark 1979 study, Reimer and Jennings established the concept of the "wavefront phenomenon" of myocardial necrosis in the canine model of acute myocardial infarction (AMI). Their study demonstrated the relationship between duration of occlusion and progressive loss of salvageable myocardium. This study has been the underpinning behind the focus on timely reperfusion in patients with ST segment elevation myocardial infarction (STEMI). This basic concept was borne out in the early trials of thrombolytic therapy and corroborated in studies of percutaneous intervention for STEMI. However, advances in the prompt recognition and reperfusion in patients with AMI resulting in dramatically shorter national average door-to-balloon times have not been mirrored by the expected improvement in mortality. This has suggested that alternative strategies to reduce mortality in this population should be investigated. Mechanical unloading of the left ventricle (LV) has been suggested to reduce infarct size after AMI. Although prior studies have investigated LV unloading during ischemia with a delay in reperfusion, little is known about the optimal timing for LV unloading in the setting of AMI.

Methods and Results: Studies were conducted in 17 adult Yorkshire swine weighing 67 ± 5 kg. A coronary balloon was inflated in the mid LAD for 60 minutes to induce a myocardial infarction. The coronary balloon was then deflated for 120 minutes (reperfusion). The animals were stratified into 3 groups: Group 1 (control, reperfusion with no LV unloading, n=5), Group 2 (LV unloading during ischemia with delayed reperfusion, n=6), and Group 3 (simultaneous LV unloading and reperfusion, n=6). Staining the hearts with Evans blue and 2,3,5-Triphenyltetrazolium Chloride was used to identify the area at risk and the infarct area respectively. Infarct percent size was defined as the area of infarcted myocardium divided by the area at risk. Of the three groups, Group 3 demonstrated significantly smaller infarct percent size compared to controls (54.7±20.3% vs. 22.2±13.4%; p=0.03). Comparison between Group 1 and Group 2 did not reveal significant difference (54.7±20.3% vs 43.3±24.6%; p=0.19).

Conclusion: We demonstrated that in our particular infarct model, a smaller infarct percent size is achieved in the setting of an acute myocardial infarct when the left ventricle is mechanically unloaded during the reperfusion, compared to reperfusion alone. Our study suggests the optimal timing of unloading may be at the initiation of reperfusion therapy with no delay in reperfusion. More broadly, our study

suggests that there may be a more complicated relationship between timing of unloading and reperfusion than found in prior studies. Further studies are warranted to investigate the factors that influence this relationship and the cellular and metabolic mechanisms of this phenomenon to guide future human trials.

AUC
Association of
University Cardiologists

2023

AUC
Association of University Cardiologists

AUC Officers 2022-2023

President
Sumeet Chugh, MD
Cedars-Sinai Health System

Immediate Past-President
Michelle A. Albert, MD MPH
University of California at San Francisco

Vice President
Barry London, MD PhD
University of Iowa

Secretary/Treasurer
Charles Lowenstein, MD
Johns Hopkins University

Councilors
Jane E. Freedman, MD
Vanderbilt University

Karol Watson, MD PhD
University of California at Los Angeles

Joseph Wu, MD PhD
Stanford Cardiovascular Institute

2023