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SCIENTIFIC SESSIONS 2017

DailyNews

WEDNESDAY, NOVEMBER 15
November 11-15 | Anaheim, California

GEMINI-ACS-1: Switching P2Y12 inhibitor in ACS patients based on pharmacogenomic testing results uncommon

An update of the GEMINI-ACS-1 trial found that switching of P2Y12 inhibitors based on the results of pharmacogenomics testing and reporting for reduced or enhanced function alleles of CYP2C19 was not common. Clopidogrel carries a black-box warning recommending testing because patients with the reduced function alleles have higher platelet reactivity and a potentially higher risk of ischemic events, especially following PCI.

Results of the update to the P2Y12 Inhibitor Switching in Response to Routine Notification of CYP2C19 Clopidogrel Metabolizer Status Following Acute Coronary Syndromes trial were presented Tuesday by E. Magnus Ohman, MD, professor of medicine and member of the Duke Clinical Research Institute in Durham, North Carolina.

"GEMINI looked at clinical outcomes for rivaroxaban versus aspirin with either clopidogrel and ticagrelor," Ohman said. "The choice of therapy was at the discretion of the clinician. This update looks at switching between these two agents."

In the trial, reporting of the CYP2C19 status was mandatory.

A central lab reported CYP2C19 metabolizer status for 99.9 percent of the 3,037 patients. A total of 34.4 percent were ultra-metabolizers (UM), 37.8 percent extensive metabolizers (EM), 24.5 percent intermediate metabolizers (IM) and 3.2 percent reduced metabolizers (RM). The trial protocol made no recommendations regarding P2Y12 inhibitors or switching agents based on CP2C19 status.

GEMINI-ACS-1 continued on page 14

STEMI ACCELERATOR-2: Regional coordination improves outcomes, FMC-to-device times in STEMI patients

Regional training and coordination interventions that provide timely reperfusion for ST-elevation myocardial infarction patients improve outcomes and the interval of first-medical-contact-to-device time, according to a study presented at Scientific Sessions on Tuesday.

In the study, investigators worked with leaders, healthcare professionals, paramedics, nurses, emergency medicine physicians and cardiologists in 12 major U.S. metropolitan regions to develop centralized STEMI plans for EMS catheterization lab activation and rapid transfer from non-PCI hospitals.

"At baseline across the 12 regions, 38 percent of patients had cath lab activation within 20 minutes," said James G. Jollis, MD, FACC, of the Duke University Clinical Research Institute in Durham, North Carolina, who presented the findings of the Regional STEMI Systems of Care: Results of the Mission: Lifeline STEMI ACCELERATOR-2 Study. "But with the new process in place, we saw that increase to more than half of patients having a cath lab activated within 20 minutes of paramedic arrival.

"For the overall project, we increased from 67 percent to 74 percent of patients reaching the national standard of first medical contact to device within 90 minutes. This coordination of training was associated with significant reductions in heart failure and death, and demonstrated a marked and statistically significant decline in mortality," Jollis said.

The study is a collaboration of Duke and the AHA's Mission: Lifeline program.


James G. Jollis, MD, FACC

ICARE-ACS

Results of a New Zealand study suggest a national clinical guidance framework that assesses patients presenting to emergency departments with possible acute coronary syndromes is effective and safely reduces hospital length of stay.

The findings were presented Tuesday by Martin Than, MD, of Christchurch Hospital in New Zealand.

In the National Implementation of a Clinical Guidance Framework for the Emergency Department Assessment of Patients with Possible Acute Coronary Syndromes trial, researchers analyzed data from 11,529 patients before the framework was implemented and 19,803 post-implementation at seven diverse hospitals in New Zealand. The primary outcome was the proportion of patients successfully discharged within six hours of emergency department arrival. A successful discharge was defined as one with no major adverse cardiac event during the following 30 days.

ACCELERATOR-2 continued on page 14

Canagliflozin results mixed for primary, secondary prevention in diabetes, CANVAS update finds

The sodium glucose co-transporter 1 inhibitor canagliflozin showed mixed results for cardiovascular prevention in a study presented Monday afternoon at Scientific Sessions.


Kenneth W. Mahaffey, MD

The agent improved cardiovascular and renal outcomes, but increased risk for lower extremity amputations in patients with diabetes.

Kenneth W. Mahaffey, MD, professor and director of the Stanford Center for Clinical Research at Stanford University in California, presented the update to the CANVAS (Canagliflozin for Primary and Secondary Prevention of Cardiovascular Events in Type 2 Diabetes) trial. Initial results of CANVAS released earlier this year showed a 14 percent reduction in cardiovascular events.

Sixty-six percent of the 10,142 patients in CANVAS had a prior cardiovascular event and were evaluated for secondary prevention. The 34 percent with two or more cardiovascular risk factors were evaluated for primary prevention.

As expected, the secondary prevention arm had a higher cardiovascular burden. These patients also showed greater benefit from canagliflozin — an 18 percent reduction in the risk for cardiovascular death, nonfatal MI or nonfatal stroke. Primary prevention patients had a 2 percent reduction.

Both groups had a similar benefit for hospitalization for heart failure — 32 percent reduction for secondary prevention and 36 percent reduction for primary prevention. Renal outcomes were also similar — 41 percent reduction for secondary prevention and 37 percent reduction for primary prevention.

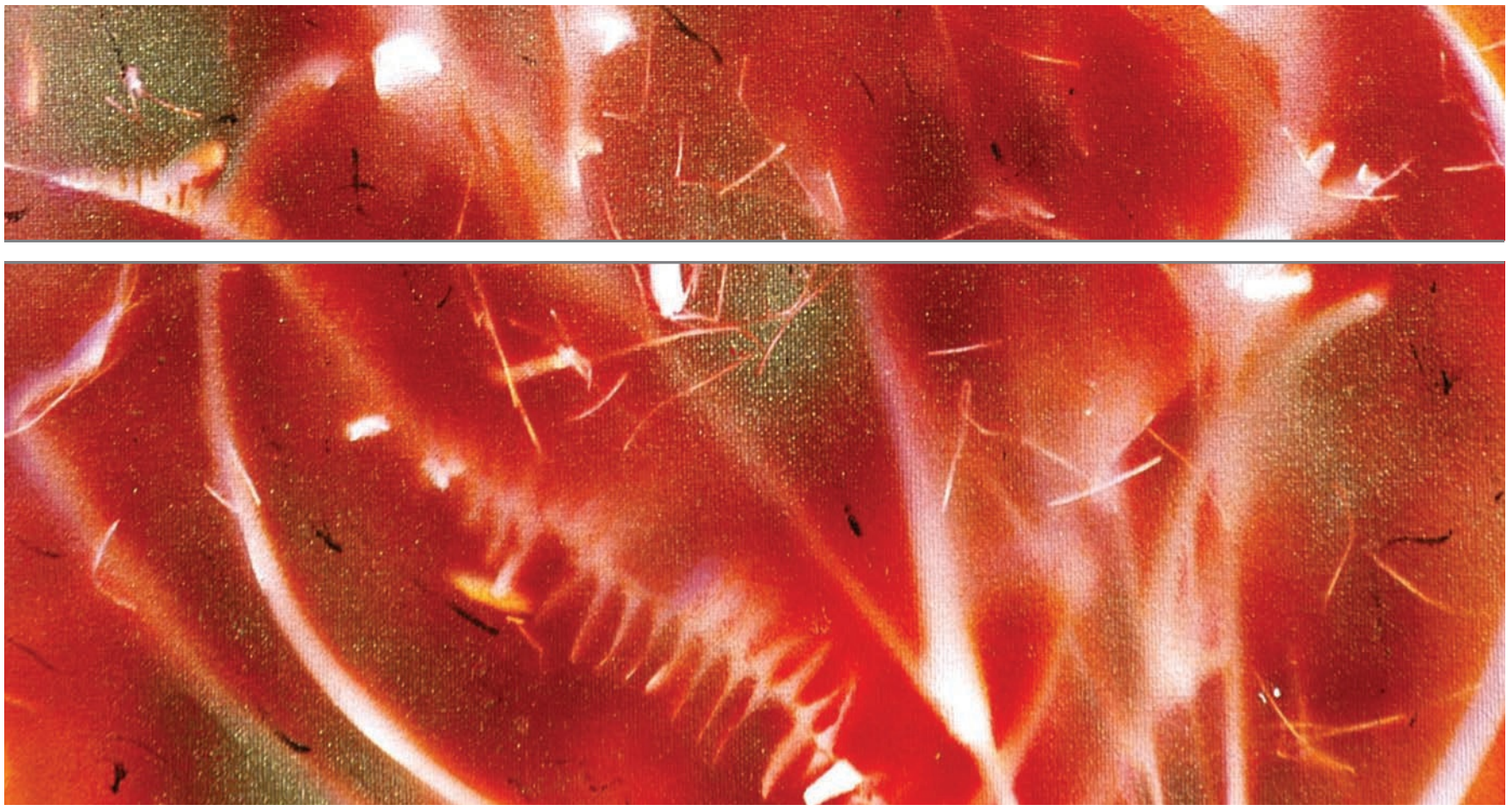
Adverse events included an expected increase in genital infections, low-trauma fracture and volume depletion events. The risk for lower-extremity amputations doubled in the secondary prevention group compared to placebo.

Larger and longer-term studies already under way will provide additional insight into the effects of canagliflozin and other SGLT2 inhibitors.

EXSCEL

The treatment effects of the GLP-1 receptor agonist exenatide don't vary based on the patient's baseline cardiovascular risk, according to an update to the Effect of Exenatide Once-Weekly on Clinical Outcomes

CANVAS continued on page 13



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HIGHLIGHTS FROM THE PROGRAM CHAIR

By Eric D. Peterson, MD, MPH, FAHA, Committee on Scientific Sessions Program Chair

Eric D. Peterson, MD, MPH, FAHA

It's the final day of Scientific Sessions! Over the past four days, we've heard exciting reports on important breakthroughs in research. Additionally, we learned about novel advances in clinical care, many of which can immediately impact how we treat our patients. And there is more to come today!

Today's program includes the week's final Late-Breaking Science session, "Innovative Therapies and Novel Applications," which begins at 9 a.m. The session will feature the latest results from the REDUCE LAP-HF, TNT-POAF, PROPEL, ALLSTAR and HOPE-Duchenne trials. The presentations feature novel findings in the fields of preventive therapies, heart failure, atrial fibrillation, peripheral artery disease, myocardial infarction and Duchenne cardiomyopathy.

The schedule also includes three Main Event sessions highlighting the hottest research in population, basic and clinical science that was presented over the past four days at Scientific Sessions. Each session offers a unique opportunity to hear commentary from international leaders.

The first of these sessions, "Trending Topics in Population Science," begins at 9 a.m. in Ballroom A, 3rd Level, Main Building. "Trending Topics in Basic Science" and "Trending Topics in Clinical Science" run concurrently at 10:45 a.m. in Ballroom A and Ballroom CD, respectively.

Before we adjourn today and head back to our practices, hospitals, clinics and labs, I want to thank my fellow members of the Committee on Scientific Sessions Program for putting together an outstanding educational program. I must also thank the AHA staff for their dedication and exceptional efforts in maintaining the Scientific Sessions' reputation as the world's premier meeting in cardiovascular science and medicine.

And finally, I want to thank all of my colleagues and friends who attended this year's meeting. I look forward to seeing all of you again next year at the 2018 Scientific Sessions in Chicago, Nov. 10-14. ▼

Late-Breaking Science VII: Innovative Therapies and Novel Applications

LBS.07 | 9-10:15 a.m. Wednesday | Ballroom CD, 3rd Level, Main Building

Trial	Description
REDUCE LAP-HF — Transcatheter InterAtrial Shunt Device for the Treatment of Heart Failure: Results from the REDUCE LAP-HF I Randomized Controlled Trial	This trial was designed to evaluate the safety and effectiveness of the InterAtrial Shunt Device to lower LA pressure in patients with heart failure.
TNT-POAF — Temporary Neurotoxin Treatment to Prevent Postoperative Atrial Fibrillation	This trial was designed to assess the efficacy and safety of epicardial botulinum toxin injection to prevent atrial fibrillation after cardiac surgery.
PROPEL — Granulocyte Macrophage Colony-Stimulating Factor With and Without Supervised Exercise to Improve Walking Performance in Peripheral Artery Disease	This trial was designed to determine whether granulocyte-macrophage colony stimulating factor (GM-CSF) combined with supervised treadmill exercise improved walking performance more than GM-CSF alone and supervised exercise alone in PAD.
ALLSTAR — 6-Month Results of ALLogeneic Heart STem Cells to Achieve Myocardial Regeneration Trial: A Randomized, Placebo-Controlled, Double-Blind Study	This trial evaluated the safety and efficacy of intracoronary allogeneic cardiac-derived stem cells in post-infarction patients.
HOPE-Duchenne — Cardiosphere-Derived Cells for the Treatment of Duchenne Cardiomyopathy: Results of the Halt cardiOmyopathy ProgrEssion-Duchenne Trial	The HOPE-Duchenne clinical trial was designed to evaluate the safety and efficacy of multivessel intracoronary delivery of allogeneic cardiosphere-derived cells in patients with cardiomyopathy secondary to Duchenne muscular dystrophy.

TODAY AT SESSIONS

Don't miss today's highlighted presentations and events. For a complete schedule, download the Mobile Meeting Guide, see the Final Program or view the online program at **scientificsessions.org.**

9-10:15 a.m.
Innovative Therapies and Novel Applications
Ballroom CD, 3rd Level, Main Building

9-10:15 a.m.
Trending Topics in Population Science
Ballroom A, 3rd Level, Main Building

10:45 a.m.-Noon
Trending Topics in Basic Science
Ballroom A, 3rd Level, Main Building

10:45 a.m.-Noon
Trending Topics in Clinical Science
Ballroom CD, 3rd Level, Main Building

HEARTY HUMOR by Jonny Hawkins

"For exercise, take two steps and one to the left and one step and two to the right..."

Claiming CME/CE at Scientific Sessions

Healthcare professionals attending Scientific Sessions can claim and print CME/CE certificates when they have attended all of the sessions for the meeting. **Physicians, nurses and EMS must claim credit by May 15, 2018. Pharmacists must claim credit by Dec. 15, 2017. ABIM MOC credit is available and must be claimed by Dec. 15, 2017.**

1. Go to **learn.heart.org**.
2. Click "Activities in Progress" in the left-hand navigation. You will be prompted to sign in using your American Heart Association username and password. You can create an account if you don't have one.
3. Review the "Activity Overview and "Activity Material" tabs.
4. Complete the evaluation.
5. Claim your credit(s).

International attendees can obtain their attendance verification certificate at the registration center. For a full list of conference accreditation statements and credit hours, visit **scientificsessions.org**.

Attendee feedback

Scientific Sessions attendees will complete a survey evaluating Scientific Sessions in the process of claiming their CME/CE credit. The American Heart Association uses these attendee surveys for feedback on programming, location, networking and more. Attendees who are not claiming CME/CE credit are invited to fill out a non-CME survey, which will be emailed following the meeting. Responses are anonymous.

WALKING CHALLENGE

Congratulations, Walking Challenge participants. You logged millions of steps at Scientific Sessions 2017. The top stepper is George Vetrovec, MD, who logged 73,903 steps in the annual competition. Miriel Ho finished second with 68,769 steps. Congratulations to the winners and thanks to all who participated! ▼

MEMBER SPOTLIGHT

Jessica Zègre-Hemsey, PhD, RN

Emergency nursing expert has passion for Mission: Lifeline

As an emergency cardiovascular care researcher and emergency department nurse, Jessica Zègre-Hemsey, PhD, RN, was intrigued and inspired by the AHA's Mission: Lifeline.

So when she was asked last year to join the cardiovascular system of care program as a representative from the Cardiovascular and Stroke Nursing Council, she eagerly accepted.

"Working with others who are passionate about improving patient care and outcomes for those afflicted with acute coronary syndrome, stroke and sudden cardiac arrest has been, thus far, one of the highlights of my career as a nurse-scientist," said Zègre-Hemsey, an assistant professor at the University of North Carolina School of Nursing in Chapel Hill.

Zègre-Hemsey's AHA membership — especially her work with Mission: Lifeline — reflects her commitment to advancing cardiovascular health and outcomes.

"I'm passionate about Mission: Lifeline and the group's commitment to its overarching goals," said Zègre-Hemsey, who was recently nominated to serve on the Mission: Lifeline Steering Committee.

"I hope to continue my work with this dynamic committee, which seeks to advance cardiovascular systems of care for time-sensitive conditions and improve patient access to definitive care and ultimately better patient outcomes. Serving as a representative of the Cardiovascular and Stroke Nursing Council gives me the opportunity to bring nursing to the table of this highly interdisciplinary committee."

Zègre-Hemsey, who is also an adjunct assistant professor in the Department of Emergency Medicine at the University of North Carolina School of Medicine, said she joined the AHA in 2002 to disseminate her research, which focuses on non-invasive monitoring strategies to improve the diagnosis of acute coronary syndrome and other time-sensitive conditions.

"I value the active engagement with colleagues — all of whom share a passion for cardiovascular science, research and strategies to improve patient outcomes — that comes with getting involved at AHA," Zègre-Hemsey said. ▼

Queen Latifah honored for her work promoting heart failure awareness

When Rita Owens was diagnosed with heart failure, her family rallied together.

They attended doctor's appointments and learned all they could about the condition. They took pictures of which pills to take at different times of the day to use as a visual checklist. Because her diet had to change, they changed theirs, too, as a show of solidarity and a step toward prevention.

Then her daughter was asked to share the family's story. Having long been in the public eye, the daughter preferred to keep this private.

"But my mother said, 'I'm all for anything I can do to prevent someone from going through what I've had to go through,'" entertainer Queen Latifah said. "My mother is that type of person — she wants to help people. I'm the mini-her, so I'm doing my job."

Since Owens' urging more than two years ago, Latifah has been the face of Rise Above Heart Failure, an AHA awareness campaign. On Sunday, AHA CEO Nancy Brown honored Latifah's work by presenting her the Woman of Distinction Award at Scientific Sessions.

"She is helping others understand the signs and symptoms of the condition and providing support so they can live a full life," Brown said. "She is truly an inspiration."

Latifah gave a brief acceptance speech, then went right back to spreading the word about heart failure. From the main stage, she crossed the Anaheim Convention Center to another stage where she joined Clyde Yancy, MD, an AHA past-president, for a Facebook Live discussion.

Queen Latifah was honored with the Woman of Distinction Award at Scientific Sessions on Sunday.

"There are so many things we can do now than before," said Yancy, a heart failure expert and chief of cardiology at Northwestern University Feinberg School of Medicine in Evanston, Illinois. "We have more drugs, devices, technologies. We can make a difference."

More than 6.5 million Americans are living with HF and more than 308,000 people die from it each year. One in five people will have heart failure in their lifetime with nearly a million new cases diagnosed each year.

"What we don't want is for people to be hospitalized," Latifah said. "We want people to be home with their family enjoying life, not in a hospital trying to fight for it or get it back together, when so much of this can be prevented."

Owens' diagnosis came about 12 years ago after she passed out at the school where she was a teacher. She's been in and out of the hospital ever since, with Latifah and a cousin sharing the duties of primary caregiver. Because her career often keeps her on the road, Latifah sometimes checks in via FaceTime. She'll even ask to see her mom's ankles to make sure she's not retaining fluid.

"It's brought us closer as a family," Latifah said.

As they discussed strategies for treatment and, better yet, prevention, Yancy said the focus shouldn't be on heart *failure*.

"It's about heart success," he said.

"I love that!" Latifah said. "Heart success."

And as the Facebook Live event ended, she smiled and pumped her arm as she turned the phrase into a chant: "Heart suc-cess! Heart suc-cess!" ▼

EHR and genomic test data can identify FH individuals at risk for adverse CV outcomes, study finds

The results of a population-based study suggest that lipid levels and other electronic health record-derived clinical data points, combined with exome sequencing for familial hypercholesterolemia (FH) variants, can be used to risk-stratify individuals for adverse cardiovascular outcomes.

Prashant Patel, MD, presented the study's findings Tuesday at Scientific Sessions.

"Our goal in this study was to employ a population-based approach using EHR-based algorithms to risk-stratify hyperlipidemia using available clinical variables," said Patel, of Geisinger Clinic and Medical Center in Danville, Pennsylvania. "In this process, we envisaged identifying the hidden burden of familial hypercholesterolemia and the associated trends of major adverse cardiovascular events. We also sought to study the role of genomic testing in the prediction of clinical outcomes."

A Geisinger Health System cohort of 41,649 patients was included in the study (57.61 percent female, median age 62 years). The researchers deployed five phenotyping methods to risk-stratify severe hypercholesterolemia in the cohort. These included an LDL-C cutoff, addition of clinical data (family and personal history of heart disease) from the EHR and presence of FH pathogenic variants. A *priori* associated confounders were used for multivariate analyses using binary logistic regression for outcome measures of myocardial infarction, coronary interventions and a composite ischemic heart disease burden.

Patel reported that baseline characteristics identified by all hypercholesterolemia phenotype definitions showed that each was associated with a high prevalence of the outcome measures. When compared to mutation-negative individuals with LDL-C ≤ 130mg/dl, there was a stepwise increase in the odds for outcomes, starting with a simple LDL-C based cutoff (≥190mg/dl) to addition of data elements from EHR and finally FH mutation positivity. Subjects with LDL ≥190 and FH mutation-positive status identified the highest risk with an OR of 28.9 (95 percent CI 15.0-55.8, p<0.0001), 26.8 (13.9-51.6, p<0.0001) and 44.3 (23.7-82.9, p<0.0001) for MI, coronary interventions and IHD burden, respectively.

"These findings suggest an important role for biochemical and genetic phenotype determination," said Vishal C. Mehra, MD, PhD, a senior author of the study. "The ever-increasing use of EHR systems may broaden the appeal of well-designed, population-based screening to identify high-risk groups, which can then be preferentially targeted by cascade genetic screening or aggressive, novel therapies to improve outcomes." ▼

Plaque regression, LDL lowering important in post-ACS management, study finds

Plaque regression of non-culprit sites in patients with acute coronary syndrome may be associated with better long-term outcomes, according to data presented Tuesday at Scientific Sessions.

Data from prospective studies of serial intravascular ultrasound (IVUS) showed that patients who achieved both plaque regression and lower LDL cholesterol had significantly reduced risk for major adverse cardiovascular events.

"The results of this study suggest reaching both plaque regression and sufficient LDL-C lowering is clinically important in post-ACS management," said Hirohisa Endo, MD, who presented the study. "In addition, this study shows that plaque regression determined by volumetric IVUS measurement could be a surrogate marker of future cardiovascular events."

According to Endo, of the department of cardiovascular medicine at Juntendo University Graduate School of Medicine in Tokyo, Japan, IVUS follow-up in patients with ACS is not routinely performed. Therefore, Endo and colleagues looked at data taken from four prospective clinical trials that included patients with ACS undergoing regular IVUS of non-culprit lesions in the culprit vessel at baseline and six months follow-up.

Of all 382 patients, they excluded the patients without available serial IVUS measurements (n=150) and without statin therapy (n=59). They looked at outcomes related to percent atheroma volume (PAV), on treatment LDL cholesterol and MACE. All patients were treated with statins.

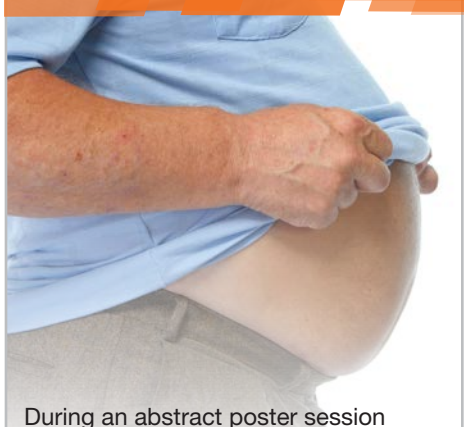

Hirohisa Endo, MD

The overall change in PAV was -1.6 and plaque regression, defined as PAV change from baseline <0, occurred in 67.6 percent of patients. The rate of MACE was lower in patients with plaque regression than in those without regression, but the difference was not statistically significant (13.7 percent vs. 19.6 percent). Among those patients with plaque regression, 40.2 percent achieved on-treatment low LDL cholesterol levels.

About 40 percent of patients achieved both plaque regression and on-treatment low LDL (group 1), 27.2 percent met only plaque regression (group 2) and 32.4 percent had plaque progression with/without LDL cholesterol (group 3). A multivariate analysis showed that those patients who achieved both regression and on-treatment LDL cholesterol had a 62 percent decreased risk of MACE (HR=0.38; 95 percent CI, 0.14-0.90; *P*=.03).

"The growing interest in treating vulnerable plaque has substantially raised the bar on current treatment approaches and, if complemented by confirmatory imaging techniques and markers, can possibly help regress plaque evolution and eliminate the possibility of atherosclerosis altogether," Endo said. ▼

BODY FAT IS MAJOR PLAYER IN CELLULAR AND CARDIAC AGING



During an abstract poster session Tuesday, investigators reported that direct measure of body fat, rather than body-mass index, is associated with telomere length. Telomere length, a marker of cellular aging, has been linked to cardiovascular disease. In the study, shorter TL was associated with diastolic dysfunction in subjects with high, but not low, body-fat mass. The results suggest that accumulation of body fat is both an important mediator of cellular aging and a modulator of the latter's impact on heart function, the researchers concluded.

Advances in PAH treatment on the horizon, says Distinguished Scientist lecturer


Marlene Rabinovitch, MD, FAHA

Tremendous progress in the use of vasodilators, endothelin receptor blockers and nitric oxide activators has improved the quality of life and the survival of patients with pulmonary arterial hypertension (PAH), but morbidity and mortality remain high, said Marlene Rabinovitch, MD, FAHA, during the Distinguished Scientist Lecture on Tuesday.

Rabinovitch, the Dwight and Vera Dunlevie Professor of Pediatric Cardiology at the Stanford University School of Medicine said that at best there's a 65 percent five-year survival rate followed by rapid attrition.

"Additionally, there's an increasing number of conditions in which PAH is recognized as a serious complication that negatively impacts survival," she said. "So, along with congenital heart disease, we now see PAH with heart failure and preserved ejection fraction, as well as reduced ejection fraction with metabolic syndrome."

Rabinovitch discussed her research exploring the fundamental mechanisms responsible for the loss and obliteration of blood vessels that cause PAH.

"In addition to lung disease, there's also increasing recognition of the adverse impact of PAH in sickle cell disease, and there's virtually an epidemic of PAH related to substance abuse," she said. "Worldwide attempts to eradicate HIV and schistosomiasis, for example, still face PAH as a complication, and treatments of scleroderma and liver disease are further challenged by the presence of this complication."

The most insidious presentation of PAH, Rabinovitch said, is the idiopathic form because there is no underlying condition to provide a clue to its presence, and the symptomatology is also vague. She noted that PAH affects females more than males, frequently in the third to fifth decade of life, but also in infants and children. Its incidence is similar to a rare disease, but about 15 percent of cases are familial.

Rabinovitch said research has identified that a BMPR2 receptor mutation is present in approximately 70 percent of familial PAH cases and 20 percent of sporadic PAH cases, adding that further studies identified reduced BMPR2 expression in all forms of pulmonary arterial hypertension. The challenge for researchers, she said, became one of relating the dysfunction of this receptor to the pathological features of PAH and to what was already understood from laboratory studies.

"The genetic basis of idiopathic pulmonary arterial hypertension has given us important clues to the pathways that are perturbed that not only target the lung vasculature but are also relevant to systemic vascular disease," she said.

Recent studies have shown that loss of BMPR2 not only induces apoptosis of endothelial cells, but also can be responsible for their transition to smooth muscle-like cells. As a consequence, in addition to losing their ability to proliferate, they lose their important function as a tight barrier, and they take on pro-inflammatory properties.

"Loss of BMPR2 recruits inflammatory cells, such as neutrophils, that release increased elastase, degrading poorly assembled elastic fibers," Rabinovitch said. "Emerging therapies, such as elafin and FK506, repress inflammation and improve BMPR2 functions. Induced pluripotent stem cells also may prove to be useful in developing patient-specific treatments." ▼

Small case series challenges thinking about fluoropyrimidine-related cardiac toxicity

With the combination of careful cardiac monitoring, calcium channel blockers and long-acting oral nitrates, researchers at the Hospital of the University of Pennsylvania were able to successfully rechallenge with fluoropyrimidines agents such as 5-FU and capecitabine in patients who experienced cardiac toxicity related to the chemotherapy.

Suparna C. Clasen, MD, presented results from the case series Tuesday in an abstract poster session.

"Fluoropyrimidines are the backbone of standard chemotherapy for gastrointestinal and other major solid malignancies," said Clasen, a fellow at the Hospital of the University of Pennsylvania in Philadelphia.

However, fluoropyrimidines use has been limited by cardiac toxicity, presenting as a spectrum of asymptomatic and symptomatic manifestations related to coronary vasospasm leading to myocardial ischemia. Clasen said experiencing these serious adverse effects has rightfully made patients and clinicians leery to reintroduce these medications.

Clasen and colleagues reported a case series of 11 consecutive patients with suspected fluoropyrimidine-induced coronary vasospasm who were successfully rechallenged to allow for chemotherapy completion.

Together with Joseph R. Carver, MD, Clasen developed two algorithms for rechallenge that varied by the type of fluoropyrimidines given, either oral or by infusion. Patients underwent a full work-up to test for underlying coronary artery disease and to try to modify underlying cardiovascular risk factors such as diabetes or hypertension.

"We never take it for granted that it is coronary vasospasm," Clasen said. "We want to rule out underlying coronary artery disease that is the culprit for the chest pain presentation and, if CAD is present, understand how much is underlying burden prior to rechallenge."

The protocols use a bolus infusion regimen of intravenous 5-FU chemotherapy and oral capecitabine with cardioprotective pretreatment of two calcium blockers and long-acting oral nitrates, which are titrated to the patient's blood pressure and heart rate.

"We pretreat with anti-anginal agents before infusion, treat during infusion, and after the infusion for up to 24 hours after the first dose," Clasen said. "Patients are then closely observed either in an inpatient setting if considered high-risk or in an outpatient setting where they are closely monitored."

All of the patients in the cohort successfully continued and completed their previously planned first-line fluoropyrimidine chemotherapy regimen with minimal therapeutic interruption. There were no cardiac events or evidence of recurrent coronary spasm after completion of therapy. Prophylactic medications were discontinued upon therapy completion.

In the case series, Clasen and colleagues took all comers presenting to the cardio-oncology clinic with suspected fluoropyrimidine-related cardiotoxicity, but future research might attempt to identify if there are certain patients with an underlying genotype that makes them more susceptible to vasospasm.

"We think this is a protocol that could potentially be widely implemented with the inclusion of very careful cardiac monitoring," Clasen said. "This has the potential to reintroduce a widely used and potentially curative chemotherapy agent for these patients." ▼

Disparities for NSTEMI angiography and revascularization are narrowing but still present, according to study

Racial disparities in the management of non ST-segment elevation myocardial infarction (NSTEMI) persist despite narrowing over time, according to results from The Atherosclerosis Risk in Communities (ARIC) Surveillance Study presented Tuesday at Scientific Sessions.

The study looked at trends in angiographic evaluation and revascularization for NSTEMI. Since 1987, the ARIC study has conducted hospital surveillance of acute MI in four U.S. states: Maryland, Minnesota, Missouri and North Carolina. Clinical data and procedures were abstracted from the medical records, and NSTEMI was classified with a validated algorithm.

Study presenter Sameer Arora, MD, and colleagues compared the probabilities of angiography and revascularization for white patients (n=21,721) relative to black patients (n=9,525) with adjustment for age, sex, TIMI risk score and hospital geographic region.

"Invasive strategy (angiography with intent to revascularize) has become the guideline-recommended standard for management of NSTEMI," said Arora, of the Division of Cardiology at the University of North Carolina School of Medicine in Chapel Hill. "The efficacy of this strategy has been widely accepted, but it appears to be utilized less when patients are black. Racial disparities in angiography and revascularization would have the potential to negatively influence mortality outcomes for black patients."


Sameer Arora, MD

In the study, black patients were more often female and younger. From 1987 to 2004, the proportion of patients undergoing angiography and revascularization increased for both black and white patients. Then from 2005 to 2013, it declined. However, data revealed that the proportion of patients evaluated by angiography was higher for white than black patients, reaching a peak disparity in 1992. A higher proportion of white patients was revascularized each year, reaching a peak disparity in 1990.

Many factors may be influencing the trend toward narrowing disparities observed in the study, Arora said. One of the most important may have been the development of NSTEMI guidelines and management algorithms in the late 1990s, he said. Greater access to medical insurance also may have been a factor.

Finally, narrowing racial disparities may have resulted from the expansion of cardiac catheterization units over the past decades, he said. Many of the black patients were sampled from economically depressed regions, which may not have had cardiac catheterization services available at the start of the surveillance. ▼

2017 Poster Winners

Early career work is extremely important to the American Heart Association. The future of cardiovascular science is in the hands of these healthcare professionals and scientists, and the poster sessions include many examples of the important work being done by this group. Here's a look at the poster winners from Scientific Sessions 2017 — all of whom are early career professionals:

Basic Science
Laurel Grisanti
β-Arrestin-Biased β2-Adrenergic Receptor Activation Confers Cardioprotection in Ischemia/Reperfusion Injury

Basic Science
Sara Vandenwijngaert
A Low-Frequency Coding Variant in Natriuretic Peptide Receptor 1 (NPR1) Increases Systolic Blood Pressure by Reducing Guanylate Cyclase Activity

Clinical Science
Erin Bohula
Atherothrombotic Risk Stratification and Magnitude of Benefit of Evolocumab in FOURIER

Population Science
Neel Chokshi
Loss-framed Financial Incentives and Personalized Goal Setting Increase Physical Activity in Ischemic Heart Disease Patients Using Wearable Devices: The ACTIVE REWARD Randomized Clinical Trial

Scenes from SESSIONS

HEALTH TECH COMPETITION

Admetsys, a company that has created a first-of-its-kind artificial pancreas for hospital and surgical care settings, took home the Judge's Choice Award in the fourth annual Health Tech Competition at Scientific Sessions. Procyrion, a company that has developed a minimally invasive circulatory assist device to treat heart failure, earned the People's Choice Award. Admetsys CEO and co-founder Jeff Valk (at right in photo at left) and Procyrion Chief Scientific Officer Jace Heuring, PhD (left), accepted the awards. Congratulations to the winners and thanks to all the finalists: Amicomed, Bodyport, MobioSense, Play-it Health, Tasso Inc. and TupeloLife.

CELEBRATING RESEARCH

Some of the current and past American Heart Association research awardees gathered for a group photo on Tuesday at Scientific Sessions. The AHA has funded more than $4.1 billion in research into heart disease, stroke and other cardiovascular diseases — more than any organization outside the federal government. The organization has funded 13 Nobel Prize winners and many lifesaving research advances such as the first artificial heart valve, cholesterol-inhibiting drugs, heart transplantation, and CPR techniques and guidelines.

Study demonstrates association between skin inflammation, high-risk coronary plaque

A study examining the effect of psoriasis treatment on high-risk coronary plaque characteristics presented Tuesday revealed additional evidence that remote inflammation can modulate coronary disease.

The architect and senior author of the study, Nehal N. Mehta, MD, MSCE, FAHA, said in an interview before the meeting that the results of the study are a warning to physicians not to ignore ongoing, low-grade sources of inflammation in patients.

"We know psoriasis is a common, chronic inflammatory skin disease, and we know inflammation is critical to atherosclerosis," said Mehta, chief of inflammation and cardiometabolic diseases at the National Heart, Lung, and Blood Institute. "This needs to be taken seriously. We recently showed that patients whose skin disease got worse over time had worsening of high-risk coronary plaque. If we follow the people with high-risk plaques for the next decade, we will see a number of preventable heart attacks."

The study results were presented in an abstract poster session by Jonathan Chung, MD, a fourth-year medical student at SUNY Downstate College of Medicine in New York. Chung worked on the study with Mehta while doing a research year at the National Institutes of Health through the NIH Medical Research Scholars Program.

For the study, Mehta's team used coronary CT angiography to measure the amount of high-risk plaque in patients with psoriasis. Participants were measured at baseline and again one year later. The study showed that when the skin condition improves, patients have a decrease in high-risk plaque features. A similar investigation by Mehta has shown the converse to also be true. That study, presented earlier this year, showed that when patients with psoriasis were not effectively treated, their high-risk coronary plaque features increased.

"When the inflammation goes down as assessed by their psoriasis skin disease severity, the high-risk coronary plaque features go down," Mehta said. "These findings add to the body of literature that uncontrolled inflammation is a dangerous thing, not only for systemic inflammation, but the blood vessels as well."

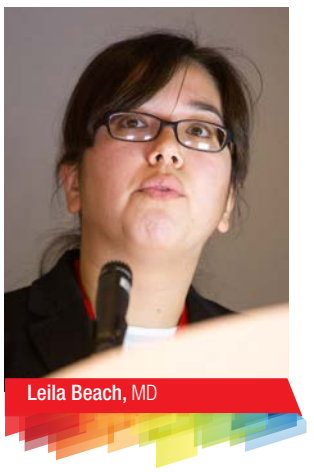
The study's cohort included 72 middle-age patients with moderate to severe psoriasis at baseline. Participants who improved their skin disease had a 68 percent decrease in their high-risk plaque score. Conversely, those who worsened had a 50 percent increase in their high-risk plaque score. Larger studies will need to be conducted to confirm these findings.

"Our findings echo recent data from the CANTOS trial, which examined whether treatment of residual inflammation in patients with prior heart attack reduced recurrent heart attack," Mehta said. ▼

Race and ethnicity influence cardiovascular risk in patients with history of hypertensive disorders of pregnancy, but does not influence MI, study finds

Research presented Tuesday at Scientific Sessions indicates that race and ethnicity modify the association between hypertensive disorders of pregnancy and heart failure, but do not modify the association between hypertensive disorders of pregnancy and myocardial infarction.

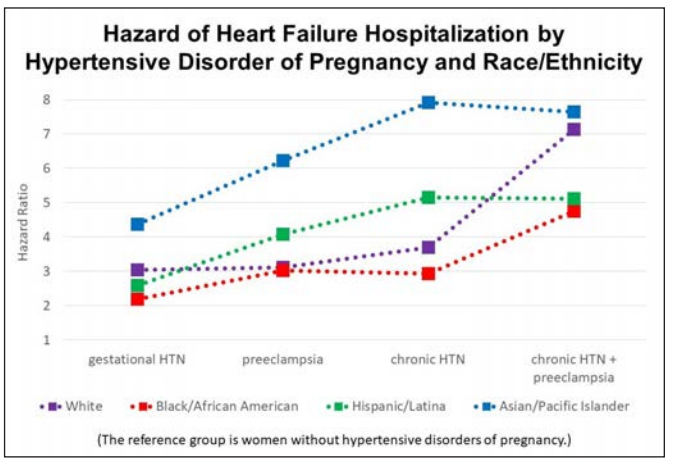
Presenter Leila Beach, MD, noted that it's well-established that race and ethnicity play a role in both cardiovascular disease outcomes and hypertensive disorders of pregnancy. But her study is the first to try to determine if race and ethnicity mediate the increased risk of cardiovascular disease following hypertensive disorders of pregnancy. The study reviewed the hospital discharge data of 1.5 million female patients in California.



Leila Beach, MD

"What was novel is that we found that African-American women who had hypertensive disorders in pregnancy were actually at much lower hazard of heart failure hospitalization than women in other racial or ethnic groups," said Beach, clinical instructor at the University of California, San Francisco, School of Medicine. "And Asian-American women who had hypertensive disorders during pregnancy had a significantly higher hazard of heart failure hospitalization. This is not necessarily what we expected to find because, for the population at large, it's well established that African-Americans are at higher risk for heart failure and that's in large part driven by hypertension."

Beach said it also was interesting that they did not see the same results for myocardial infarction. The study showed that hypertensive disorders of pregnancy were associated with future heart attack risk, but the results did not indicate that race or ethnicity significantly mediated the hazard for MI hospitalization. In the study, hazard ratios for future MI ranged from 2.7 for gestational hypertension to 6.0 for chronic hypertension.



"Why race and ethnicity mediate the hazard for heart failure and not for MI is something we don't have pinned down at this point," she said. "Even without understanding the mechanisms that are driving the difference, I think the implications are significant for the care of women who have a history of hypertensive disorders of pregnancy, especially as medicine becomes more personalized."

Beach said the study also confirmed a lot of what is generally known in the literature.

"We found that, indeed, women had a much higher hazard for heart failure and heart attack hospitalization if they had hypertensive disorders of pregnancy," she said. "We also found that the prevalence of hypertensive disorders of pregnancy was highest among black women and lowest in Asian-American women. That's something that has been seen before in other cohorts in other states." ▼

Pulmonary autograft associated with improved long- and short-term outcomes in pediatric AVR

Children undergoing aortic valve replacement had improved short-term and long-term outcomes with pulmonary autograft (Ross procedure) compared to mechanical or tissue AVR procedures, according to the results of a retrospective study presented Tuesday at Scientific Sessions. Amber Leila Sarvestani, a third-year medical student at the University of Missouri-Kansas City, presented the research.

Based on the study's results, clinicians may need to revisit this issue and give more consideration to the Ross procedure, according to senior author Lazaros Kochilas, MD.

"Even after adjustment for a patient's age, era effect and co-existing conditions, the Ross procedure still seems to be holding its place as the more favorable choice compared with any of the other choices," said Kochilas, medical director of cardiac clinical research at Children's Healthcare of Atlanta.

The study was designed to compare long-term, transplant-free survival of children undergoing AVR with several procedures: pulmonary autograft, mechanical valve or tissue valve prosthesis. The Ross procedure, or pulmonary autograft, is a more complex surgery; it involves replacing the diseased aortic valve with the patient's own pulmonary valve and then placing a pulmonary allograft in the right ventricular outflow and re-attaching the coronary arteries to the neoaorta.

In the study, the researchers looked at data from Pediatric Cardiac Care Consortium, a large multi-institutional, U.S-based registry of interventions for congenital heart diseases. The study included 1,068 children who had undergone their first AVR after 1991.

The median age of the children in the study was 12.7 years. The most common AVR procedure in the study cohort was the Ross procedure (44 percent) followed by mechanical valve replacement (40 percent) and then tissue prosthesis (16 percent). The in-hospital mortality was lowest for Ross procedures (3.1 percent), followed by mechanical replacement (4.9 percent). It was highest in patients undergoing tissue prosthesis (11.9 percent).

Of the 1,037 patients that survived to discharge, the transplant-free survival up to 15 years was 92.9 percent for those who underwent a Ross procedure, 84 percent for mechanical procedure and 77.6 percent for tissue prosthesis.

There was increased long-term survival for patients after the Ross procedure compared with mechanical or tissue valve replacement with increasing advantage five years after the AVR procedure. A multivariable analysis showed that outcomes with the Ross procedure were still three times better than with the mechanical valve.

The results are encouraging, Kochilas said, because the Ross procedure is associated with improved quality of life compared to the other AVR procedures.

"An additional benefit to the autograft is the low risk for blood clots and, thus, no need for anticoagulation, which can have big implications for children's quality of life," Kochilas said. "With the mechanical valve, children need to take blood thinners, which can be very demanding as it requires frequent blood tests and dose adjustment, and it imposes dietary restrictions and limits participation in certain physical activities." ▼

Diastolic-systolic velocity ratio may be useful in assessing functional stenoses in coronary arteries, study finds

An international study has identified the diastolic-systolic velocity ratio (DSVR) as potentially useful in assessing functional stenoses in coronary arteries. The technique, which can be performed either invasively via angiography or noninvasively by echocardiography, could be a useful adjunct to clinical practice, according to Guus de Waard, MD, a cardiology research fellow at VU University Medical Center in Amsterdam, the Netherlands.

de Waard presented the findings from the study during the Melvin Judkins Young Investigator Award Competition on Sunday at Scientific Sessions.

"We found a reasonable diagnostic accuracy for DSVR when we compared it to invasive measurements, such as fractional flow reserve (FFR) to determine whether a stenosis is functionally significant," de Waard said. "Coronary angiography with FFR remains the gold standard for assessing the functional importance of stenosis, but DSVR could be a useful adjunct in certain scenarios."

Researchers at four cardiology centers in Great Britain, Spain and the Netherlands collaborated on the project, which compared the diagnostic accuracy of DSVR and FFR, and explored the physiologic mechanisms that underlie DSVR.

Researchers obtained simultaneous measurements of intracoronary pressure and Doppler flow velocity using coronary angiography in 228 stable patients. Measurements also were analyzed after percutaneous intervention in 39 patients.

de Waard reported that DSVR declines with worsening of the FFR, classified into 0.05 unit groups (P_{trend}<0.001), and that DSVR shows acceptable diagnostic agreement with FFR at an ischemic threshold of 0.75 and a hyperemic stenosis resistance index threshold of 0.80 mmHg·cm^{-1}·s. The optimal cutoff value for DSVR is 1.74. Because DSVR has a close inverse correlation with the diastolic-systolic resistance ratio (r^2=0.83, p<0.001), de Waard said the distribution of vascular resistance among diastole and systole could be interrogated.

The difference between systolic and diastolic stenosis resistance as a percentage of total vascular resistance gradually increases as FFR class worsens (P_{trend}<0.001). After PCI, DSVR increased from a mean of 1.56 to 1.77 (p<0.01).

"The most important finding is that we were able to unravel how the DSVR index works," de Waard said. "Because microvascular resistance is lower during diastole than during systole, while stenosis resistance does not differ for both phases of the cardiac cycle, a stenosis that is functionally significant has a higher impact on diastole than on systole. This results in a decrease of DSVR, which can be measured immediately using ultrasonographic echocardiography."

However, de Waard noted, DSVR should not be viewed as a replacement for coronary angiography or FFR because ultrasound cannot provide pressure data and is less precise than direct angiographic measurement. He said there are several situations, though, in which a quick, reasonably accurate substitute may be useful.

Guus de Waard, MD

The most common scenario is the patient who presents in the emergency room with chest pain. Electrocardiography may be inconclusive and a troponin assay may not be immediately available.

Another potentially useful application, he said, might be in noninvasive follow-up for patients after CABG or PCI to monitor graft patency and in-stent restenosis.

"I am not recommending that the DSVR index replace any of the clinical tools we already have in place," de Waard said. "It should be viewed as an interesting and potentially useful tool to add to our current armamentarium." ▼

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Study: *PCSK9* variation produced low LDL associated with low risk for CV, all-cause death

Having genetically low LDL cholesterol due to proprotein convertase subtilisin/kexin 9 *(PCSK9)* was associated with a reduced risk for cardiovascular and all-cause mortality in the general population, according to data presented Tuesday at Scientific Sessions.

"The results suggest that more prolonged reductions in LDL cholesterol with, for example, *PCSK9* inhibitors, might eventually translate into a reduction in both cardiovascular and all-cause mortality," said Marianne Benn, MD, PhD. "However, randomized clinical intervention trials of PCSK9 inhibitors with long follow-up are needed to document such effects."

Marianne Benn, MD, PhD

According to Benn, associate professor and chief physician in the Department of Clinical Biochemistry at Rigshospitalet, a function of Copenhagen University Hospital in Denmark, PCSK9 degrades LDL receptors and lowers the amount of LDL cholesterol that can be removed by the liver. Genetic variation in the *PCSK9* gene reducing protein function (similar to PCSK9 inhibition) increases the number of LDL receptors and lowers LDL cholesterol.

In this study, Benn and colleagues tested whether genetically low LDL due to *PCSK9* was causally associated with reduced cardiovascular and all-cause mortality in the general population. They genotyped for *PCSK9* R46L (rs11591147), R237W (rs148195424), I474V (rs562556) and E670G (rs505151) in 109,566 individuals from the Copenhagen General Population study and the Copenhagen City Heart Study. With a median follow-up of 8.6 years and more than 1 million person years, they observed 2,261 cardiovascular deaths and 14,651 deaths from any cause.

Results of the study revealed that genetically low LDL cholesterol due to *PCSK9* variation (corresponding to pharmacologic inhibition of *PCSK9* by alirocumab or evolocumab) was causally associated with low risk of cardiovascular mortality. Specifically, an increasing number of weighted *PCSK9* alleles were associated with stepwise lower LDL cholesterol of up to 0.61 mmol/L (P for trend <.001), and with lower cardiovascular (*P*=.0002) and all-cause mortality (*P*=.045).

"Mortality data on low LDL cholesterol via *PCSK9* has not been reported before," Benn said. "There is only one study which has shown that lowering LDL cholesterol as primary prevention reduces mortality."

The researchers conducted causal genetic analyses and found a 1 mmol/L lower LDL cholesterol was associated with significantly reduced risk for cardiovascular death (risk ratio=0.33; 95 percent CI, 0.19-0.58; *P*<.001) and all-cause mortality (risk ratio=0.72; 95 percent CI, 0.60-0.88; *P*=.001). ▼

Prophylactic ablation for atrial flutter reduced onset of new AF, study finds

The use of prophylactic pulmonary vein isolation (PVI) in patients with typical atrial flutter significantly reduced new onset of atrial fibrillation and burden, the associated number of hospitalizations and repeat ablation for AF, according to three-year results of the PREVENT AFI study presented Tuesday at Scientific Sessions.

These results confirmed the benefit of PVI seen after one-year follow-up in the study. Patients were assessed using continuous implantable loop recorder with a battery life of about three years that allowed Jonathan Steinberg, MD, and colleagues to continue to follow outcomes for an extended period.

"Over three years, there was still a substantial reduction in the incidence of atrial fibrillation," said Steinberg, a cardiologist with the University of Rochester in New York. "Because we documented this with the implantable loop recorder, we saw a substantial reduction of about two-thirds of atrial fibrillation burden over time. Prophylactic ablation worked in greatly reducing the amount of new onset atrial fibrillation."

The study included 50 patients with documented atrial flutter randomly assigned to either cavo-tricuspid isthmus (CTI) ablation alone (n=25) or CTI with concomitant PVI (n=25). All patients received an implantable loop recorder and had regular follow-up for three years. The primary endpoint of the study was the occurrence of any atrial tachyarrhythmia including AF or atrial flutter after ablation with the monthly burden exceeding 0.5 percent on the recorder.

Jonathan Steinberg, MD

At three years, 80 percent of patients who did not have prophylactic PVI developed AF or atrial flutter compared with only about half (52 percent) of patients in the CTI plus PVI group (hazard ratio=2.40; 95 percent CI, 1.18-4.86; *P*=.015).

Because the researchers were able to follow patients for this extended period they could clinically track other outcome events, Steinberg said.

"We found that one-third of patients who did not have prophylactic ablation were referred back for ablation for atrial fibrillation," he said. "We also found that patients who did not undergo prophylactic ablation had a much higher likelihood of visiting the hospital or emergency room, or being hospitalized for cardiovascular causes, which we suspect were largely atrial fibrillation."

Specifically, 32 percent of patients in the CTI alone group underwent repeat ablation compared with 8 percent in the PVI plus CTI group (*P*=.037). The three-year AF burden was only 6.2 percent for prophylactic PVI compared with 16.8 percent for the CTI alone group (*P*=.038). Finally, about half (48 percent) of patients in the CTI alone group were hospitalized during the follow-up period compared with 16 percent of patients who underwent prophylactic ablation (*P*=.032).

"We may be moving in a different direction now when it comes to applying prophylactic ablation for AF," Steinberg said. "In future research, we may be looking at groups that have high risk of AF who may be candidates for additional clinical investigation or for prophylactic ablation procedures." ▼

Study: Cardiosphere-derived cell infusion improved several outcomes of functional single ventricle

Intracoronary autologous cardiosphere-derived cell (CDC) infusion in patients with functional single ventricle resulted in significant improvements at two years in ventricular function, somatic growth, heart failure status and event-free survival, according to the results of a study presented Tuesday by Toshikazu Sano, MD.

"Cardiosphere-derived cell infusion in patients with single-ventricle physiology was associated with improved cardiac function at two years regardless of the proceeding stage procedure," said Sano, of the department of vascular surgery at Okayama University Hospital in Japan. "These better outcomes may be attributed to decreased incidence of rehospitalization or repeated cardiac surgery for recurrent heart failure, as well as reduced the parenting stress during child care for their families."

Toshikazu Sano, MD

Cardiosphere-derived cells are enriched with a cardiac progenitor cell population that can give rise to cardiomyocytes, smooth muscle and endothelial cells *in vitro* and *in vivo*. Along with these direct-differentiation capabilities toward cardiovascular-lineage specification for myocardial repair, recent studies have shown that cardiosphere-derived cells are able to transfer exosomes, which contain various molecular constituents of their cell of origin, including proteins and micro RNA, as biologically active cell-derived small vesicles.

In this study, Sano and colleagues assessed the long-term effects and clinical outcomes of intracoronary infusion of autologous CDCs in patients with single-ventricle physiology compared with patients treated by staged palliation alone. The study included 101 patients who underwent stage 2 or stage 3 surgical palliation with single-ventricular physiology between January 2011 and March 2015. Forty-one patients were assigned to receive CDC infusion into coronary arteries four weeks after staged palliation. Sixty patients were treated by staged palliation alone.

Compared with stage palliation alone, patients treated with the CDC infusion had significantly improved cardiac function (*P*<.05) and somatic growth (*P*<.01). In addition, CDC infusion was associated with improved event-free survivals such as late failure, adverse events and catheter intervention.

Multivariate analyses showed that both CDC infusion (*P*<.02) and heart failure status (*P*<.03) were significant affecters for adverse events at two years.

The researchers also categorized study patients into two subgroups: heart failure with preserved or reduced ejection fraction (cardiac function <50 percent). CDC infusion improved cardiac function at two years in both groups. In patients with reduced ejection fraction receiving CDC, the incidence of all-cause mortality, late failure, adverse events and unplanned catheter intervention were significantly reduced compared with those treated by surgical reconstruction alone.

"In patients with preserved ejection fraction, the functional benefits brought by cell therapy was neither associated with improved mortality nor reduced late complication after staged palliation. It may require further studies to investigate the underlying mechanisms to innovate novel therapy to treat these patients," Sano said. ▼

CANVAS continued from page 1

in Patients with Type 2 Diabetes Mellitus and Cardiovascular Disease (EXSCEL) trial.

The primary EXSCEL trial had more than 14,000 participants with Type 2 diabetes from 35 countries and showed a 15 percent reduction in the risk for all-cause mortality compared to placebo. About 70 percent of the trial population had a prior cardiovascular event.

"The question was whether the magnitude of the treatment benefit depends on a patient's baseline risk," said Robert J. Mentz, MD, assistant professor of medicine at Duke University in Durham, North Carolina. "Our hypothesis was that patients who are at increased risk for mortality and MACE have a relatively greater benefit with exenatide than those at lower risk."

However, data showed no significant difference in treatment benefit based on baseline cardiovascular risk. Instead, the study showed that familiar baseline characteristics — including age, prior cardiovascular events, comorbidity burden and lab values — provide good prognostic value for mortality and MACE.

EMPA-REG OUTCOME

Patients with diabetes and peripheral artery disease at baseline benefit more from empagliflozin added to standard care compared to patients with diabetes and other types of cardiovascular disease, according to results from a sub-analysis of the Empagliflozin Reduces Mortality and Hospitalization for Heart Failure in Patients with Type 2 Diabetes and Peripheral Artery Disease (EMPA-REG OUTCOME) trial.

Adverse events, including rates of lower limb amputations, were similar in both groups.

PAD is among the most common comorbidities in patients with Type 2 diabetes. Similarly, PAD patients often have diabetes. PAD is a predictor of cardiovascular death and is associated with an increased risk of heart failure.

The primary EMPA-REG OUTCOME trial of empagliflozin in patients with Type 2 diabetes and CVD showed good cardiovascular results. The risk of cardiovascular death was reduced by 38 percent, all-cause mortality by 32 percent, heart failure hospitalization by 35 percent and incident or worsening neuropathy by 39 percent compared to placebo.

The primary analysis didn't explore the effect of empagliflozin on the 1,461 patients who had PAD.

The trial update compared cardiovascular death, all-cause mortality, MACE, heart failure hospitalization, a composite of heart failure hospitalization or death, neuropathy and adverse events in patients with and without PAD.

The biggest difference in the PAD group was an excess of former and current smokers.

"That's not surprising," said Subodh Verma, MD, PhD, FAHA, Professor and Canada Research Chair in Atherosclerosis at the University of Toronto in Ontario. "In patients with PAD, 70 percent are current or former smokers. The presence of PAD identifies a group at higher risk of cardiovascular events and death."

In EMPA-REG, adding empagliflozin to standard care for patients with PAD reduced the risk of cardiovascular death by 43 percent, all-cause mortality by 38 percent and heart failure hospitalization by 44 percent versus placebo. In patients without PAD, risk reduction was 36 percent for cardiovascular death, 30 percent for all-cause mortality and 32 percent for heart failure hospitalization.

"There's a profound and precocious separation of curves favoring empagliflozin in patients with PAD," Verma said. "This is reflective of the higher baseline risk of this population. The substantial risk reductions seen in patients with PAD have important translational implications for clinical practice."

BiomarCaRE

Serum metabolites could become the next generation of predictors and prognosticators for coronary heart disease, according to the largest study performed on serum metabolites.

Serum Metabolomic Profiles Predict Coronary Heart Disease in the General Population (BiomarCaRE) used the Biomarker for Cardiovascular Risk Assess in Europe database to create a cohort of 10,741 people that included 2,166 patients with coronary heart disease.

"Metabolites are good candidates because they reflect genomic changes in individuals and indicate changes in phenotypes," said Tanja Zeller, PhD, professor for genomics and systems biology at the University of Hamburg in Germany. "In our cohort of middle-aged individuals, we found four metabolites that are significantly associated with coronary heart disease."

The four metabolites are phosphatidylcholines and have an inverse relationship to coronary heart disease. Lower metabolite levels increase risk while higher levels are protective. The predictive strength of metabolite markers is similar to classical risk factors such as BMI, systolic blood pressure, diabetes and total cholesterol, Zeller said.

More research and validation are needed before metabolites are ready for clinical use, she said. But the BiomarCaRE study indicates the value of metabolomics to develop novel biomarkers and improve risk stratification. ▼

ACCELERATOR-2 continued from page 1

Than reported that all sites had an increase in proportion of patients discharged within six hours (pre-implementation mean 8.3 percent; post-implementation mean 18.4 percent). Researchers found no difference in the proportion of patients with a MACE within 30 days of patients discharged within six hours: pre-implementation (0.52 percent) compared with post-implementation (0.44 percent).

ACS QUIK

The results of a recent trial conducted across 63 hospitals in Kerala, India, demonstrated that a quality improvement intervention led to improvements in in-hospital and discharge medications, but not in the rate of 30-day MACE in acute MI patients.

Findings from the Effect of a Quality Improvement Toolkit on Acute Myocardial Infarction in India: The ACS QUIK Cluster Randomized, Stepped Wedge Trial were presented Tuesday by Mark D. Huffman, MD, of Northwestern University in Chicago.

The researchers evaluated the effect of a locally adapted, evidence-based quality improvement toolkit on process measures and outcomes among 21,374 patients from November 2014-November 2016. The toolkit included audit and feedback, admission and discharge checklists, patient education materials and linkage to emergency cardiovascular care and quality improvement training.

"We saw improvements in process measures, including in-hospital and discharge medications, and clinical outcomes, including a reduction in our primary outcome of the rate of death, recurrent heart attack, stroke and major bleeding at 30 days — from 6.4 percent in the control group to 5.3 percent in the intervention group," Huffman said.

STIC2IT

A novel, technologically enabled, behaviorally targeted, pharmacist-based intervention improves adherence to medications for chronic diseases and disease control, according to findings from the Results of the Study of a Tele-Pharmacy Intervention for Chronic Diseases to Improve Treatment Adherence trial.

A total of 4,078 patients with diabetes, hypertension or hyperlipidemia who were both non-adherent and had poor disease control were randomized in equal numbers to the intervention and usual-care arms. The intervention consisted of a brief pharmacist-delivered telephone consultation, text messaging, mailed reports providing patients with updated biometric and adherence information and feedback from the pharmacists to patients' primary care physicians.

"The intervention increased medication adherence but did not improve measures of disease control, including LDL cholesterol, blood pressure and hemoglobin A1C," said Niteesh K. Choudhry, MD, PhD, of Brigham and Women's Hospital and Harvard Medical School in Boston. "Future work should focus on strategies to increase the uptake of similar interventions and on improving the understanding of which patient groups derive the most clinical benefit from adherence improvement efforts."

SWEDEHEART

An analysis of data from a national myocardial infarction registry in Sweden shows a dramatic improvement in long-term survival and reduction in the risk of new ischemic events and heart failure in non-ST-elevation MI patients over the last 20 years.

The researchers believe these improvements in outcomes are attributable to the gradual uptake and widespread use of in-hospital coronary interventions and evidence-based medications.

Findings from the Improved Outcomes in Patients with Non-ST-Elevation Myocardial Infarction During 20 years are Related to Implementation of Evidence-Based Treatments study were presented Tuesday by Karolina Szummer, MD, of Karolinska University Hospital in Stockholm.

Szummer reported that the standardized, one-year mortality ratio in NSTEMI compared to the control population decreased from 5.53 (5.30-5.77) in 1995-96 to 3.03 (2.89.3.19) in 2013-14. After adjusting for differences in baseline characteristics, the change of one-year CV-death or MI corresponded to a linearly decreasing trend of 0.930 (95 percent CI: 0.926-0.935) per two-year period. This trend was substantially attenuated after adjusting for changes in coronary interventions, and almost eliminated after also adjusting for changes in discharge medications.

DECIDE-LVAD

The findings of another recent trial suggest that a shared decision-making intervention for destination therapy left ventricular assist device (DT LVAD) improved patient decision quality based on patient knowledge and concordance between stated values and patient-reported treatment preference.

Results from the Effectiveness of a Shared Decision Making Intervention for Patients Offered a Destination Therapy Left Ventricular Assist Device for End-Stage Heart Failure trial were presented Tuesday by Larry A. Allen, MD, of the University of Colorado-Denver.

After randomly varying time in usual care, LVAD implanting centers were transitioned to an intervention consisting of clinician education and use of a DT LVAD pamphlet and video patient decision aids. Patients being considered for DT LVAD were enrolled and followed up at one and six months.

Allen reported that patient knowledge (mean test performance) during the decision-making period improved from 59.5 percent to 64.9 percent in control versus 59.1 percent to 70 percent in intervention. Correlation between stated values and patient-reported treatment preference at one month was stronger in intervention than control. However, there was no improved correlation between stated values and actual treatment received by six months for intervention compared to control. There were no differences in decision conflict, decision regret or preferred control. ▼

GEMINI-ACS-1 continued from page 1

A total of 6.5 percent of patients switched agents, with 8.5 percent of the ticagrelor group switching to clopidogrel and 4 percent of clopidogrel patients switching to ticagrelor.

CP2C19 status played a small role in switch decisions, Ohman said. The vast majority of patients did not switch, irrespective of their metabolizer status. And while patients with RM status were five times more likely to switch compared to UM patients, only 43 percent of RM patients switched from clopidogrel to ticagrelor because of metabolizer status. The other 57 percent switched due to nonbleeding adverse events, recurrent ischemic events, or another reason.

Only one patient switched from ticagrelor to clopidogrel because of metabolizer status. Other switches were due to nonbleeding adverse events, recurrent ischemic events or other reasons.

"Our findings do not support the utility of mandatory pharmacogenomics testing for P2Y12 inhibitor use because clinicians do not act on it," Ohman said. "And we saw no increased risk of ischemic events or increased bleeding with the RM phenotype, suggesting the information is of little clinical value."

COMPASS

Rivaroxaban 2.5 mg bid plus aspirin has the potential to reduce direct care costs an average of $682 for every patient treated. The estimate comes from a trial update of COMPASS, which compared cardiovascular outcomes for patients treated with rivaroxaban plus aspirin versus aspirin alone.

The primary trial found a 24 percent reduction in the risk for cardiovascular death, stroke or MI, said Andre Lamy, MD, associate professor of surgery at McMaster University in Hamilton, Ontario. The trial update examined the potential cost impact in the United States, Canada, France and Germany based on direct medical and procedural costs for all cardiovascular events in the trial.

U.S. treatment costs ranged from $6,871 for severe limb ischemia to $48,859 for stroke. Costs in the other four countries were lower, particularly for procedures, Lamy said.

"We are looking only at direct-care costs for cardiovascular events and procedures," he said. "And the 2.5 mg dose of rivaroxaban has not been approved anywhere, nor do we know the list price. But we saw that rivaroxaban decreases the direct costs of hospitalization, procedures and other treatments for major cardiovascular events."

RE-DUAL PCI

Clinicians should not expect any significant subgroup differences when using dabigatran dual-therapy for patients undergoing PCI. The results of a subgroup analysis of the RE-DUAL PCI trial found no differences between the primary outcome and subgroups with acute coronary syndrome as the index event, drug-eluting versus bare metal stents or ticagrelor versus clopidogrel.

The primary trial compared two dabigatran doses, 150 mg and 110 mg, plus a P2Y12 inhibitor versus warfarin triple-therapy with a P2y12 inhibitor plus aspirin. Both doses of dabigatran showed non-inferior outcomes vs. warfarin therapy. And while the trial was not powered to show superiority with 2,725 patients, both dabigatran doses showed better efficacy.

"There were no interactions in the subgroups based on ACS, the type of stent used or the antiplatelet agent," said Jonas Oldgren, MD, professor of medicine at Uppsala University in Sweden. "The benefits of dabigatran dual therapy were entirely consistent with the main results."

POISE-2 PCI

Patients with previous PCI who are taking aspirin probably do not need to interrupt aspirin for noncardiac surgery. For every 1,000 patients with prior PCI, perioperative aspirin will prevent 59 MIs and cause eight major bleeds, according to findings from a post-hoc analysis of a subgroup of the 10,010 patients in the POISE-2 study comparing aspirin to placebo in patients undergoing noncardiac surgery.

"This was not a prespecified analysis because the steering committee did not expect to randomize patients with prior PCI," said Michelle M. Graham, MD, professor of cardiology at the University of Alberta and the Mazankowski Alberta Heart Institute in Edmonton. "But 470 patients with prior PCI were randomized, which give us the opportunity to look at any potential subgroup effect."

The subgroup analysis found that in patients with prior PCI, those taking aspirin had a 50 percent risk reduction for death or MI compared to placebo.

"Among those with prior PCI undergoing noncardiac surgery, perioperative aspirin may be more likely to benefit patients than to harm them," Graham said.

PRAGUE-18

Patients who take prasugrel or ticagrelor following MI and then switch to clopidogrel are not at increased risk for ischemic events, according to findings from PRAGUE-18, an academic study that examined one-year outcomes comparing patients who did and did not switch to clopidogrel. Because there was no industry support, patients had to pay for antiplatelet agents after discharge.

"Patients commonly switch to clopidogrel after discharge for economic reasons," said co-principal investigator Zuzana Motovska, PhD, professor and head of acute cardiology at Charles University Third Medical Faculty in Prague.

"Most patients who switched because of cost did so immediately after discharge. Whether they switched or not, we saw no difference in the key endpoint of cardiovascular death or nonfatal stroke or MI," Motovska said. ▼

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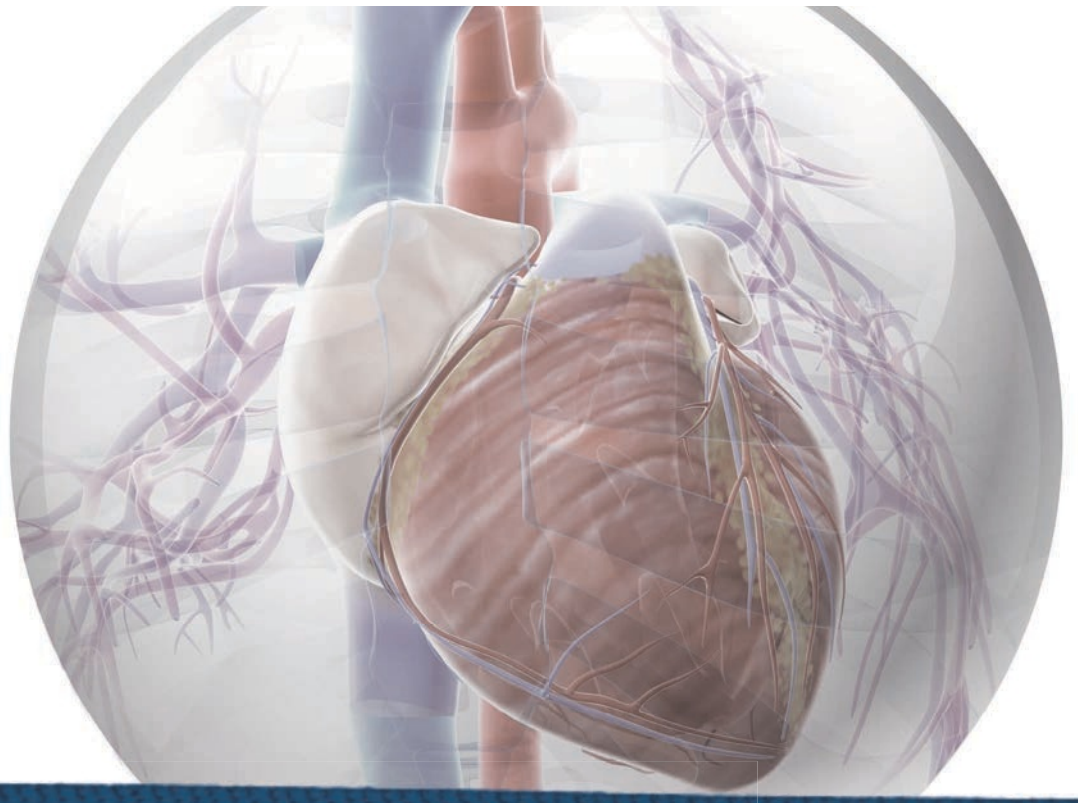

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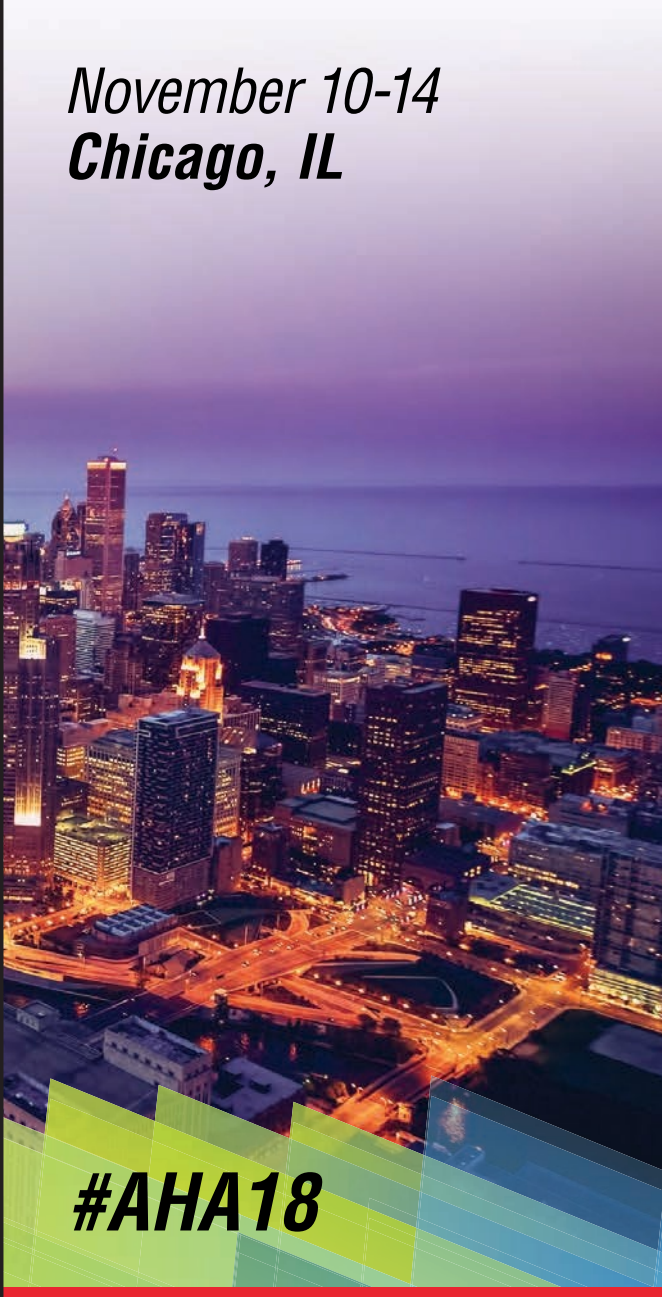

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