KSC 2021 DAILY

Today's Highlights

New Frontiers in Cardiology 1
Precision Medicine in Cardiovascular Disease
08:30-10:00 / Channel 1

Cross Specialty: Neurology & Intervention
Stroke Prevention in PFO and Carotid Artery Disease
08:30-10:00 / Channel 3

Education Workshop 1~4
08:30-16:00 / Channel 6

New Frontiers in Cardiology 2
Digital Therapeutics
10:10-11:40 / Channel 1

Cross Specialty: Myocardial Infarction & Cardiogenic Shock
Optimal Management for Cardiogenic Shock with AMI
10:10-11:40 / Channel 3

Cross Specialty: Neurology & Arrhythmia
AF Detection and Stroke Prevention in Patients with Stroke
12:50-14:20 / Channel 3

Basic Research Hot Session 1, 2
14:30-17:40 / Channel 3

ESC-KSC Joint Session: Arrhythmia
Clinical Updates in Treatment of Atrial Fibrillation
16:10-17:40 / Channel 2

New Frontiers in Cardiology 1

Atrial Fibrillation, Its Genetic Landscape and Recent Progress

Seung Hoan Choi, PhD
Broad Institute of MIT and Harvard, USA

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with substantial morbidity and mortality. Prior genome-wide association studies (GWAS) have identified over 100 genomic loci associated with AF. While GWAS for AF have rapidly expanded, there are numerous inherent limitations with this approach. For example, the disease-associated variants identified by GWAS typically confer only small effects, and identifying the correct gene at a GWAS locus is challenging. In contrast, whole genome sequencing (WGS) and whole exome sequencing (WES) studies provide greater resolution for genetic discovery and enable the discovery of rare variants conferring large genetic effects. However, due to the high cost of sequencing, many prior studies were performed within small sample sizes or with low sequencing depth, both of which greatly reduce the resolution for genetic discovery.

In the recent years, large international collaborations have facilitated a massive expansion in the sequencing data available. The National Heart Lung and Blood Institute (NHLBI) and the National Health Genetic Research Institute (NHGRI) have built the Trans-Omics for Precision Medicine Program (TOPMed) and the Centers for Common Disease Genomics (CCDG) to perform deep coverage WGS for a range of complex diseases. The CCDG has further produced WES data to identify the genetics underpinning several common diseases, such as AF. Finally, the UK Biobank, a population-based study from the United Kingdom, released over 200,000 WES samples in December 2020, following an industry-funded partnership.

To date, only a limited number of studies were able to leverage sequencing data to identify reproducible rare variant associations for AF. In 2018, a family-based study and an early-onset AF study identified the important association between rare loss-of-function (LOF) variants in titin (TTN) and early-onset AF. The association between rare mutations in TTN to AF risk has been subsequently replicated, yet these variants only explain ~0.2% of the variance in AF susceptibility.

Here, they will present a meta-analysis of over 52K AF cases and 267K controls from sequenced samples from TOPMed-CCDG, CCDG, four thrombolysis in myocardial infarction (TIMI) trials, and the UK Biobank. This project leverages the largest scale of sequencing data for this complex trait to date and allows us to assess the role of rare genetic variants in risk stratifying AF through exome-wide tests of protein-coding genes. Our results identify several novel associations of genes with AF and highlight a shared biological basis between AF and various inherited forms of cardiomyopathy. This finding may have implications for the diagnosis, longitudinal evaluation, and treatment of this common arrhythmia. More broadly, our findings underscore the value of large-scale sequencing to understand the rare genetic underpinnings of complex, adult-onset diseases.

Continued on page 13

Ethics Workshop [필수교육]

무엇이 아름다운 연구인가?

›› Sunday, Oct. 17, 16:10-17:40, Channel 5

- 16:10-16:40 윤리의 탄생: 성찰하는 삶, 소크라테스와 만남
- 16:40-17:10 참다운 연구: 위변조, 표절의 예방과 저자 윤리
- 17:10-17:20 KCJ의 경험: 사례로 알아보는 연구윤리 위반
- 17:20-17:30 Discussion

KSC 2021 DAILY

Program at a glance: Day 2, Oct 17, 2021

	Channel 1	Channel 2	Channel 3	Channel 4	Channel 5	Channel 6	Abstract Library
08:30-10:00	**New Frontiers in Cardiology 1** Precision Medicine in Cardiovascular Disease	**Arrhythmia 3** Clinical EP-1 (SVT, Atrial Tachyarrhythmia & EP Procedure)	**Cross Specialty: Neurology & Intervention** Stroke Prevention in PFO and Carotid Artery Disease	**Echocardiography 3** Heart as the Victim	**Case 3 (Intervention)** 14-17 **Case 4 (AMI & CAD)** 18-21	**Education Workshop 1: Heart Failure** 2021 Pharmacologic and Non-pharmacologic Therapy of Heart Failure	
10:10-11:40	**New Frontiers in Cardiology 2** Digital Therapeutics	**Arrhythmia 4** Clinical EP-2 (Ventricular Tachyarrhythmia)	**Cross Specialty: Myocardial Infarction & Cardiogenic Shock** Optimal Management for Cardiogenic Shock with AMI	**Echocardiography 4** Learning from Faults, A Word from the Masters	**Case 5 (Pediatric Cardiology)** 22-25 **Case 6 (Echo & Imaging)** 26-29	**Education Workshop 2: Intervention** Recent Update of ACS Treatment	
11:50-12:30	**Scientific Session [Viatris]** When and Why Atorvastatin Portfolio is Needed	**Scientific Session [BMS/Pfizer]** Anticoagulation for Better Patient Outcomes	**Scientific Session [Novartis]** ARNI: The Essential Standard of Care for Heart Failure	**Scientific Session [Samjin]** Updates on Antiplatelet Treatment Strategies	**Scientific Session [Boryung]** New Insights of Hypertension & SPAF		
12:30-12:50	**Break**						**Abstract** 1-270
12:50-14:20	**TSOC[1]-KSC Joint Session: Intervention** Contemporary Approach to Coronary Bifurcation Lesion Treatment	**Heart Failure 1** 2021 Update on HF Guidelines	**Cross Specialty: Neurology & Arrhythmia** AF Detection and Stroke Prevention in Patients with Stroke	**Lipid** Perspective on Anti-atherosclerotic Therapy in the Next Decade	**Pediatric Cardiology 1** Right Heart Failure in Congenital Heart Disease 1	**Education Workshop 3: Echocardiography** Applying Updated Guidelines to Clinical Practice: Case-based Approach	
14:30-16:00	**Intervention 3** Which is the Winner for Long-term Management of Patients Undergoing Complex PCI?	**Heart Failure 2** Essence of Recent HF Trials	**Basic Research Hot Session 1**	**Hypertension** Hypertension and Women	**Pediatric Cardiology 2** Right Heart Failure in Congenital Heart Disease 2	**Education Workshop 4: Arrhythmia** Essentials in Atrial Fibrillation Diagnosis and Management	
16:10-17:40	**Intervention 4** CTO Recorded Live Session	**ESC[2]-KSC Joint Session: Arrhythmia** Clinical Updates in Treatment of Atrial Fibrillation	**Basic Research Hot Session 2**	**Women Heart Disease** Korean Big Data on Sex Difference in Cardiovascular Disease	**Ethics Workshop [필수교육]** 무엇이 아름다운 연구인가?	**Epidemiology** Recent Advances in Cardiovascular Risk Prediction	
17:50-	**정기 총회**						

1) TSOC: Taiwan Society of Cardiology 2) ESC: European Society of Cardiology

Scientific Session

Scientific Session [Viatris]	
When and Why Atorvastatin Portfolio is Needed	
11:50-12:10	Let Start High Intensity Statin for ACS Patients, Let's Start
12:10-12:30	The Lower the Better: Atorvastatin's Next Option for Dyslipidemia Management
›› Oct 17, 11:50-12:30, Channel 1	
Scientific Session [BMS/Pfizer]	
Anticoagulation for Better Patient Outcomes	
11:50-12:10	Dosing Strategies for Long-term Persistence and Adherence
12:10-12:30	Real World Updates in Anticoagulation Management
›› Oct 17, 11:50-12:30, Channel 2	
Scientific Session [Novartis]	
ARNI: The Essential Standard of Care for Heart Failure	
11:50-12:10	Optimal Treatment of Heart Failure According to 2021 ESC Heart Failure Guideline
12:10-12:30	Reinforce Your Strategies to Improve Outcomes in POST-MI Heart Failure
›› Oct 17, 11:50-12:30, Channel 3	
Scientific Session [Samjin]	
Updates on Antiplatelet Treatment Strategies	
11:50-12:05	Role of Clopidogrel for ACS
12:05-12:20	Review of HOST-EXAM: Patients Management after PCI
12:20-12:30	Discussion
›› Oct 17, 11:50-12:30, Channel 4	
Scientific Session [Boryung]	
New Insights of Hypertension & SPAF	
11:50-12:10	New Clinical Trial of Fimasartan: FANTASTIC, FITNESS
12:10-12:30	Current Evidence in SPAF: From RE-VOLUTION to Gloria AF
›› Oct 17, 11:50-12:30, Channel 5	

New Frontiers in Cardiology 2

Digital Therapeutics in Diet and Glucose Control

Jung Eun Lee, ScD
Seoul National University, Korea

In the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD 2017), suboptimal dietary factors were responsible for 11 million deaths (22% of all deaths) and 255 million disability-adjusted life years (DALYs) (15% of all DALYs). It highlighted the importance of improving diet for non-communicable disease (NCD) prevention and management, and such dietary modification requires monitoring, reinforcement, interactive communications, and personalized approaches. As information and communication technologies evolved and became increasingly widespread, digital therapeutics devices, such as diet-tracking applications (apps), have become tools to help facilitate dietary changes.

Diet is the key to managing blood glucose, and therefore medical nutrition therapy is the major approach for managing diabetes. Recent systematic reviews and meta-analyses of randomized controlled trials (RCT) observed a significant reduction of hemoglobin A_{1c} (HbA_{1c}) with app-based interventions or telemedicine programs. A meta-analysis of 11 RCTs of type 2 diabetes patients found -0.35 (95% CI: -0.48 to -0.21) of HbA_{1c} in the app group vs. control group. In a meta-analysis of 31 telemedicine trials among type 2 diabetes patients, the mean difference in the change of HbA_{1c} level for telemedicine intervention compared to usual care was -0.63 (p<0.001).

Dietary intake monitoring function is contained in 68% of commercially available apps and 75% of apps reported in a journal literature review summarizing the features of mobile apps (Aug 2021). Diet-tracking apps often implement dietary assessment and dietary monitoring. Many studies evaluated the clinical effectiveness of the app use in health-related outcomes, but only a few studies validated the dietary assessment function of the apps. The main contents of diet-tracking apps include food composition, diet-health resources, feeding practices, feedback, general nutritional information, nutritional tools, and nutritional supports.

We developed a diet-tracking app and found its potential to have positive effects on managing chronic conditions. However, there was insignificant difference in weight loss and clinical biomarkers compared to the conventional paper-based diary method, which is in alignment with previous data. When we compared nutrient intake data from the app with those from 24-hour recalls, we found modest-to-high correlations.

Emerging technologies have paved the way for effective diet-tracking, such as video and image analysis based on machine learning, speech recognition, and personalized devices including smartphones and wearables, computing resources on clouds, low-latency connectivity, and Mechanical Turk. However, it remains a challenge to acquire easy food logging, continued update of food database, tailored nutrition counseling, and sustainable engagement.

Given the widespread use of digital devices and growing interest in the efficacy of digital health for lifestyle modification in NCD prevention and control, it is important to understand and implement digital therapeutics in nutrition care. Further prospective and intervention studies are warranted.

New Frontiers in Cardiology 2
Digital Therapeutics
›› Sunday, Oct 17, 10:10-11:40, Channel 1

Women Heart Disease

Sex Difference in Atrial Fibrillation

So-Ryoung Lee, MD, PhD
Seoul National University Hospital, Korea

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice. There are differences in the risk of AF incidence as well as AF-related adverse events depending on the sex. For the incidence of AF, the male sex is associated with a higher risk of AF by 1.5-fold than the female sex, even after adjusting for age and other risk factors. Although many risk factors have been identified for AF, the magnitude of relative effect differs between the sexes. Heart failure and valvular heart disease contribute to the increase of AF risk in women than men. In contrast, hypertension, diabetes mellitus, myocardial infarction, and obesity have a similar effect in both sexes on the risk of AF. In the aspect of pathophysiology, several possible mechanisms have been suggested, including the role of sex hormones, and the differences in the electrophysiologic remodeling or the structural remodeling, including tissue fibrosis. Although women with AF have greater symptom burden and a higher risk of AF-related adverse events than men with AF, female patients are treated more conservatively. Understanding the sex differences in AF patients and implementing optimal treatment strategy based on these differences should be emphasized to improve the clinical outcomes in both female and male patients.

Women Heart Disease
Korean Big Data on Sex Difference in Cardiovascular Disease
›› Sunday, Oct 17, 16:10-17:40, Channel 4

KSC 2021 DAILY

Arrhythmia

How to Perform Fluoroless Electrophysiology Procedures

Hong Euy Lim, MD, PhD
Hallym University Sacred Heart Hospital, Korea

Catheter ablation (CA) is more effective than antiarrhythmic drugs, and increasing evidence suggests that the procedure can be used as a first-line therapy for most patients with various arrhythmias. Previously, operators in the field of electrophysiology (EP) incorporated the imaging with fluoroscopy for insertion and manipulation of intracardiac catheters because this was the only imaging modality available. As EP procedures became more complex, radiation exposure to patients and operators has extended. As a result, the cumulative risk of cancer may increase. Moreover, medical staff are required to wear heavy protective equipment, also increasing the risk of musculoskeletal injuries and disabilities.

With technological advancement, the abundance of non-fluoroscopic imaging techniques provides better anatomic and electrical detail without the risk, cost, and hassle of fluoroscopy. Additionally, heavy dependency on fluoroscopy had been questioned and has been minimized at most EP centers with the invention and continued evolution of non-fluoroscopic imaging modalities such as intracardiac echocardiography (ICE) and three-dimensional (3D) electroanatomical mapping system. Recent prospective, randomized controlled trials have shown the effectiveness and safety of implementing a zero-fluoroscopy approach in the EP labs. The most vulnerable populations, including children and pregnant patients, are best served by using a zero-fluoroscopy ablation approach. However, there are still concerns that fluoroless methods will lead to increased procedural duration, procedure-related complication rate, and reduced effectiveness of CA.

With more image sophistication as well as early adoption in training or practice, EP operators may feel less and less need to verify positions or anatomy by fluoroscopy. Education of the next generation of trainees is pivotal in transformational technology adoption. Since EP labs have promoted zero to near-zero fluoroscopy, most new fellows are likely to continue this trend into their practice following graduation. Comprehensive instruction in multi-imaging modalities for training fellows optimally helps the field of EP to shift towards a fluoroless procedure. In the future, fluoroless methods for CA may become the standard-of-care.

Arrhythmia 3
Clinical EP-1 (SVT, Atrial Tachyarrhythmia & EP Procedure)
›› Sunday, Oct 17, 08:30-10:00, Channel 2

How to Use 3D Electroanatomical Mapping Systems

Seil Oh, MD, PhD
Seoul National University Hospital, Korea

Cardiac mapping is a procedure to interpret the mechanism of arrhythmia and to localize the site of origin or critical region of tachyarrhythmia. The three-dimensional (3D) electroanatomical mapping systems can provide spatial information in a 3D manner as well as local electrogram data to allow us to better understand arrhythmia mechanism more intuitively and facilitate ablation procedures. It can track sites of ablation and project generated cardiac anatomy that can be used to recognize adjacent anatomical structures.

However, 3D map is not always accurate because it is highly dependent on the reference electrode (or electrogram) and window of interest. It is important to confirm that reference electrogram has not shifted. When mapping a focal tachyarrhythmia, it is of key importance that the beginning of the window be set far enough before the reference to allow for acquisition of signals from early sites responsible for arrhythmia propagation. In case of macro-reentry, deciding on an appropriate window is even more critical. The window should not exceed the tachycardia cycle length. Most mapping systems allow the user to define a region where "early meets late". However, this is arbitrary and depends on where the offset and onset of the windows are defined. Designation of the activation time of locally acquired signals is generally arbitrary during macro-reentry, and defining critical sites of ablation may require the additional maneuvers such as entrainment. As missing areas could result in false activation map, all possible regions and chambers should be included in the map. In addition, electrogram quality is of number-one importance because the 3D map is reconstructed based on the electrogram. Therefore, contact of the mapping electrode should be good, and annotation process should be consistently correct. When annotating a point, one has to consider whether the earliest portion of the electrogram (peak, maximum upstroke of the bipolar electrogram, or maximum upstroke velocity [dV/dt] of the unipolar electrogram) will be used to determine the local activation. Annotation can become even more complex at sites of diseased tissue. Thus, one should consider how each individual electrogram is annotated during mapping, including differentiating far-field from near-field potentials.

Even though mapping technology evolves quite accurately, it must be considered that there are still potential limitations and pitfalls for successful procedures.

Arrhythmia 4
Clinical EP-2 (Ventricular Tachyarrhythmia)
›› Sunday, Oct 17, 10:10-11:40, Channel 2

Hypertension

Hypertension in Korean Women

Hyeon Chang Kim, MD, PhD
Yonsei University Severance Hospital, Korea

The prevalence of hypertension is known to be higher in men than women, but not in all age groups. Korea is one of the world's fastest aging countries, while the average life expectancy difference between men and women is wide, resulting in a rapid increase in the elderly female population.

Analysis of the Korea National Health and Nutrition Examination Survey (KNHANES) shows that women with hypertension, especially in older age groups, are rapidly increasing. In 1998, about 3.5 million women and 4.3 million men had hypertension, but currently (2016-2018), about 5.2 million women and 6.5 million men have hypertension. However, if limited to those aged 65 or older, currently 2.7 million women and 1.8 million men have hypertension (**Figure 1**).

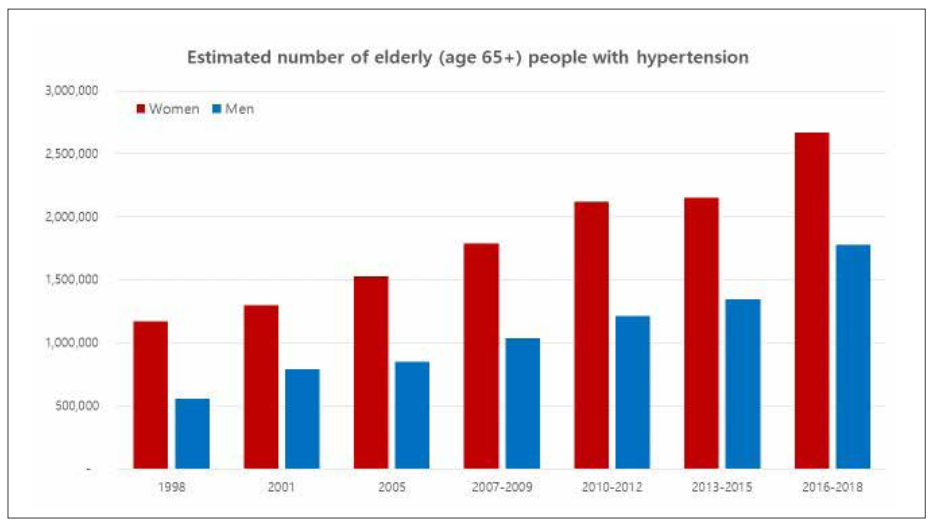

Figure 1. Estimated number of elderly (age 65+) people with hypertension (Data source: Korea National Health and Nutrition Examination Survey [KNHANES] 1998-2018.)

Prevalence of hypertension is higher in men up until the age of 50s, but the prevalence becomes higher in women after age of 70s. Undiagnosed hypertension and diagnosed-but-untreated hypertension are more common in men, while treated-but-uncontrolled hypertension is more common in women. Moreover, elderly female patients with hypertension are suffering from more frequent co-morbidities compared to younger or male counterparts.

A multi-pronged approach is needed to increase awareness of hypertension in women and to achieve better blood pressure control especially for elderly women.

Hypertension
Hypertension and Women
›› Sunday, Oct 17, 14:30-16:00, Channel 4

Cross Specialty: Neurology & Intervention

The Causality of PFO in Cryptogenic Stroke

Bum Joon Kim, MD, PhD
Ulsan University Asan Medical Center, Korea

Patent foramen ovale (PFO) can be found in one-fourth of individuals in the general population. The rate increases to one in two among those with cryptogenic stroke. Theoretically, only half of PFO in cryptogenic stroke may be the culprit for the ischemic event. Therefore, it is critical to determine which PFO is truly the cause of the stroke.

Two strategies can be used to investigate the suspect. First, the characteristics of the crime itself (the PFO) can be investigated by the cardiologist. The size of PFO, shunt amount, and presence of an atrial septal aneurysm are taken into consideration to define high-risk PFO (**Figure 1**). Additionally, the crime scene (brain) should be investigated. As a neurologist, first thing to consider is the infarction pattern. As the PFO-stroke is mainly embolic, it is generally located in the cortical area.

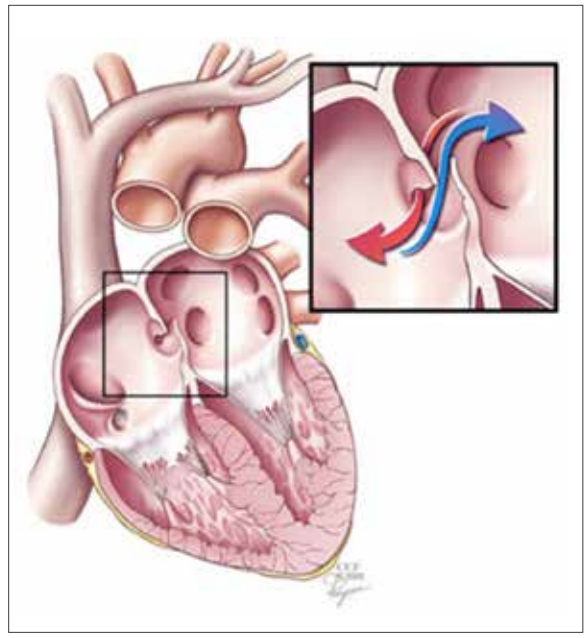

Figure 1. Foramen ovale (Adapted from Cleveland clinic)

The emboli must pass through the PFO, which is not a large structure, but as the ischemic lesions are usually small, the magnetic resonance angiography reveals no occlusive lesion. Second, the ischemic lesions are more dominant in the posterior circulation. During the release of the Valsalva maneuver, right-to-left shunt increases. At the same time, the flow-through posterior circulation also increases. This is explained by the less sympathetic innervation of the posterior circulation. A similar pathophysiology is also involved in the posterior reversible encephalopathy syndrome. Hence, PFO can be characterized as two types; some are opened only at the release of the Valsalva maneuver, whereas the remaining are consistently opened regardless of the Valsalva maneuver. The type which only opens at the release of the Valsalva maneuver shows a more predominance of infarction located at the posterior circulation due to the mechanism mentioned above.

In the same vein, the condition of the stroke is also considered. If the stroke has occurred after the intra-abdominal pressure increase, it may provoke the Valsalva maneuver and the right-to-left shunt, which as a result may increase the chance of paradoxical embolism. Other clinical factors such as age and conventional risk factors are also considered. Younger patients with fewer risk factors – which may be presented by a high risk of paradoxical embolism (RoPE) score - may have a higher chance for the ischemic stroke to be attributed by PFO. On the contrary, caution is needed when judging the causality of PFO on stroke among elderly patients. If there is any chance for another potential embolic source, such as those with left atrial enlargement or non-sustained tachycardia, an in-depth rhythm evaluation with an implantable loop recorder may be considered before determining the treatment strategy. PFO closure is not an emergent procedure and can be delayed in those at the gray zone. The causality of PFO for stroke must be checked by a multidisciplinary approach, including neurologists and cardiologists.

Cross Specialty: Neurology & Intervention
Stroke Prevention in PFO and Carotid Artery Disease
›› Sunday, Oct 17, 08:30-10:00, Channel 3

Pediatric Cardiology 1

Mechanism of Right Heart Failure in Congenital Heart Diseases

Hwa Jin Cho, MD, PhD
Chonnam National University Hospital, Korea

As major advances have been made in both diagnosis and management of congenital heart disease (CHD), the majority of children are now surviving into adulthood. In patients with CHD, the right ventricle (RV) may function as either the subpulmonary or the systemic ventricle (e.g., transposition of great arteries). Among CHDs that affect the RV more commonly are atrial septal defect, tetralogy of Fallot (TOF), pulmonary stenosis, Ebstein anomaly, arrhythmogenic right ventricular cardiomyopathy (ARVC), and pulmonary valve atresia.

The right heart failure (RHF) is characterized by the inability of the right heart to sufficiently eject blood or fill at sufficiently low pressure to meet the needs of the body. In patients with CHD, both systolic and diastolic RV dysfunction often occurs. As the RV dilates, tricuspid regurgitation may also aggravate the RHF syndrome. Cardiac arrhythmias may also be a notable feature of patients with CHD and RHF, especially in patients with previous ventriculotomy, severe right atrial enlargement or ARVC.

Several mechanisms may contribute to RHF in CHD depending on the specific pathogenesis of the CHD, including pressure or volume overload or intrinsic myocardial disease. Myocardial ischemia may also contribute to the progression of right ventricular failure (RVF). In patients with CHD affecting the right heart, pressure and volume overload may combine to cause progressive RHF. This is often observed in patients with TOF who may have both pulmonary stenosis and regurgitation, even after surgical correction.

Regarding the compensation, the RV adapts better to chronic volume overload than to pressure overload. For example, patients with ventricular septal defect (VSD) and Eisenmenger physiology often show a better ventricular compensation than patients with later onset pulmonary arterial hypertension. To prevent 'irreversible' RHF, timely diagnosis and corrective/palliative surgery are required for patients with CHD affecting the RV.

Pediatric Cardiology 1
Right Heart Failure in Congenital Heart Disease 1
›› Sunday, Oct 17, 12:50-14:20, Channel 5

KSC 2021 DAILY

Cross Specialty: Neurology & Arrhythmia

How Long of AF Detected by Implantable Loop Recorder is Significant for Recurrence of Stroke?

Ki Yung Boo, MD
Jeju National University Hospital, Korea

Nonvalvular atrial fibrillation (AF) or atrial flutter is the cause of one-third of all ischemic strokes and the majority of strokes related to cardiac embolism. The diagnosis of AF requires rhythm documentation with an electrocardiogram (ECG) tracing showing AF. By convention, an episode lasting at least 30 seconds is diagnostic for clinical AF. Among patients with recent ischemic stroke but without evidence of AF on ECG and Holter monitoring, the guidelines suggest etiologic investigations, including additional ECG monitoring for 2 to 4 weeks. This recommendation is based on the evidence that evaluation with both external and implantable loop recorders (ILR) improves the detection of AF in patients with stroke of undetermined etiology. Randomized studies evaluating 30 days of ECG monitoring after stroke diagnosed new AF in 14% to 16% of patients, whereas monitoring with an ILR for a longer duration detected AF in 12.4% of patients after 6 months.

Owing to short monitoring, detection of atrial high-rate episodes (AHRE)/subclinical AF via external ECG is less likely. Cardiovascular implantable electronic devices (CIEDs) with an atrial lead can monitor atrial rhythm and store the tracings. Implantable cardiac monitors (ICMs) have no intracardiac leads but continuously monitor cardiac electrical activity by recording and analyzing a single lead bipolar surface ECG based on a specific algorithm. Very short episodes (<30 sec/day) are considered clinically irrelevant, as they are not significantly associated with longer episodes or an increased risk of stroke or systemic embolism. However, longer episodes of AHRE/subclinical AF are associated with an increased risk of clinical AF, ischemic stroke, major adverse cardiovascular events, and cardiovascular death (**Figure 1**). Overall, the absolute risk of stroke associated with AHRE/subclinical AF may be lower than with clinical AF. The temporal dissociation from acute stroke suggests that AHRE/subclinical AF may represent a marker rather than a risk factor for stroke. AHRE/subclinical AF is increasingly reported in a variety of patients undergoing cardiac monitoring. Clinical AF will reportedly develop in 1 in 5-6 patients within 2.5 years after diagnosis of AHRE/subclinical AF. Notwithstanding that more high-quality evidence is needed to inform optimal management of these patients, more intense follow-up and monitoring to detect clinical AF early is prudent.

The use of oral anticoagulant (OAC) may be considered in selected patients with longer durations of AHRE/subclinical AF (≥24 h) and an estimated high individual risk of stroke, accounting for the anticipated net clinical benefit and informed

Continued on page 7

Six-month incidence of transition to higher AHRE burden[a]
(n = 6,580, pooled from three prospective studies)

	Baseline burden			
6-month progression	5 min to <1 h	1 h to <6 h	6 h to <12 h	12 h to <23 h
Transition to ≥1 h	33.5%			
Transition to ≥6 h	15.3%	42.2%		
Transition to ≥12 h	8.9%	27.5%	55.8%	
Transition to ≥23 h	5.1%	16.0%	40.6%	63.1%

Stroke rates[b] per AHRE burden and CHA_2DS_2VASc category
(n = 21,768 device patients not taking OAC)

	Baseline maximum daily burden		
CHA_2DS_2-VASc score	No AF	AF 6 min–23.5 h	AF >23.5 h
0	0.33%	0.52%	0.86%
1	0.62%	0.32%	0.50%
2	0.70%	0.62%	1.52%
3-4	0.83%	1.28%	1.77%
≥5	1.79%	2.21%	1.68%

CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age 65-74 years, sex category (female).
[a]The higher the burden at diagnosis, the greater the incidence of progression in the next 6 months and thereafter. [b]Stroke rates above the threshold for OAC are shown in red.

Figure 1. Progression of atrial high-rate episode burden (left panel) and stroke rates according to AHRE daily burden and CHA_2DS_2-VASc score (right panel) (Adapted from Hindricks G, et al. Eur Heart J 2021;42(5):373-498.)

Lipid

ANGPTL3 and Apolipoprotein C-III as Novel Lipid-Lowering Targets

Chan Joo Lee, MD, PhD
Yonsei University Severance Hospital, Korea

Recent studies have shown that angiopoietin-like protein 3 (ANGPTL3) and apolipoprotein C-III (ApoC-III)-targeted therapies have the potential for overcoming cardiovascular diseases. ANGPLT3, involved in angiogenesis and lipid metabolism, has the ability to inhibit lipoprotein lipase and hepatic lipase activity. Its inhibition enhances lipase activity and accelerates lipoprotein degradation and removal. Based on animal studies and a human Mendelian randomization study, ANGPLT3 can be a promising therapeutic target in the treatment of dyslipidemia, and drug development using monoclonal antibody and antisense oligonucleotide is in progress. Evinacumab, a monoclonal antibody of ANGPLT3, was effective in reducing low-density lipoprotein (LDL) cholesterol regardless of LDL receptor activity in a phase 2 study with homozygote familial hypercholesterolemia patients.

Another therapeutic strategy that inhibits ANGPLT3 is transcriptional modulation by antisense oligonucleotides (ASO). *Angplt3* ASO (IONIS-ANGPLT3-L_{Rx}) effectively reduced ApoB-containing lipoprotein concentration in a mouse model. ApoC-III, a major lipoprotein constituting very-low-density lipoprotein (VLDL) and chylomicron, inhibits lipoprotein lipase to decrease lipolysis and decrease hepatic uptake, thereby increasing triglyceride (TG)-rich lipoprotein. Genome-wide association studies and Mendelian randomization studies demonstrated that the loss-of-function mutation in *APOC3* is associated with low TG levels and a low atherosclerotic risk. Large long-term studies showed an association between ApoC-III and cardiovascular risk. High-density lipoprotein (HDL) particles containing ApoC-III have lower cholesterol efflux capacity than classical HDL. Therefore, *APOC3* silencing using small interfering ribonucleic acid (siRNA) is being studied. Volanesorsen, a second-generation siRNA targeting *APOC3*, can reduce serum TG level by up to 90%. In two phase 3 studies, volanesorsen showed significant reductions in TG, VLDL cholesterol, and chylomicron with an increased risk of thrombocytopenia.

Lipid
Perspective on Anti-atherosclerotic Therapy in the Next Decade
›› Sunday, Oct 17, 12:50-14:20, Channel 4

TSOC-KSC Joint Session: Intervention

Upfront 2-stent Approach for Bifurcation Lesions: When and How?

Chi-Jen Chang, MD
Chang Gung Memorial Hospital, Taiwan

Provisional stenting is currently the standard recommendation for most of the bifurcation lesions treated with percutaneous coronary intervention. In most of the randomized trials comparing the effects of provisional strategy and upfront 2-stent strategy, upfront 2-stent strategy was not shown to be associated with a lower rate of major adverse cardiac events.

Recently, the DEFINITION II trial demonstrated that in patients with complex true bifurcation lesions, defined according to the DEFINITION criteria, upfront 2-stent strategy was associated with a lower rate of target vessel failure, driven by a lower rate of target vessel myocardial infarction and target lesion revascularization, compared with the provisional strategy. These findings suggest that the upfront 2-stent strategy may not be beneficial for all true bifurcation lesions. However, for complex bifurcation lesions, the upfront 2-stent technique is beneficial in reducing adverse cardiac events. According to the DEFINITION criteria, bifurcation lesions meeting one major criterion and two minor criteria are defined as complex bifurcation lesions. The major criteria (side branch lesion length ≥10 mm and diameter stenosis ≥70% for left main [LM] bifurcation and ≥90% for non-LM bifurcation) reflect the disease severity of the side branch. The six minor criteria cover other factors such as calcification, thrombus containing, etc.

For bifurcations that do not meet the criteria of complexity, if delivery of the stent to the side branch is anticipated to be difficult after stenting for the main vessel, the upfront 2-stent strategy may also be indicated. For bifurcation with critical stenosis at the ostium of the side branch, indicating high risk of occlusion after stenting for the main vessel, but the complexity does not meet the criteria, usage of the jailed balloon may secure the access to the side branch after stenting for the main vessel and avoid upfront 2-stent technique.

When treating bifurcation lesions with the upfront 2-stent strategy, the most important points to remember are to do the procedure properly and completely no matter which 2-stent technique is used. The procedure of each 2-stent technique has been refined in the past decade. The procedures such as the proximal optimization technique, rewiring through the correct cell, sequential high-pressure post-dilation, and kissing balloon technique, are proposed to minimize overlapping of stent struts, minimize redundant struts at the carina, avoid incomplete stent coverage, maximize the stent expansion and optimize the stent geometry. It is pivotal to understand extensively each step of different 2-stent techniques since adherence to best practice impacts largely on acute and late clinical outcomes.

TSOC-KSC Joint Session: Intervention
Contemporary Approach to Coronary Bifurcation Lesion Treatment
›› Sunday, Oct 17, 12:50-14:20, Channel 1

Continued from page 6

patient's preferences. In the recent trials, OAC was initiated in 76.4% and 56.3% of patients with ≥2 clinical stroke risk factors and insertable cardiac monitor detected physician-confirmed AF episodes of ≥6 min, respectively, but follow-up bleeding rates were not reported. In a large retrospective cohort study using remote monitoring data on daily AF burden, there was a large practice variation in the OAC initiation. Across increasing AF burden strata (from >6 min to >24 hr), the risk of stroke in untreated patients increased numerically, and the strongest association of OAC with a reduction in stroke was observed among patients with device detected AF episodes of >24 hr.

Cross Specialty: Neurology & Arrhythmia
AF Detection and Stroke Prevention in Patients with Stroke
›› Sunday, Oct 17, 12:50-14:20, Channel 3

Basic Research Hot Session

Simultaneous Induction of Vasculogenesis and Angiogenesis Elicits Comprehensive Cardiac Repair Following Myocardial Infarction

Hun-Jun Park, MD, PhD
The Catholic University of Korea Seoul St. Mary's Hospital, Korea

Since impaired coronary blood supply following myocardial infarction (MI) deteriorates the heart function, therapeutic neovascularization in the ischemic hearts has been considered as a major target for cell-based cardiac repair. We developed a multifaceted combined platform to regenerate vasculatures by simultaneously promoting postnatal vasculogenesis and angiogenesis, the two core mechanisms of neovascularization, utilizing CD31+ endothelial cells derived from human induced pluripotent stem cells (hiPSC-ECs) and engineered human mesenchymal stem cells (SDF-eMSCs) that continuously secrete stromal cell-derived factor 1α (SDF-1α) within a three-dimensional (3D) cardiac patch, implanted in the epicardium of MI hearts. We hypothesized that intramyocardially injected hiPSC-ECs produce *de novo* vessels via vasculogenesis, whereas epicardially implanted SDF-eMSC patch (SDF-eMSC-PA) simultaneously enhances angiogenesis of host vessels through prolonged secretion of paracrine factors including SDF in MI hearts. Subsequently, SDF1α-eMSC-PA improved vasculogenic potential of hiPSC-ECs and promoted survival and retention when they were injected into the MI-induced rat hearts, ultimately achieving comprehensive neovascularization and restoring cardiac function to the MI hearts (**Figure 1**). These results provide compelling evidence that this combined platform for vascular regeneration can be an effective means for treating ischemic heart disease.

Comprehensive Quantification of Fuel Use by the Failing and Non-failing Human Heart

Cholsoon Jang, PhD
University of California, USA

The heart consumes circulating nutrients to fuel lifelong contraction, but a comprehensive mapping of human cardiac fuel use is lacking. We used metabolomics on blood from artery, coronary sinus, and femoral vein in 110 patients with or without heart failure to quantify the uptake and release of 277 metabolites, including all major nutrients, by the human heart and leg. The heart primarily consumed fatty acids and, unexpectedly, little glucose; secreted glutamine and other nitrogen-rich amino acids, indicating active protein breakdown, at a rate ~10 times that of the leg; and released intermediates of the tricarboxylic acid cycle, balancing anaplerosis from amino acid breakdown. Both heart and leg consumed ketones, glutamate, and acetate in direct proportionality to circulating levels, indicating that availability is a key driver for consumption of these substrates. The failing heart consumed more ketones and lactate and had higher rates of proteolysis. These data provide a comprehensive and quantitative picture of human cardiac fuel use.

Basic Research Hot Session 1
›› Sunday, Oct 17, 14:30-16:00, Channel 3

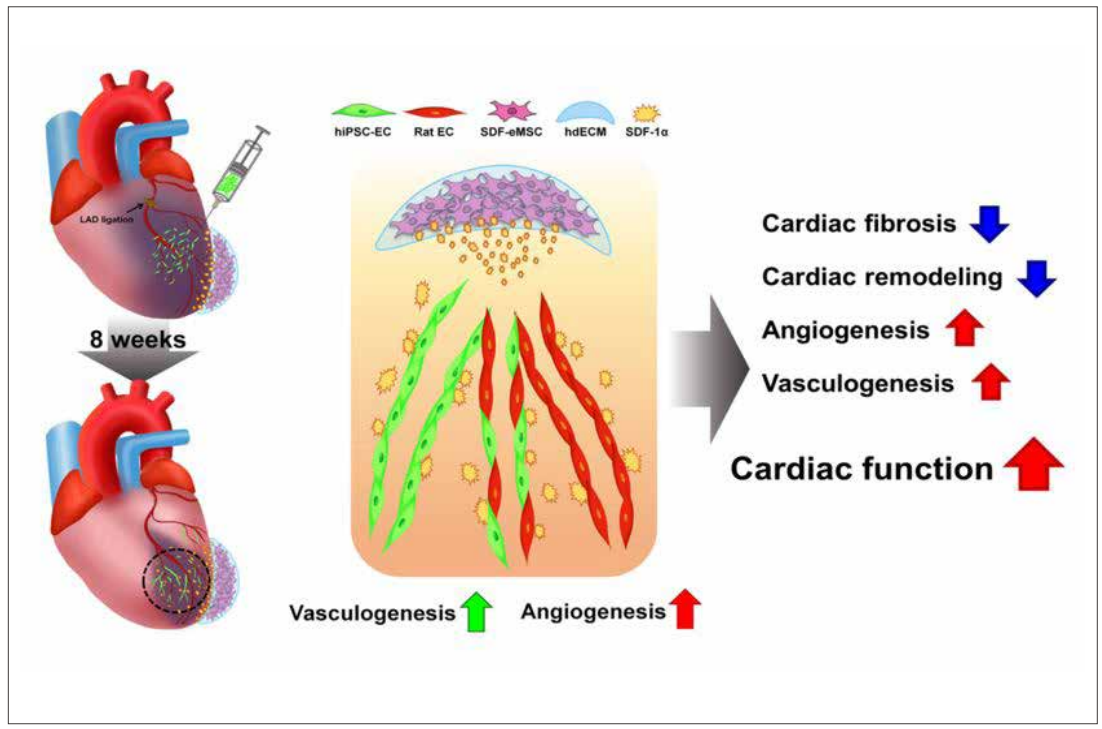

Figure 1. Simultaneous induction of vasculo-angiogenesis using hiPSC-ECs and SDF1α-eMSC-PA

Dynamic Regulation of Mitochondrial Metabolism in Metabolic Disease

Haejin Yoon, PhD
Harvard Medical School, USA

Rapid alterations in cellular metabolism allow tissues to maintain homeostasis during changes in energy availability. The central metabolic regulator acetyl-CoA carboxylase 2 (ACC2) is robustly phosphorylated during cellular energy stress by AMP-activated protein kinase (AMPK) to relieve its suppression of fat oxidation. While ACC2 can also be hydroxylated by prolyl hydroxylase 3 (PHD3), the physiological consequence thereof is poorly understood. We find that ACC2 phosphorylation and hydroxylation occur in an inverse fashion. ACC2 hydroxylation occurs in conditions of high energy and represses fatty acid oxidation. PHD3-null mice demonstrate loss of ACC2 hydroxylation in heart and skeletal muscle and display elevated fatty acid oxidation. Interestingly, PHD3 senses glucose and suppresses lipid metabolism, which is the most important dynamic regulation of fuel utilization in muscle in the exercise model. To understand the loss of PHD3 in skeletal muscle in physiology, we investigated muscle function with exercise capacity. Whole body or skeletal muscle-specific PHD3 loss enhances exercise capacity during an endurance exercise challenge. In sum, these data identify an unexpected link between AMPK and PHD3, and a role for PHD3 in acute exercise endurance capacity and skeletal muscle metabolism.

Basic Research Hot Session 2
›› Sunday, Oct 17, 16:10-17:40, Channel 3

Cross Specialty: Myocardial Infarction & Cardiogenic Shock

Percutaneous Coronary Intervention Strategy for Cardiogenic Shock with Acute Myocardial Infarction

Min Chul Kim, MD, PhD
Chonnam National University Hospital, Korea

Cardiogenic shock (CS) is a leading cause of death in patients with acute myocardial infarction (AMI). About two-thirds of CS develops from AMI, and CS develops in approximately 7% of patients with AMI. The case fatality rate of these patients is very high, up to 40-50%, despite widespread use of percutaneous coronary intervention (PCI), advances in cardiac intensive care medicines, and improved antithrombotic regimens. Although the incidence of CS is higher in patients with ST-segment elevation myocardial infarction (STEMI; 10-12%) than those without ST-segment elevation (NSTEMI; 3-4%), mortality is comparable regardless of ST-segment change. The mainstay of therapy for CS with AMI is early revascularization. The SHOCK (SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK) trial demonstrated the short- and long-term benefits of early revascularization in patients with AMI complicated by CS. Current guidelines for both STEMI and NSTEMI recommend early revascularization in AMI patients with CS. However, emergency coronary artery bypass surgery should be done if patient's coronary anatomy is not suitable for PCI or if PCI failed.

Multi-vessel disease is a common clinical condition, about 70-80% of all PCI cases in AMI with CS, and it is associated with poorer clinical outcomes than single-vessel disease. Older guidelines recommended multi-vessel PCI (MVI) in patient that are hemodynamically unstable or CS status. However, there has been many observational studies that showed inconsistent results. There has been no consensus of optimal revascularization strategy in this circumstance. However, a large-sized randomized trial, the CULPRIT-SHOCK (culprit lesion only PCI versus multivessel PCI in cardiogenic shock) trial, recently demonstrated no benefit of MVI over culprit vessel-only PCI (CVI). The 30-day risk of a composite of death or renal-replacement therapy was lower among those who initially underwent CVI only than those received immediate MVI. Therefore, CVI is recommended as the initial interventional strategy in AMI patients with CS who has multi-vessel disease.

Recently, several large-scaled randomized controlled trials regarding the use of mechanical circulatory support are being conducted for these high-risk patients. Optimal use of mechanical circulatory support combined with early revascularization may help reduce mortality in AMI patients with CS.

Cross Specialty: Myocardial Infarction & Cardiogenic Shock
Optimal Management for Cardiogenic Shock with AMI
›› Sunday, Oct 17, 10:10-11:40, Channel 3

Pediatric Cardiology 2

Medical Therapy for Chronic Right Ventricular Failure in Congenital Heart Disease

Soo In Jeong, MD
Ajou University Medical Center, Korea

With advances in pediatric cardiology and cardiac surgery, more patients with congenital heart disease (CHD) are surviving into adulthood. This as a result has led to many patients confronting the cardiac sequelae of residual hemodynamic problems. Right heart failure (RHF) is a frequent complication in both children and adults with CHD. The pathophysiology of RHF in CHD includes pressure overload, volume overload, or primary cardiomyopathy. The treatment approach to RHF in CHD patients consists of 1) medical management including drug therapy, 2) cardiac rehabilitation or 3) a more radical approach, such as structural correction by surgery, percutaneous intervention or assist device implantation.

Because of the broad spectrum of CHD and lack of evidence-based guidelines derived from large randomized controlled trials, medical management of CHD-specific RHF remains a challenge. The knowledge from guidelines in left ventricular (LV) failure is often extrapolated to treatment of RHF conditions, but this should be done with extreme caution because the right ventricle significantly differs anatomically and functionally from the left ventricle.

Symptomatic adult patients with CHD have neurohormonal activation of the natriuretic, endothelin, sympathoadrenergic, and renin-angiotensin-aldosterone systems (RAAS). However, the beneficial effects of RAAS blockade or β-blockers for RHF in CHD patients have not been demonstrated. A randomized clinical trial of β-blocker therapy for young adults with right ventricular (RV) dysfunction secondary to corrected CHD has shown no significant improvements in the clinical status, hemodynamic measurements, cardiorespiratory performance, or neurohormonal activation of the patients. The APPROPRIATE (ACE inhibitors for Potential PRevention Of the deleterious effects of Pulmonary Regurgitation In Adults with repaired TEtralogy of fallot) trial studying the effect of angiotensin-converting enzyme inhibition also found no improvement in exercise capacity but showed improvement of the LV volume in a subgroup with restrictive physiology. Recently, the REDEFINE (Right vEntricular Dysfunction in tEtralogy of Fallot: INhibition of the rEnin-angiotensin-aldosterone system) trial showed no beneficial effect of losartan on RV dysfunction or secondary outcomes in adults with repaired tetralogy of Fallot (TOF). The 2016 European Society of Cardiology (ESC) heart failure guidelines suggest diuretics for morphological subpulmonary RV failure in adult CHD. According to the 2018 American Heart Association (AHA) guideline for the management of adults with TOF, there are currently no recommendations on medical treatment for RV failure following CHD.

If RHF is secondary to precapillary pulmonary hypertension, pulmonary arterial hypertension-targeted therapy is recommended. The pressure overloaded RV is often very preload-dependent and therefore, loop diuretics must be used with caution in this group of patients.

In general, pharmacologic management of RHF in CHD is rather empirical and recommendations are mainly based on expert opinions. Besides drug therapy, early detection of RV dysfunction is critical, together with timely surgery, intervention, or other assist device implantation.

Pediatric Cardiology 2
Right Heart Failure in Congenital Heart Disease 2
›› Sunday, Oct 17, 14:30-16:00, Channel 5

KSC 2021 DAILY

Intervention

Dual Antiplatelet Therapy (DAPT) is the Only Reliable Regimen for Patients at High Risk

Ki Hong Choi, MD, PhD
Samsung Medical Center, Korea

After the introduction of the CURE (Clopidogrel in Unstable angina to prevent Recurrent Events) trial sub-study for percutaneous coronary intervention (PCI), $P2Y_{12}$ (purinergic receptor P2Y) inhibitor in addition to aspirin has become the standard treatment for patients with coronary artery disease after PCI. Despite the beneficial effects of DAPT after PCI in the drug-eluting stent era to reduce the risk of the future ischemic event is well-established, the appropriate duration for DAPT remains controversial, especially for patients who underwent complex PCI. Patients who undergo complex revascularization procedures are well-known to be at a substantially higher risk of ischemic events, in a graded fashion, with increased procedural complexity. Therefore, the intensifying anti-thrombotic strategy should be needed for these patients. To date, we have three options for more intensifying the anti-thrombotic therapy. First, we can use the potent $P2Y_{12}$ inhibitor instead of clopidogrel after PCI. However, the recent ALPHEUS (Assessment of Loading with the $P2Y_{12}$ inhibitor ticagrelor or clopidogrel to Halt ischemic Events in patients Undergoing elective coronary Stenting) and SASSICAIA (Strategies of Loading With Prasugrel vs. Clopidogrel in PCI-Treated Biomarker Negative Angina) trials failed to prove the benefits for the early use of potent $P2Y_{12}$ inhibitor (ticagrelor or prasugrel) in patients with complex high-risk indicated procedure (CHIP). Second, we can try the dual pathway inhibition strategy using novel oral anticoagulation therapy in addition to aspirin. In fact, the COMPASS (Cardiovascular OutcoMes for People using Anticoagulation StrategieS) trial demonstrated that rivaroxaban (2.5 mg twice daily) plus aspirin had better cardiovascular outcomes and more major bleeding events than aspirin alone. However, this trial included not solely a population treated with PCI, and the lesion complexity was not considered for the inclusion criteria. Finally, extended DAPT is one of the options for CHIP patients. In the sub-study of the DAPT trial, the benefits of extending DAPT for reducing the future ischemic risk were similar in subjects with and without complex lesions. Furthermore, a patient-level meta-analysis of four randomized trials for comparing the outcomes between short and long DAPT showed that long-term DAPT (≥1 year) significantly reduced the risk of cardiac ischemic events with a magnitude that was greater for higher procedural complexity, compared with a short period of DAPT (3-6 months). Therefore, among the intensifying anti-thrombotic strategy, only extended DAPT has concordant evidence for patients who underwent complex PCI and should be considered as the default strategy if significant bleeding is absent.

The HOST-EXAM Trial Clarified the Benefit of Clopidogrel Monotherapy Even in Patients at High Risk

Jung-Kyu Han, MD, PhD
Seoul National University Hospital, Korea

Previously, the only one randomized controlled study, the CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events) trial, had directly compared the efficacy and safety of clopidogrel with aspirin in patients with atherosclerotic vascular disease. The CAPRIE trial demonstrated that long-term administration of clopidogrel was more effective than aspirin in reducing the combined risk of ischemic stroke, myocardial infarction (MI), or vascular death. However, no study has assessed which is the better choice between the two antiplatelet agents for the chronic maintenance therapy in patients undergoing percutaneous coronary intervention (PCI) in the drug-eluting stent era. In the HOST-EXAM (Harmonizing Optimal Strategy for Treatment of coronary artery diseases-EXtended Antiplatelet Monotherapy) trial, we sought to compare head-to-head the efficacy and safety of aspirin and clopidogrel monotherapy in this clinical situation. A total of 37 study sites participated in this investigator-initiated, prospective, randomized, open-label, multicenter trial. We enrolled patients aged at least 20 years old, who maintained dual antiplatelet therapy without clinical events for 6–18 months after PCI

Continued on page 11

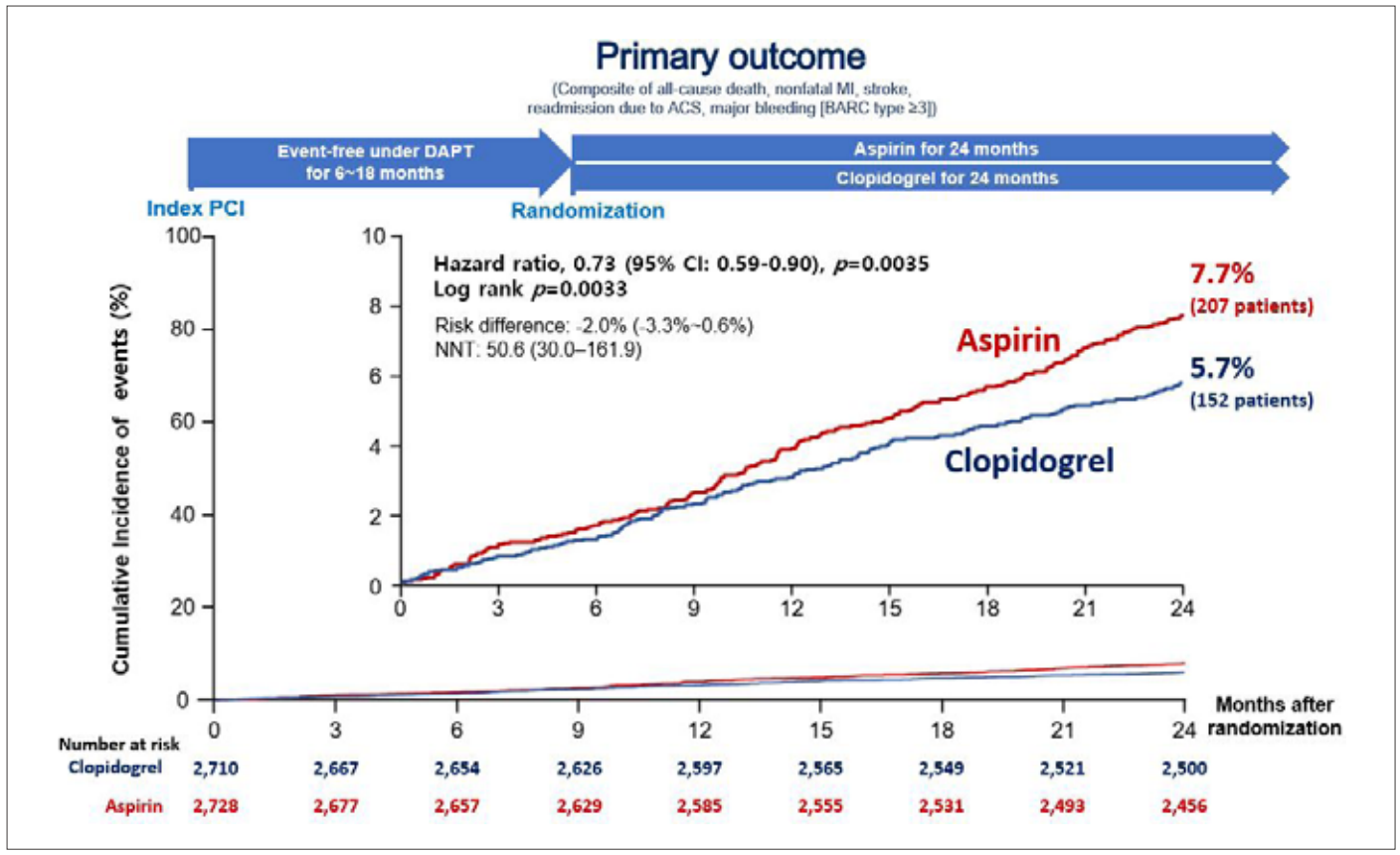

Figure 1. 24-month cumulative incidence of the primary composite outcome (Adapted from Koo BK, et al. Lancet 2021;397(10293):2487-96.)

Continued from page 10

with drug-eluting stent. We excluded patients with any ischemic and major bleeding complications. Patients were randomly assigned 1:1 to receive a monotherapy agent of clopidogrel 75 mg once daily or aspirin 100 mg once daily for 24 months. The primary endpoint was a composite of all-cause death, non-fatal MI, stroke, readmission due to acute coronary syndrome, and Bleeding Academic Research Consortium (BARC) bleeding type 3 or greater, in the intention-to-treat population. Between March 26, 2014 and May 29, 2018, we enrolled 5,530 patients. 5,438 (98.3%) patients were randomly assigned to either the clopidogrel group (2,710 [49.8%]) or to the aspirin group (2,728 [50.2%]). Ascertainment of the primary endpoint was completed in 5,338 (98.2%) patients. During the 24-month follow-up, the primary outcome occurred in 152 (5.7%) patients in the clopidogrel group and 207 (7.7%) in the aspirin group (hazard ratio (HR) 0.73 [95% confidence interval (CI): 0.59–0.90]; *p*=0.0035) (**Figure 1**). The per-protocol analyses yielded similar results to the intention-to-treat analyses for the primary study endpoint (HR 0.72 [95% CI: 0.58–0.89]; *p*=0.002). *Post hoc* analysis demonstrated that the beneficial effect of clopidogrel monotherapy was consistent in the various subgroups (acute MI, diabetes, multivessel disease, complex PCI, high bleeding risk) without any significant interaction. Interestingly, clopidogrel was better than aspirin not only in the thrombotic composite endpoint (HR 0.68 [95% CI: 0.52-0.87]; *p*=0.0028), but also in the major (BARC type ≥3, HR 0.63 [95% CI: 0.41-0.97]; *p*=0.035) or any bleeding (BARC type ≥2, HR 0.70 [95% CI: 0.51-0.98]; *p*=0.036) outcomes (**Figure 2**). In conclusion, the HOST-EXAM trial demonstrated that clopidogrel monotherapy is superior to aspirin monotherapy in preventing future adverse clinical events, including both the thrombotic composite as well as any bleeding in patients who received PCI and successfully maintained the intended duration of dual antiplatelet therapy (6~18 months).

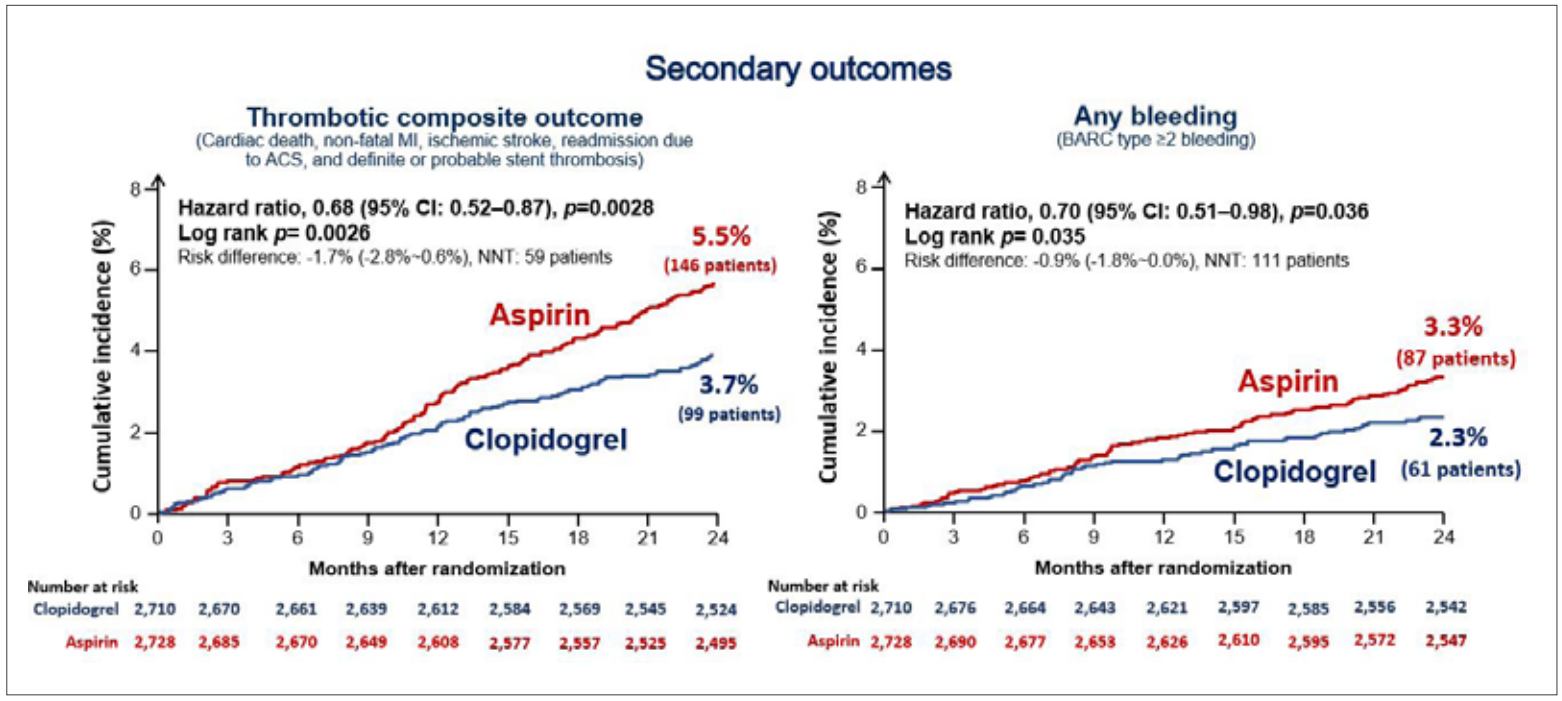

Figure 2. 24-month cumulative incidence of the secondary outcomes (Adapted from Koo BK, et al. Lancet 2021;397(10293):2487-96.)

Intervention 3
Which is the Winner for Long-term Management of Patients Undergoing Complex PCI?
›› Sunday, Oct 17, 14:30-16:00, Channel 1

Epidemiology

Machine Learning-based Models for Cardiovascular Risk Prediction

Sang-Yeong Cho, MD
Gyeongsang National University Changwon Hospital, Korea

Predicting the risk of cardiovascular disease (CVD) is the key to primary prevention. Contemporary guidelines recommend several risk assessment tools that have been proposed to accurately predict the risk of CVD, among which the Framingham risk score, pooled cohort equation, systematic coronary risk evaluation, and QRISK3 are widely used. However, there is still room for improvement in their accuracy; the range of the area under the curve (AUC) has been shown to be between 0.65 and 0.85. In addition, the overestimation of CVD risk, as well as underestimation, have been reported for specific individuals and population subgroups.

Recent years have seen remarkable advances in the application of machine learning (ML) in healthcare and medical research. However, a meta-analysis of 71 studies demonstrated no definite evidence of superior performance of ML over logistic regression.

Thus, we evaluated calibration and discrimination of pre-existing CVD risk models among Korean adults and developed ML-based risk prediction models using the National Health Insurance Service-Health Screening (NHIS-HEALS) cohort from Korea. This study demonstrated that ML-based algorithms could provide higher accuracy in cardiovascular risk prediction over contemporary cardiovascular risk models in statin-naïve healthy Korean adults without CVD.

Epidemiology
Recent Advances in Cardiovascular Risk Prediction
›› Sunday, Oct 17, 16:10-17:40, Channel 6

Heart Failure

Do We Agree on the New Universal Definition and Classification of HF?

In-Cheol Kim, MD, PhD
Keimyung University Dongsan Hospital, Korea

In 2021, the universal definition of heart failure (HF) was released by the writing committee consisting of 38 experts in HF, cardiomyopathy, and cardiovascular disease from the Heart Failure Society of America (HFSA), the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) and the Japanese Heart Failure Society (JHFS). This new universal definition was developed in need for standardization of the definition of HF and is expected to guide treatment, clinical trials, and health care policies. The pivotal elements needed to define HF are symptoms and/or clinical signs caused by a structural and/or functional cardiac abnormality, which are corroborated by either elevated natriuretic peptide levels or objective evidence of cardiogenic pulmonary or systemic congestion (**Figure 1**). In the first step, echocardiography is a key diagnostic modality to evaluate the structural and functional cardiac abnormalities. Evidence of systolic dysfunction (left ventricular ejection fraction [LVEF] <50%), high filling pressure (ratio of early transmitral flow velocity to early diastolic velocity of the mitral annulus [E/e'] >15), abnormal chamber enlargement, ventricular hypertrophy or valvular dysfunction can be evaluated by routine transthoracic echocardiography (ECHO). Considering the pathophysiology of HF, objective evidence of pulmonary and systemic congestion also needs to be confirmed by a chest X-ray, ECHO, right heart catheterization or pulmonary artery catheter. At the same time, the importance of natriuretic peptide is emphasized in this new definition of HF. The working group proposed modified HF stages: Stage A (at risk of HF); Stage B (Pre-HF); Stage C (HF); and Stage D (Advanced HF). Although this universal definition and stages of HF cannot be a perfect measure, it can provide more plausible and standardized criteria to classify HF in current era compared to the previous ones. Professor Kim will mention additional issues to be considered in the future, which are as follows: classification of asymptomatic pre-HF stages; setting different cut-off values for the natriuretic peptide levels among patients; and genetic background and etiologic differences. All in all, Professor Kim believes that while it is reasonable to adopt the new universal definition and classification of HF in our clinical practice, every effort should be made to adopt it properly based on the circumstances in every specific situation.

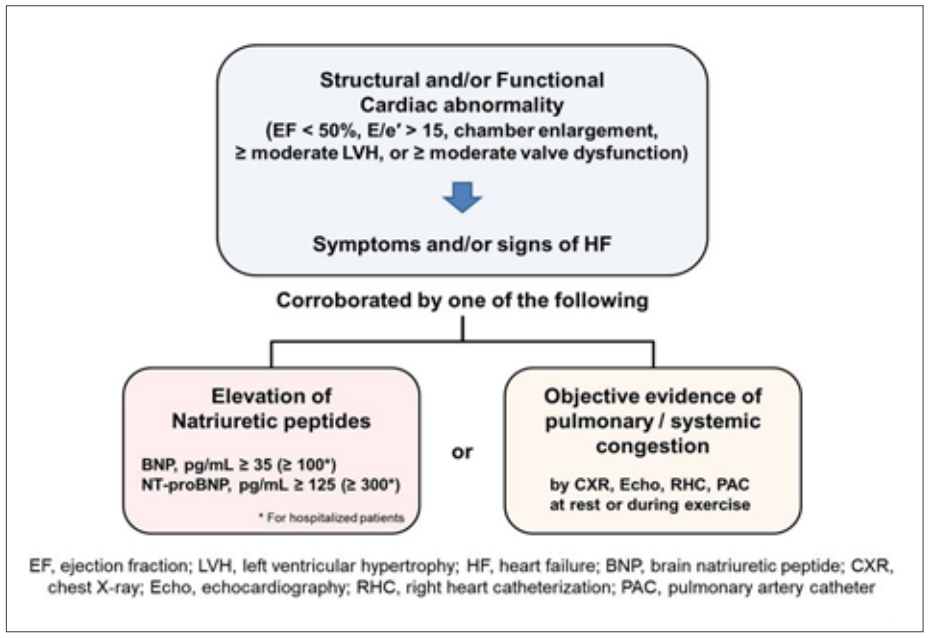

Figure 1. Summary of the universal definition of heart failure (Modified from Bozkurt B, et al. Eur J Heart Fail 2021;23(3):352-80.)

Heart Failure 1
2021 Update on HF Guidelines
›› Sunday, Oct 17, 12:50-14:20, Channel 2

EMPEROR-Preserved Trial: Empagliflozin, the First Win Against a Formidable Foe (HFpEF)

Jong-Chan Youn, MD, PhD
The Catholic University of Korea, Seoul St. Mary's Hospital, Korea

Heart failure (HF) with preserved ejection fraction (HFpEF) is one of the largest unmet clinical needs in the current cardiovascular medicine. The proportion of patients and the number of hospitalization due to HFpEF are increasing. Although there have been steady developments regarding pharmacologic treatment for use in patients with HF with reduced ejection fraction (HFrEF), no drugs have shown clear mortality benefits in patients with HFpEF. It is clear that the survival of patients with HFrEF has improved significantly over time, while the survival of patients with HFpEF has not.

HFpEF is currently understood as a heterogeneous syndrome originating from the interplay of cardiac (central) and extracardiac (peripheral) abnormalities. Until recently, randomized trials of a variety of potentially promising interventions have not been able to demonstrate a definitive benefit in HFpEF patients. Professor Youn considers this lack of demonstrative benefit in HFpEF trials may have been due to failed trial designs or ineffective study interventions. The stagnation of therapeutic progress in HFpEF has been explained by heterogeneity of HFpEF patients, thereby incomplete understanding of the various pathophysiology and inadequate diagnostic criteria, which resulted in development of an inappropriate therapeutic target.

Professor Youn will present the results of a recent HFpEF trial using empagliflozin, becoming the first drug to improve outcomes. The EMPEROR-preserved trial randomly assigned 5,988 patients with class II–IV HF and an EF of more than 40% to receive empagliflozin or placebo, in addition to usual guideline directed medical therapy. The primary outcome was a composite of cardiovascular death or hospitalization for HF. Over a median of 26.2 months, a primary outcome event occurred significantly less in the empagliflozin group (13.8%) than in the placebo group (17.1%) (**Figure 2**). This effect was mainly related to a lower risk of hospitalization for HF in the empagliflozin group. The effects of empagliflozin appeared consistent in patients with or without diabetes. The total number of hospitalization for HF was significantly lower in the empagliflozin group than in the placebo group. In conclusion, the EMPEROR-preserved trial demonstrated empagliflozin improving the clinical outcomes of HFpEF patients, making a critical paradigm shift in the pharmacological treatment of HFpEF.

Heart Failure 2
Essence of Recent HF Trials
›› Sunday, Oct 17, 14:30-16:00, Channel 2

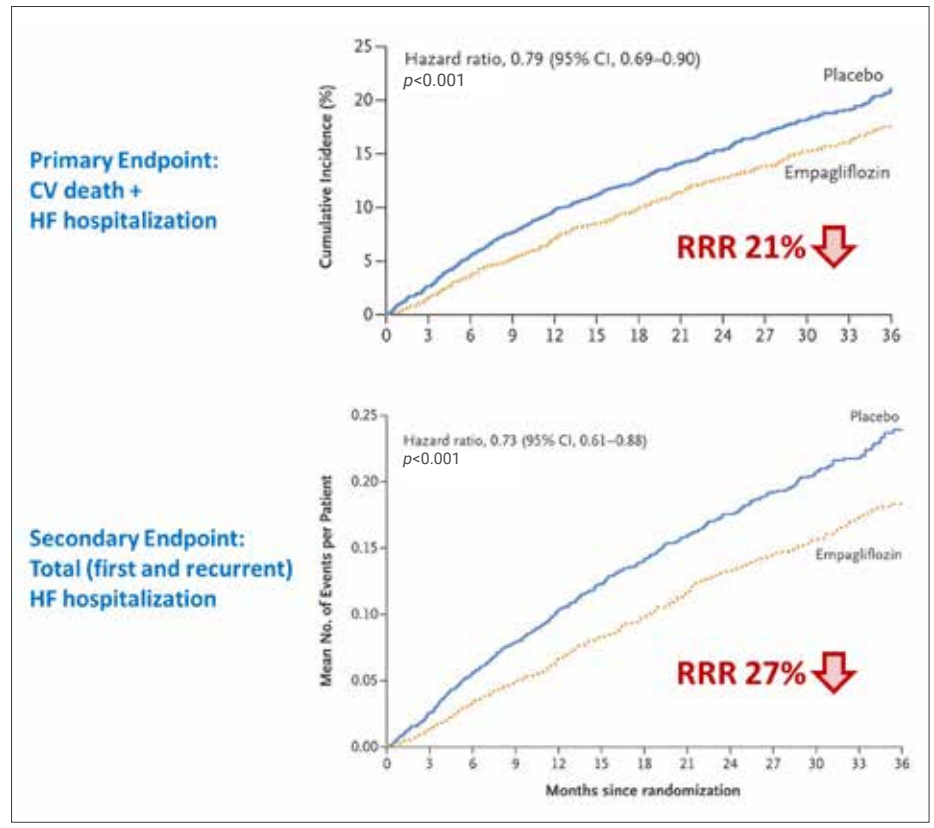

Figure 2. Key results of the EMPEROR-preserved trial (Adapted from Anker SD, et al. N Engl J Med 2021;385 (16):1451-61.)

Continued from page 1

New Frontiers in Cardiology 1

Public DBs and New Analytic Tools-Potentials for Future Research

Seunggeun Lee, PhD
Seoul National University, Korea

An important basis of precision health research is large-scale biobanks that combines multi-omics bio-data and extensive clinical data from electronic health records (EHR). The prime example is the UK-Biobank, which harbors whole-genome scale genotype data, whole-exome sequencing (WES) data, thousands of complex traits and exposures from hospital EHR, web surveys, medical image, biomarkers and metabolomics on ~500,000 individuals. Other examples include the All of Us biobank in the US, BioBank Japan, and the Korean Genome and Epidemiology Study (KoGES). These biobanks aim to capture vast information on health, and rich data will help advance prevention and treatment of complex diseases.

The first and most important step in the biobank data analysis is massive-scale genome- and phenome-wide association tests that identify genetic variants associated with the entire phenome. The analysis is typically done for all pairs of every single genetic variant and phenotype, resulting in billions of tests. The single variant test can be extended to gene- or pathway-based tests, especially for rare variants. Using the association test results, researchers can construct genome-based disease risk prediction model, called polygenic risk scores, find causal biomarkers and estimate drug effects using Mendelian randomization, and identify drug targets (**Figure 1**).

The size and complex structure of biobanks is a huge challenge for effective analysis of the data. For example, the numbers of genetic variants and phenotypes are more than 10 million and several thousands, respectively, which increase with the advancement of technology. Additionally, there are not enough methods and tools to analyze highly informative but complicated phenotypes, such as time-to-disease onset and patient diagnosis/treatment history, and rare variant associations in sequencing data.

Our group has developed multiple tools for genome-wide analysis on the phenome-wide scale. One example is Scalable and Accurate Implementation of GEneralized mixed model package (SAIGE), a scalable method to accurately test genetic associations of unbalanced case-control phenotypes with very low case count. We extended this approach to time-to-event phenotype analysis using disease-onset age and categorical phenotypes from survey data. Another example is SAIGE-GENE and SAIGE-GENE+ that can carry out gene-based rare variant association analysis.

Utilizing SAIGE, we analyzed the genome-wide association study (GWAS)-chip-based genome data and WES data of the UK-Biobank. The analysis results are hosted in a web-based browser, called PheWEB, which visualizes the analysis results and enables to query the results. PheWEB was originally built for the single variant test, and we have modified it to host gene-based test results as well.

Our analysis highlights some interesting findings. For example, from the WES analysis, we have found rare exonic variants in 19 and 23 genes associated with low-density lipoprotein (including APOB, PCSK9, and ANGPTL3) and high-density lipoprotein (including APOC3, ABCA1, and LCAT), and 2 genes (*TTL* and *ZDHHC13*) with atrial fibrillation. These results will help to identify the genetic basis of heart disease-related phenotypes as well as find new prevention and treatment schemes.

New Frontiers in Cardiology 1
Precision Medicine in Cardiovascular Disease
›› Sunday, Oct 17, 08:30-10:00, Channel 1

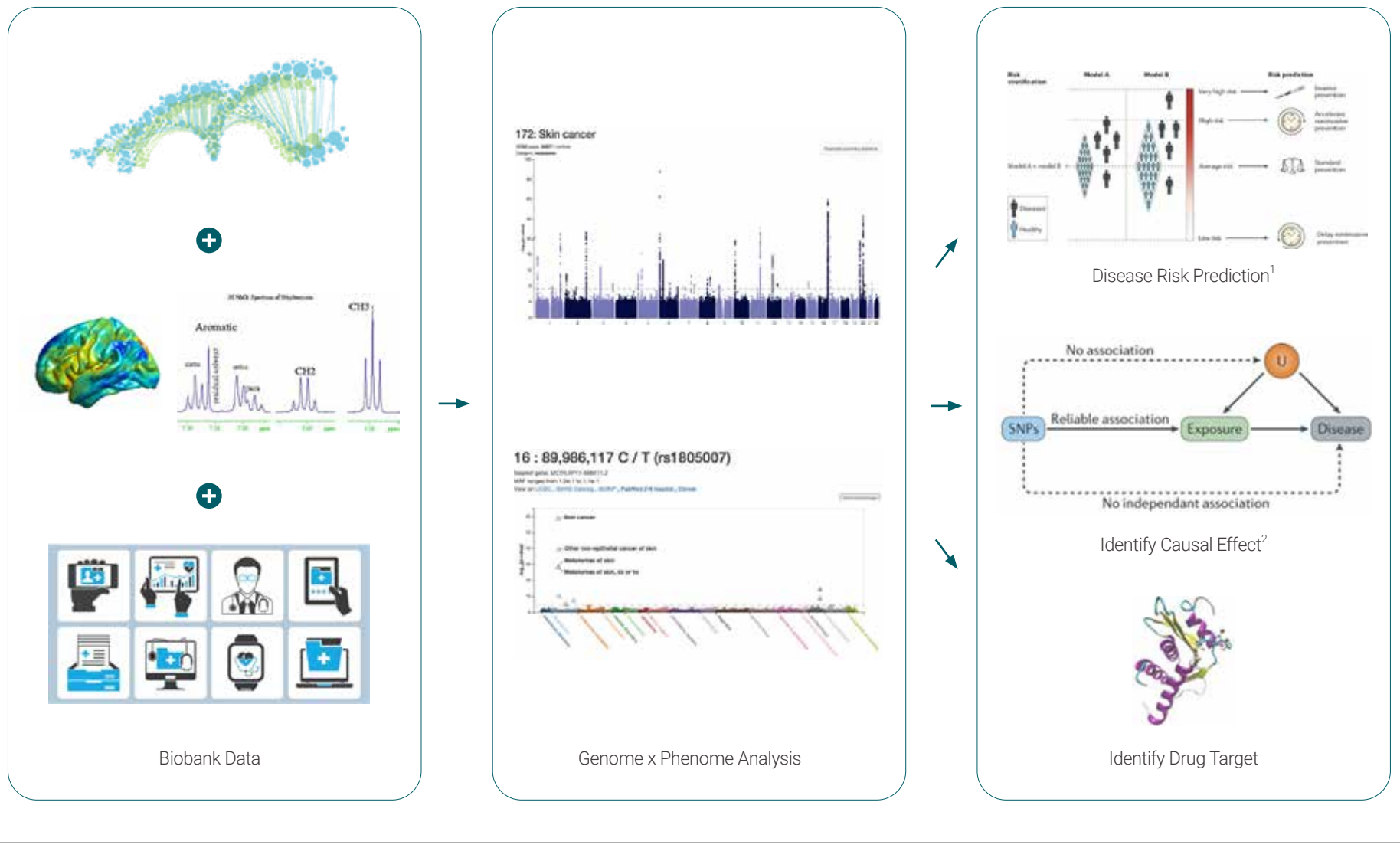

Figure 1. Biobank data and analysis framework (Adapted from 1. Torkamani A, et al. Nat Rev Genet 2018;19(9):581-90 and 2. Holmes MV, et al. Nat Rev Cardiol 2017;14(10):577-90.)

KSC 2021 DAILY

Echocardiography

Poisoning

Dong-Hyuk Cho, MD, PhD
Yonsei University Wonju College of Medicine, Korea

In Korea, approximately 10,000 patients are admitted to the emergency department annually for carbon monoxide (CO) poisoning. CO inhibits oxygen delivery and subsequently causes ischemic changes that can ultimately lead to multi-organ failure and death. Myocardial injury, defined as the elevation of cardiac enzyme levels or global myocardial dysfunction, has been commonly observed in patients with CO poisoning requiring hyperbaric oxygen therapy. Although most cardiac functions tend to normalize, it remains unclear why more cardiovascular events occur despite normalization of CO-induced elevated troponin I (TnI) and myocardial dysfunction.

We hypothesized that CO poisoning could result in myocardial fibrosis that can be detected by cardiac magnetic resonance (CMR) during the acute phase (i.e., days after poisoning) and the chronic phase (i.e., months after poisoning). We therefore evaluated residual myocardial fibrosis after acute CO poisoning using CMR (**Figure 1**). We also evaluated its association with short-term adverse outcomes and cardiac function by using transthoracic echocardiography.

The prevalence of late gadolinium enhancement (LGE) in patients with acute CO poisoning with elevated TnI levels was 69.2%; the pattern on LGE was primarily comprised of midwall patterns of injury. Of the 37 patients who underwent follow-up CMR, most chronic phase images showed no interval change. These findings suggest myocardial fibrosis in CO intoxication may affect long-term subsequent clinical events.

Advances in Cardiovascular Imaging to Inform Cancer Therapy Cardiotoxicity

Bonnie Ky, MD
University of Pennsylvania, USA

Cardio-oncology is a field in rapid evolution and growth. Both cancer and cardiovascular disease are substantial contributors to morbidity and mortality globally. Highly effective cancer therapies can result in significant adverse cardiovascular effects, including cardiomyopathy and heart failure.

Despite this tremendous public health burden, there are fundamental gaps in our understanding of the disease and in the application of evidence-based strategies for the clinical care of this growing population. A critical need for the field of cardio-oncology is to understand the

Continued on page 15

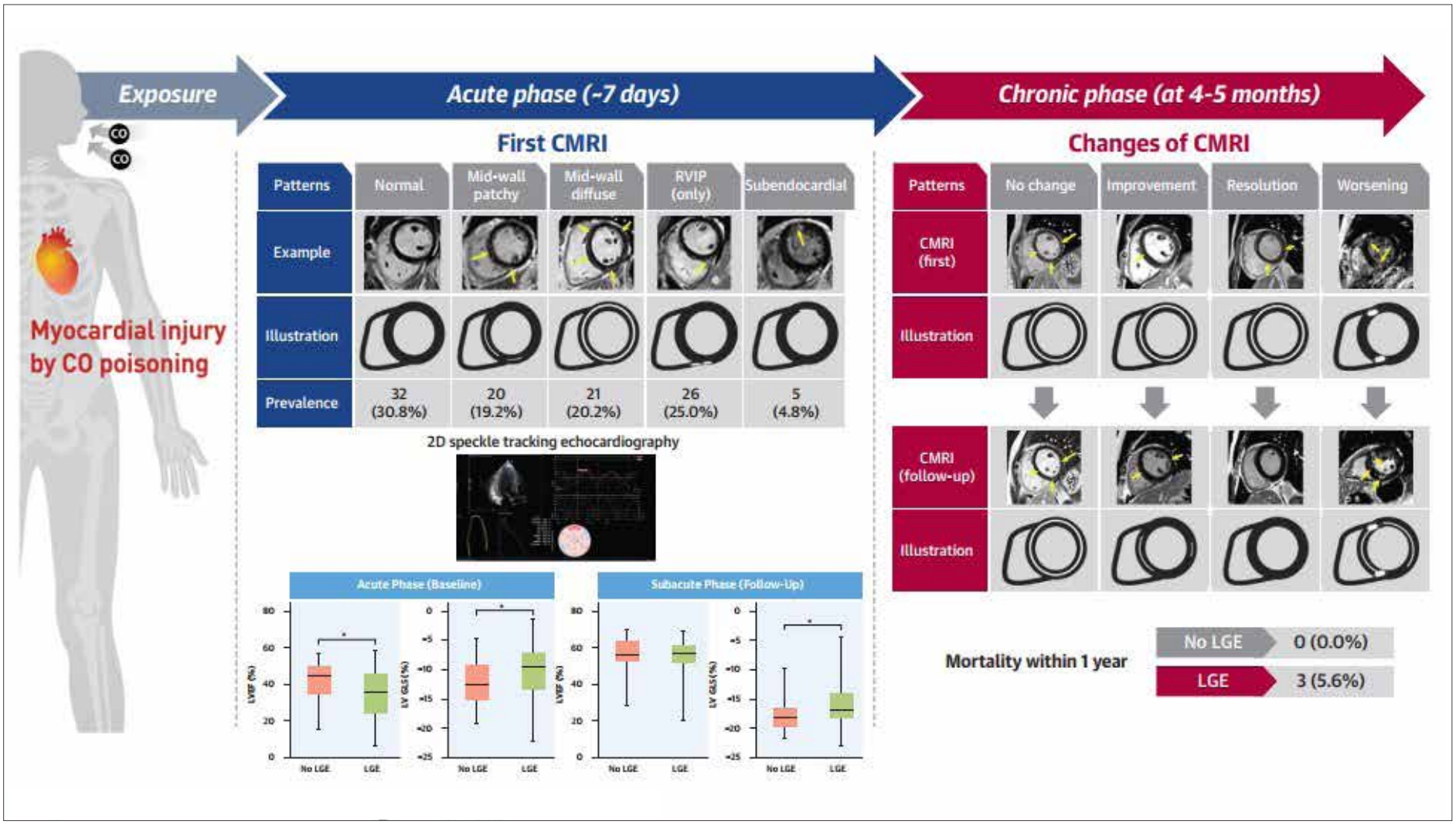

Figure 1. Myocardial injury detected by cardiac magnetic resonance imaging in carbon monoxide poisoning (Adapted from Cho DH, et al. J Am Coll Cardiol Img 2021;14(9):1758-70.)

ESC-KSC Joint Session: Arrhythmia

Can We Perform Atrial Fibrillation Ablation First Line?

Dipen Shah, MD
University Hospital of Geneva, Switzerland

Catheter ablation of atrial fibrillation (AF) has become increasingly popular and well-accepted since the earliest performance of the ablation of pulmonary vein (PV) foci in 1998.

PV isolation (PVI), initially performed at the ostium guided by circular mapping catheters, and more recently, by circumferential antral ablation has become the cornerstone of the strategy of catheter ablation of AF. A similar clinical and procedural efficacy has been shown with balloon cryo-ablation PVI as with radiofrequency ablation-based PVI.

Catheter ablation as a strategy of rhythm control has been shown to be superior to medical therapy in preventing atrial tachyarrhythmia recurrence, providing better quality of life and even in reducing hospitalization and mortality – the latter in selected populations of AF patients with systolic dysfunction.

In this respect, the EAST-AFNET 4 (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial 4) also showed better cardiovascular outcomes of an early rhythm control strategy compared to usual care, thus emphasizing the importance of maintaining sinus rhythm.

Typically, patients with an initial diagnosis of AF are treated with medical therapy, usually a combination of anticoagulation and rate control with or without rhythm control drugs. Catheter ablation is unanimously recommended for patients with resistant arrhythmias, symptoms or intolerant to drugs.

'First line' catheter ablation or initial therapy with catheter ablation is considered less well-established because of concerns about the invasive nature of the procedure, attendant complications and sustained efficacy.

Chen, et al. recently described a pooled analysis of first line catheter ablation for AF, summarizing the data from five randomized trials including 997 patients. Their mean age was 57.4 years old, 68.6% were male, and 98% had paroxysmal AF. Over a mean follow-up of 1.4 years, first line catheter ablation resulted in significantly higher freedom from arrhythmia, significantly greater improvement in quality of life scores with no differences in the incidence of serious adverse events compared to medical therapy with anti-arrhythmic drugs.

Thus, there is an increasing body of rigorous evidence that first line catheter ablation is more effective and as safe as anti-arrhythmic therapy in younger patients with paroxysmal AF. Improvements in ablation technology have shortened procedure times, and tailored ablation strategies of individualized substrate ablation are being actively evaluated to provide better outcomes in patients with non-paroxysmal AF as well.

ESC-KSC Joint Session: Arrhythmia
Clinical Updates in Treatment of Atrial Fibrillation
›› Sunday, Oct 17, 16:10-17:40, Channel 2

Continued from page 14

changes in cardiac structure and function that occur to identify patients at increased risk for the development of cardiotoxicity.

Our work has focused on understanding the changes in cardiac remodeling and function that occur with cancer therapies and how early changes predict risk of subsequent cardiotoxicity. Our ongoing research focuses on the use of two-dimensional and three-dimensional measures of cardiac mechanics such as strain and ventricular-arterial coupling, and diastolic function measures to understand the effects of cancer therapies. Our ultimate goal is to establish a robust paradigm of risk-guided cardioprotection. This lecture will also highlight ongoing advances in cardio-oncology across additional imaging modalities.

Echocardiography 3
Heart as the Victim
›› Sunday, Oct 17, 08:30-10:00, Channel 4

Leading Science, Saving Lives

2022년

춘계심혈관통합학술대회 & ACC Asia

2022 Annual Spring Scientific Conference of the KSC with Affiliated Cardiac Societies & ACC Asia 2022

대한심장학회 | 대한부정맥학회 | 대한소아심장학회 | 대한심부전학회 | 대한심혈관중재학회 | 심장대사증후군학회 | 한국심초음파학회 | 한국지질·동맥경화학회

4. 15 (Fri.) - **16** (Sat.)

HICO, Korea

LEADING SCIENCE, SAVING LIVES KSC 2022

대한심장학회 THE KOREAN SOCIETY OF CARDIOLOGY 심장학연구재단 THE KOREAN CARDIAC RESEARCH FOUNDATION

KSC

THE KOREAN SOCIETY OF CARDIOLOGY 2022

2022. 10. 14. Fri. - 16. Sun.

Grand Walkerhill Seoul, **Korea**