Clinical and translational science in cardiovascular research: highlights from the American Heart Association Scientific Sessions 2017

Changing view on the concept of cardiovascular risk and blood pressure targets

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The annual flagship meeting of the American Heart Association (AHA) (AHA Scientific Sessions 2017), held between 11–15 November 2017 in Anaheim, California, was attended by almost 18 000 professionals from more than 100 countries, featuring almost 5000 individual sessions, and 4000 original presentations. A wide selection of topics were presented, ranging from basic research to clinical and population science, with a particular focus on risk factor management and prevention. In his Presidential Address and a speech inspired by personal and family experiences, Dr John J. Warner, highlighted the impact of cardiovascular disease on families around the world and his commitment to fight heart disease through his professional- and community-based work. Other outstanding lectures included the Paul Dudley White International Lecture by Sir Rory Collins, who stressed out the importance of evidence-based medicine and ‘hard facts’ in an era of disinformation, the Lasker lecture by Dr Bruce M. Alberts, who underlined the need to expand the National Institute of Health (NIH) New Innovator Award program to support innovative research by younger scientists, as well as the AHA Distinguished Scientist Lecture by Dr Marlene Rabinovitch on the pathophysiological mechanisms and genetic determinants of pulmonary arterial hypertension.

The main topic that dominated the discussion in the conference as well as in the US and international news media was the announcement of the new 2017 Guidelines for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults, a joint report issued by the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.1 Readings higher than 130/80 mmHg now qualify for a diagnosis of Stage 1 Hypertension (previously defined as pre-hypertension), raising the percentage of the US adult population with high blood pressure levels from 32% to an estimated 46%. However, the guidelines emphasize the importance of lifestyle interventions and risk factor control, reserving pharmacologic treatment only for patients with readings ≥130/80 mmHg with a calculated 10-year atherosclerotic cardiovascular disease (ASCVD) risk ≥10% or with known cardiovascular or chronic kidney disease and/or diabetes mellitus. These guidelines emphasize the need to improve blood pressure control in the general population and identify new ways to prevent the deleterious effects of hypertension on the cardiovascular system such as vascular complications and left ventricular hypertrophy, a topic that has been extensively discussed in the recent issues of Cardiovascular Research.2,3

A wide number of very interesting Late Breaking Clinical Trials attracted the attention of the attendees and scientific community. In the field of cardiometabolism, Gastric Bypass Surgery to Treat Patients with Study Hypertension (GATEWAY) showed that gastric bypass surgery can reduce or eliminate the need for anti-hypertensive medications in obese, hypertensive patients, following up on previously published findings on the beneficial effects of bariatric surgery on diabetes and the close association between obesity and hypertension.4

A secondary analysis of the recently published Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS trial) which originally

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demonstrated the efficacy of targeting inflammation through an anti-interleukin-1β (IL-1β) agent in reducing adverse cardiovascular events in patients with prior myocardial infarction (MI), 7 showed that a reduction of high-sensitivity C-reactive protein levels to <2 mg/dL could reliably predict the efficacy of canakinumab in reducing both cardiovascular events and lung cancer mortality and incidence. 6 This observation underlines the importance of inflammatory pathways in cardiovascular and cancer pathogenesis 8,9 and suggests that longitudinal follow-up of inflammatory biomarkers may provide early hints on the efficacy of anti-inflammatory interventions in atherosclerosis.

Two subanalyses of recent trials have shed more light on the beneficial effects of sodium glucose co-transporter-2 (SGLT-2) inhibition on diabetes and cardiac function. 9,10 A secondary analysis from the previously published Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients—Removing Excess Glucose (EMPA-REG) trial revealed the efficacy of empagliflozin (an SGLT-2 inhibitor) in reducing mortality, hospitalization for heart failure, and renal failure particularly in the vulnerable group of patients with type 2 diabetes mellitus and peripheral arterial disease. 11 Similarly, post hoc analysis of the Canagliflozin Cardiovascular Outcomes Assessment Study (CANVAS) trial data has revealed a consistent benefit for canagliflozin in diabetic patients with and without prior cardiovascular events. 12

In a detailed analysis of the Randomized Evaluation of the Effects of Anacetrapib through Lipid Modification (REVEAL) study, anacetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, reduced adverse coronary events independently of the presence of diabetes mellitus and was further linked to a decrease in the incidence of new-onset diabetes mellitus, among high-risk patients on statin treatment. 13

Moreover, new findings have been presented on Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) inhibitors, a class of drugs that has revolutionized anihyperlipidaemic management. 14–16 New data from the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) trial show that evolocumab (a PCSK9 inhibitor) is further associated with a reduction in recurrent cardiovascular events in addition to first major events. 17 Post hoc analysis of the EXenatide Study of Cardiovascular Event Lowering (EXSCEL) trial which explored the cardiovascular efficacy of an extended-release formulation of exenatide, a glucagon-like peptide-1 (GLP-1) receptor agonist, revealed that the beneficial effects of exenatide were consistent across different baseline risk groups, suggesting a protective role independent of the baseline cardiovascular risk. 18 Nevertheless, traditional subgroup analysis may fail to detect Heterogenous Treatment Effects, as discussed in a recent commentary written by Dr Tomasz J. Guzik, published in Cardiovascular Research. In his commentary, Prof. Guzik highlighted the importance of ensuring that pathophysiological and pharmacological heterogeneity is taken into account in the design of such trials and the key role of Basic Science research in identifying these sources of heterogeneity. 19

Finally, Randomized Evaluation of Aggressive or Moderate Lipid-Lowering Therapy With Pitavastatin in Coronary Artery Disease (REAL-CAD) confirmed the superiority of high- vs. low-intensity statin (pitavastatin) treatment in a Japanese population of stable coronary artery disease. 20

Taken together, these findings highlight the significant cardiovascular benefit associated with targeting a range of pathways involved in metabolic disease, 21 including dyslipidemia, 22 and diabetes mellitus. 23

In the field of antiacogulation, the Efficacy of Different Antiplaque Therapy Strategy after Coronary Artery Bypass Grafting (DACAB) study demonstrated the superiority of dual antiplaque therapy (DAPT) with aspirin plus ticagrelor vs. single treatment with aspirin or ticagrelor alone in maintaining 1-year saphenous vein graft patency rates in patients undergoing coronary artery bypass grafting surgery (CABG). 24 Three other landmark trials challenged common clinical practices in cardiovascular intervention. The Prevention of Serious Adverse Event Following Angiography trial (PRESERVE trial) showed no benefit for the use of intravenous sodium bicarbonate or oral acetylcysteine for the prevention of adverse events in patients at high-risk of renal complications referred for coronary angiography. 25 In the Transfusion Requirements in Cardiac Surgery (TRICS) III study, a restrictive strategy for red-cell transfusion using a haemoglobin cut-off of 9.5 vs. 7.5 g/L was non-inferior with respect to adverse cardiovascular and renal events in patients undergoing cardiac surgery at moderate-to-high risk for death. 26 Furthermore, the BRUISE CONTROL-2 study showed no significant difference in the incidence of device pocket haematoma for interrupted vs. non-interrupted anticoagulation with direct oral anticoagulants in patients undergoing pacemaker or defibrillator implantation. 27

In the field of Basic Science research, late-breaking abstracts covered new mechanisms that regulate cardiac fibrosis, highlighting novel roles for proteins such as prolyl-transfer ribonucleic acid (tRNA) synthetase, 28 and the cytosolic isoform of RBFox1 in regulation of cardiac fibrosis. 29 Other abstracts focused on pathways mediating inflammatory responses, cardiomyocyte death, hypertrophy, metabolism and cardiac bioenergetics, topics that have been extensively addressed in recent issues of Cardiovascular Research. 30–32

Novel technologies were also presented, such as a method using sphero-toids consisting of induced pacemaker cells to reverse-engineer the function of the sinoatrial node. 33 Machine learning and big data were also discussed in several sessions, ranging from machine learning-based analysis of arterial pulses waves using a wearable biosensor to detect obstructive cardiomyopathy, 34 to big data analysis in the era of omics and precision medicine. The vast opportunities that arise from these new approaches in the diagnosis and treatment of heart disease were highlighted in a recent Position Paper of the European Society of Cardiology Working Group on Cellular Biology of the Heart published in Cardiovascular Research. 35

In summary, the AHA 2017 Scientific Sessions were marked by several exciting new studies covering a wide range of topics in basic, translational, clinical, and population research in cardiovascular science and medicine. We look forward to the translation and integration of these findings into clinical practice, with the ultimate goal to improve prevention, management, and treatment of heart disease.

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References

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