FRAME OF REFERENCE

Perspective
The Ethics of Conducting Clinical Trials With Sodium-Glucose Cotransporter-2 Inhibitors in Heart Failure: Is Placebo Assignment Justified in Patients With Comorbid Diabetes Mellitus and Heart Failure?
Javed Butler, MD, MPH, MBA; Stefan D. Anker, MD, PhD

ORIGINAL RESEARCH ARTICLES

Efficacy and Safety of a Pharmaco-Invasive Strategy With Half-Dose Alteplase Versus Primary Angioplasty in ST-Segment–Elevation Myocardial Infarction: EARLY-MYO Trial (Early Routine Catheterization After Alteplase Fibrinolysis Versus Primary PCI in Acute ST-Segment–Elevation Myocardial Infarction)
Jun Fu, MD; Song Ding, MD; Heng Ge, MD; Yaling Han, MD; Jinchen Guo, MD; Rong Lin, MD; Xi Su, MD; Heng Zhang, MD; Lianglong Chen, MD; Ben He, MD; EARLY-MYO Investigators

Editorial
Recalibrating Reperfusion Waypoints
Paul W. Armstrong, MD; Robert C. Welsh, MD

Experimental Modeling Supports a Role for MyBP-HL as a Novel Myofilament Component in Arrhythmia and Dilated Cardiomyopathy
David Y. Barefield, PhD; Megan J. Puckelwartz, PhD; Ellis Y. Kim, BS; Lisa D. Wilsbacher, MD, PhD; Andy H. Vo, BS; Emily A. Waters, PhD; Judy U. Earley, BS; Michele Hadhazy, BS; Lisa Delletave-Castillo, MS; Lorenzo L. Pesce, PhD; Elizabeth M. McNally, MD, PhD

Editorial
Closing the Genotype-Phenotype Loop for Precision Medicine
Calum A. MacRae, MB, ChB, PhD; Christine E. Seidman, MD

Direct Comparison of Cardiac Myosin-Binding Protein C With Cardiac Troponins for the Early Diagnosis of Acute Myocardial Infarction
Thomas E. Kaier, MD, MBA; Raphael Twerenbold, MD; Christian Puelacher, MD; Jack Marjot, MBBS, BSc; Nazia Imamabaccus; Jasper Boedinghaus, MD; Thomas Nestelberger, MD; Patrick Badertscher, MD; Zaid Sattib, MD; Maria Rubini Giménez, MD; Karin Wildi, MD; Petra Hillinger, MD; Karin Grimm, MD; Sarah Loefelt; Samyut Shrestha, MD; Dayana Flores Wildner, MD; Janosch Cupa, MD; Nikola Kozhubarov, MD, Oscar Miró, MD, F. Javier Martin-Sánchez, MD; Beata Morawiec, MD; Katharina Rentsch, PhD; Jens Lohrmann, MD; Wanda Kloor, MD; Stefan Osswald, MD; Tobias Reichlin, MD; Ekkehard Weber, Ph.D; Michael Marber, MD, PhD; Christian Mueller, MD

In Vivo Functional Selection Identifies Cardiotrophin-1 as a Cardiac Engraftment Factor for Mesenchymal Stromal Cells
Francesca Bordolotti, PhD; Giulia Ruizi, PhD; Antonella Falcione, PhD; Sara Daina, MD; Matteo Dal Ferro, MD; Pierluigi Lesizza, MD; Lorenza Zentilin, PhD; Lawrence Banks, PhD; Serena Zacchigna, MD, PhD; Mauro Giacca, MD, PhD

On the Cover: Circulation Doodle
This month’s doodle was submitted by Caitlin E. Kiehl, reader of the journal from Cleveland, Ohio. Caitlin’s husband, Erich, is an electrophysiology fellow at Cleveland Clinic. It is in honor of the United Nations. UN Day is celebrated on October 24.
For more information about the doodle, go to http://circ.ahajournals.org/content/circulation-cover-doodle.
ORIGINAL RESEARCH ARTICLES

Editorial
FunSel: Mesenchymal Stromal Cells Stay for the Party
James E. Hudson, PhD; Enzo R. Porrello, PhD

Epigenome-Wide Association Study Identifies Cardiac Gene Patterning and a Novel Class of Biomarkers for Heart Failure
Benjamin Meder, MD; Jan Haas, PhD; Farbod Sedaghat-Hamedani, MD; Elham Kayvanpour, MD; Karen Frese, PhD; Alan Lai, PhD; Rouven Nietsch, MSc; Christina Scheiner, MSc; Stefan Mester, MSc; Diana Martins Bordalo, MSc; Ali Amr, MD; Carsten Dietrich, PhD; Dietmar Pils, PhD; Dominik Siede, MSc; Hauke Hund, MSc; Andrea Bauer, PhD; Daniel Benjamin Holzer, MD; Arjang Ruhparwar, MD; Matthias Mueller-Hennesen, MD; Dieter Weichenhan, PhD; Christoph Plass, PhD; Tanja Weis, PhD; Johannes Backs, MD; Maximilian Wuerstle, PhD; Andreas Keller, PhD; Hugo A. Katus, MD; Andreas E. Posch, PhD

Editorial
DNA Methylation and Human Heart Failure: Mechanisms or Prognostics
Christoph D. Rau, PhD; Thomas M. Vondriska, PhD

STATE OF THE ART

In Depth
Activation and Inhibition of Sodium-Hydrogen Exchanger Is a Mechanism That Links the Pathophysiology and Treatment of Diabetes Mellitus With That of Heart Failure
Milton Packer, MD

CORRESPONDENCE

Research Letter
Increases in Natriuretic Peptides Precede Heart Failure Hospitalization in Patients With a Recent Coronary Event and Type 2 Diabetes Mellitus
Emil Wolsk, MD, PhD; Brian Claggett, PhD; Rafael Diaz, MD; Kenneth Dickstein, MD, PhD; Hertzel C. Gerstein, MD; Lars Kober, MD; Francesca C. Lawson, MD; Eldrin F. Lewis, MD, MPH; Aldo P. Maggioni, MD; John J. V. McMurray, MD, PhD; Jeffrey L. Probstfield, MD; Matthew C. Riddle, MD; Scott D. Solomon, MD, Jean-Claude Tardif, MD; Marc A. Pfeffer, MD, PhD

Correspondence
Letter by Musso et al Regarding Article, “Cardiac Outcomes After Ischemic Stroke or Transient Ischemic Attack: Effects of Pioglitazone in Patients With Insulin Resistance Without Diabetes Mellitus”
Giovanni Musso, MD; Maurizio Cassader, PhD; Roberto Gambino, PhD

Letter by Jin-Shan and Xue-Bin Regarding Article, “Cardiac Outcomes After Ischemic Stroke or Transient Ischemic Attack: Effects of Pioglitazone in Patients With Insulin Resistance Without Diabetes Mellitus”
He Jin-Shan, MD; Li Xue-Bin, MD

Response by Young et al to Letters Regarding Article, “Cardiac Outcomes After Ischemic Stroke or Transient Ischemic Attack: Effects of Pioglitazone in Patients With Insulin Resistance Without Diabetes Mellitus”
Lawrence H. Young, MD; Catherine M. Viscoli, PhD; Silvio E. Inzucchi, MD; Walter N. Kernan, MD
**CLINICAL STATEMENTS AND GUIDELINES**

**AHA Scientific Statement**

Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association

Sean van Diepen, MD, MSc, FAHA, Chair; Jason N. Katz, MD, MHS, Vice Chair; Nancy M. Albert, RN, PhD, FAHA; Timothy D. Henry, MD, FAHA; Alice K. Jacobs, MD, FAHA; Navin K. Kapur, MD; Ahmet Kilic, MD; Venu Menon, MD, FAHA; E. Magnus Ohman, MD; Nancy K. Sweitzer, MD, PhD, FAHA; Holger Thiele, MD; Jeffrey B. Washam, PharmD, FAHA; Mauricio G. Cohen, MD; On behalf of the American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline

**CORRECTIONS**

Correction to 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society
