Cardiology in 2011—Amazing Opportunities, Huge Challenges

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THE HEART HAS ALWAYS HELD A SPECIAL FASCINATION for humans: it has been the seat of the soul; the home of emotions; and the pump that when beating, symbolizes life, and when silent, signifies death. Perhaps no other organ in the body has been so closely scrutinized. Therefore it is appropriate that as scientists and clinicians from around the globe gather at the 2011 American Heart Association (AHA) Scientific Sessions, we devote this theme issue of *JAMA* to cardiovascular disease (CVD). It is our hope that readers will clearly see that cardiovascular medicine remains a vital and rapidly changing discipline, filled with innovation yet also confronting significant challenges.

Only 50 years ago, atherosclerosis was thought to be inevitable, a natural consequence of the aging process. However, carefully performed epidemiologic studies from the Framingham Heart Study and others identified the major CVD risk factors including hypertension, elevated cholesterol levels, smoking, and diabetes. These seminal works changed the view of CVD from a preordained fate to a preventable disorder.

Much has been learned since that time regarding the etiology of CVD, yet multiple mysteries persist. For example, although the onset of CVD is directly related to the burden of CVD risk factors, Canto and colleagues,[1] in their report in this issue of *JAMA*, found, paradoxically, that in-hospital mortality following an initial myocardial infarction (MI) was inversely associated with the number of baseline risk factors. This interesting finding either could represent residual confounding or may indicate that patients without traditional risk factors who have an acute coronary event may harbor novel but as-yet uncharacterized and deadly CVD risk factors.

Another "known but unknown" in CVD risk centers on blood pressure. Although it is known that high blood pressure can lead to CVD and stroke, the optimal therapeutic target for blood pressure control remains unclear. In their study of patients following a stroke, Ovbiagele and colleagues[2] found a U-shaped association between longitudinal blood pressure levels and risk for recurrent events. The higher risk at lower levels of blood pressure could be the result of residual confounding, but these observational data raise the possibility that there may be harm if blood pressure management is too aggressive or too lenient.

Cholesterol management is another important and modifiable risk factor. Scientists have unraveled the complexities of cholesterol metabolism and identified several therapeutic targets for manipulation. Statins effectively lower low-density lipoprotein (LDL) cholesterol levels and subsequently reduce CVD events when used in select primary and secondary populations. In this issue of *JAMA*, Nicholls and colleagues[3] report on the first large experience with evacetrapib, a novel, potent, and selective inhibitor of cholesteryl ester transfer protein (CETP). In their clinical trial, the authors found that this new drug, when added to a statin regimen, further favorably improved lipid profiles by not only decreasing LDL levels but also by substantially increasing high-density lipoprotein (HDL) cholesterol levels. Although these findings are promising, subsequent larger outcome trials will be needed to confirm that these modifications in lipid profile translate into lower long-term CVD risk.

The past few decades have seen the emergence of a number of acute and chronic interventions that prevent events, improve the quality of life, and save lives for patients with CVD. The tradition of exploration of novel concepts in CVD therapy continues in the research on the potential for pleuripotent stem cells to repair and replace damaged myocardium. To date, animal models have demonstrated that stem cell infusions following experimental infarction can restore ventricular function, yet the role of this intervention in humans remains controversial. In this issue, Traverse and colleagues[4] report the primary findings of the LateTIME trial, the first of a series of human clinical stem cell trials sponsored by the National Heart, Lung, and Blood Institute (NHLBI). Their clinical trial was designed to specifically address the optimal timing of stem cell

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therapy, particularly whether the infusion of intracoronary bone marrow stem cells 2 to 3 weeks after acute MI can affect downstream ventricular function.

Although scientific discoveries offer much promise, translations of such innovations to routine clinical practice can present challenges and require careful evaluation. Novel blood biomarker and cardiac imaging modalities are being developed at an amazing pace, yet clinicians in practice often struggle to understand their appropriate application. Prasad and Bonow[5] provide a thoughtful Commentary on cardiac biomarkers, arguing that the major metric for the success of a biomarker should predict hard clinical outcomes and ultimately should affect subsequent treatment selection. In a contemporary example of this principle, Shreibati and colleagues[6] describe the adoption of a new cardiac imaging modality, coronary computed tomography angiography (CCTA), into clinical practice. Using Medicare administrative data, the authors found that patients undergoing CCTA were more likely to undergo subsequent confirmatory testing, cardiac catheterization, and coronary revascularization relative to those receiving traditional stress testing. Yet despite this increased utilization, short-term outcomes were similar. Even though these data cannot delineate an ideal diagnostic testing pattern, the findings support the need for future evaluation.

Three other Commentaries in this issue highlight the need for unified and synchronized efforts to address the challenges of CVD. Mack, current president of the Society of Thoracic Surgeons, and Holmes, current president of the American College of Cardiology, provide an uplifting Commentary on how the major cardiothoracic surgery and cardiology societies are collaborating to promote the responsible adoption of a transcutaneous aortic valve replacement (TAVR).[7] Although TAVR can save lives when performed by experienced operators and in specific patients, translation of these innovations to community practice will require the training of clinicians, appropriate patient case selection, close monitoring and feedback of procedural outcomes, and a better understanding of the long-term benefits, risks, and costs of the procedure. This appropriate adoption of a new technology can be stimulated by clear practice recommendations, educational and training programs, and a national registry to track performance.

In another Commentary, Lauer, director of the Division of Cardiovascular Sciences at the NHLBI, describes how federal funding of CVD basic, translational, outcome, and population science has and continues to be vital for the health and overall strength of the United States.[8] Similarly, the Commentary by Tomaselli, current president of the AHA, emphasizes that even with reductions in CVD deaths in the United States, there is an increasing global threat from CVD.[9] Despite this, he identifies several examples whereby collaborations among multiple entities, such as the Million Hearts Campaign, are working to improve CVD treatment, increase CVD prevention efforts, and ultimately save millions of lives.

JAMA will continue to strive to be an important contributor in the fight against CVD. The journal has a long tradition of publishing leading studies on CVD treatment and prevention. Moving forward, we reaffirm this open call for the very best CVD science, including major clinical trials and innovative observational and implementation studies. We hope that the publication of such studies will continue to foster the special fascination medicine has with the heart, encourage new insights needed to address contemporary CVD challenges, and meet the huge challenge of continuing to reduce the burden of CVD in the next generation.

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