

Global Perspectives on Cardiovascular Health

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Despite advances in cardiovascular (CV) research, global disparities concerning life expectancy, health care resource allocation, and clinical implementation remain. In 2005, the global rate of death from CV causes was 3.3 times greater than AIDS, tuberculosis, and malaria combined. Additionally, four-fifths of all CV events occur in developing countries [Sanz G & Fuster V. *Nature Clin Practice Cardiovasc Med* 2009]. Due to the magnitude of the problem, biomedical research in developing countries is essential.

Magdi Yacoub, FRS, Imperial College and Founder Patron of Chain of Hope, London, UK, discussed the Chain of Hope program, which has taken measures to promote research and health care in Africa and other regions in need. The objective is to develop local expertise and educate local providers while building a global network and generating region-specific solutions to health care issues, noted Prof. Yacoub. In early 2009, the first Heart Research Center was opened in Addis Ababa, Ethiopia. This new state-of-the-art facility will allow for advanced research in local “neglected” diseases at epidemiological, cellular, and molecular levels and will include continentwide databases, translational research studies, educational programs, and international collaborative efforts. These components are the key to sustainable solutions for global health care, added Prof. Yacoub. Similar projects are also underway in Kenya and Mozambique.

Valentin Fuster, MD, PhD, FACC, Mt. Sinai Medical Center, New York, NY, discussed the global challenges of cardiovascular disease (CVD) and what the future may hold. Conventional CVD risk factors, such as abnormal lipids, smoking, hypertension, diabetes, and abdominal obesity, will contribute to more than 90% of serious CV events (including coronary death, myocardial infarction, and stroke) worldwide in the next decade [Yusuf S et al. *Lancet* 2004; Vasan RS et al. *Ann Intern Med* 2005; Pencina MJ et al. *Circulation* 2009]. Therefore, risk factors, early detection, and prevention must remain a focus moving forward.

Bioimaging is a critical component of early CVD detection. Dr. Fuster and colleagues (in collaboration with the Humana Health Plan) have launched a bioimaging study in the United States that consists of 7300 participants, 6000 of whom will be characterized with respect to their Framingham risk score and imaging features, including coronary calcification, carotid intima-media thickness, the presence of atherosclerotic plaques, and lower extremity arterial insufficiency, as determined by ankle brachial index. The remaining 1300 participants will be excluded from the imaging arm of the study.

The purpose of this study is to identify imaging and/or circulating biomarkers that predict 3-year CV events, improve upon traditional risk assessment, and determine the predictive value of biological and/or imaging markers for 1- to 3-year outcomes. Enrollment began in January 2008, and the study will continue through July 2012. Results from this study could impact CVD detection and prevention approaches worldwide.

Pharmacological therapy is another strategy for prevention that may help with the mounting global CVD crisis in the coming years. However, 50% of patients do not take the prescribed medication [Sanz G & Fuster V. *Nat Clin Pract Cardiovasc Med* 2009]. Dr. Fuster



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pointed out that several factors may impede adherence, including complexity of treatment, limited availability of medications, the financial burden of treatment, and inadequate prescription of medication. Therefore, a fixed-dose combination therapy (“polypill”) approach may be a better solution for low-income countries.

The ongoing Centro Nacional de Investigaciones Cardiovasculares fixed-dose combination (CNIC-FDC) therapy project focuses on patients who have suffered an acute myocardial infarction (AMI) and will introduce a polypill that consists of aspirin, a statin, and an angiotensin-converting enzyme inhibitor along with behavioral modification strategies as part of a worldwide prevention program. Another CNIC program, the FOCUS study, will test the efficacy of the polypill post-AMI and assess the magnitude of inadequate prevention and factors that contribute to poor adherence in different socioeconomic environments.

The first phase (n=4000) of the FOCUS study will evaluate economic and health care characteristics, such as the accessibility of care and treatment, out-of-pocket expenditure, food prices, and affordability of treatment. Adherence evaluations, clinical variables, demographics, and patient psychosocial factors will also be assessed during this phase of the study. The second phase (n=1340) of the study will evaluate the efficacy of the three drugs taken separately compared with the polypill. Participants will be seen at 1 month, 4 months, and 6 to 9 months for evaluation of clinical status, adverse effects, adherence and pill counting, lipid profile, and blood pressure.

Results from The Indian Polycap Study (TIPS) indicated that tolerability of the fixed-dose combination pill was similar to that of individual treatments, with no evidence of increased intolerance that resulted from the consolidation of the medications into one pill. The polypill may reduce multiple risk factors and CV risk while offering a convenient adherence solution [TIPS. *Lancet* 2009]. Based on these data and preliminary findings from CNIC-FDC and FOCUS, Dr. Fuster noted that a polypill might improve secondary prevention worldwide due to its affordability and reduction in treatment complexity.

The polypill has the potential to impact CVD on a global scale, particularly in developing countries, where resources are scarce and adherence is more problematic. Further outreach initiatives and biomedical research programs are needed in order to manage the growing CVD challenges. Identifying biomarkers and sustainable treatment solutions are the first steps in decreasing the global prevalence of CVD and mortality.

Integrating Imaging

The integration of imaging modalities may provide a broader picture of disease anatomy, burden, and molecular activity. Edward T. Martin, MD, Oklahoma Heart Institute, Tulsa, OK, discussed the utility of magnetic resonance (MR) and computed tomography (CT) imaging in the setting of electrophysiology.

One of the main factors in deciding whether a patient is a candidate for an implantable cardioverter defibrillator is whether the left ventricular ejection fraction is below 35%. Accurate ejection fraction assessment can be difficult for a 2-D technique, like echocardiography, especially in patients with prior myocardial infarction. A 3-D imaging modality, such as MRI, offers a more accurate method to quantify left ventricular function, which can save lives as well as money.

Using either MR or CT imaging prior to radiofrequency ablation for atrial fibrillation allows the clinician to evaluate the anatomy and assess for the presence of a common ostium and the number, position, and location of pulmonary veins, reducing the risk of complications. Additionally, these CT or MR images may be incorporated into the fluoroscopic images for a highly detailed intraprocedure evaluation, which may also reduce radiation exposure and fluoroscopic time. In a study by Ector and colleagues, CT images of the pulmonary veins, merged with fluoroscopic images, resulted in detailed anatomical and electrical activation maps [Ector J et al. *Circulation* 2005; Ector J et al. *Circulation* 2007]. Delayed enhancement MRI of the left atrium prior to a radiofrequency ablation procedure for atrial fibrillation can predict postprocedure atrial fibrillation recurrence, noted Dr. Martin [Oakes RS et al. *Circulation* 2009].

Zahi Fayad, PhD, FAHA, FACC, Translational and Molecular Imaging Institute, Mt. Sinai School of Medicine, New York, NY, discussed the benefit of multimodality imaging, particularly with regard to MRI and fluorodeoxyglucose positron emission tomography (FDG-PET). The benefit of this combination imaging technique is that it is highly reproducible and noninvasive and provides quantitative data about vessel morphology, metabolic activity and glycolysis, tissue composition, and inflammation. The level of radiation that is used with CT is decreasing, but the exposure can be further reduced with combination MRI/PET imaging, Dr. Fayad noted. However, the protocol for this combination is more complex and may require more experience and/or close attention to the guidelines for this technique.