

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 intolerability 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].

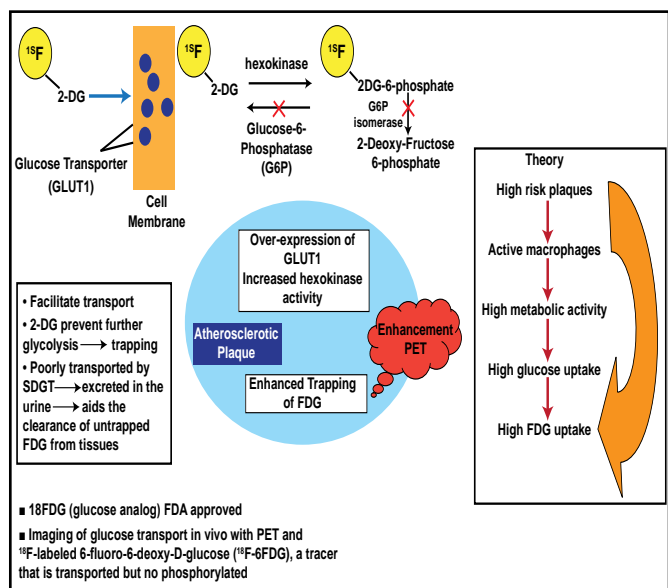
Zahi Fayad, PhD, FAHA, FACC, Translational and Molecular Imaging Institute, Mt. Sinai School of Medicine, New York, NY, discussed the benefit of multimodality imaging, particularly with regard to MRI and fluorodeoxyglucose positron emission tomography (FDG-PET). The benefit of this combination imaging 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.

Studies have shown that FDG-PET is a useful tool for detecting molecular markers of inflammation and plaque vulnerability, which may have implications for stroke prevention and carotid atherosclerotic intervention assessment (Figure 1) [Tawakol A et al. *J Am Coll Cardiol* 2006; Graebe M et al. *Eur J Vasc Endovasc Surg* 2009]. Strong correlations have been found with FDG-PET uptake in carotid plaques and gene expression of the macrophage-specific marker CD68 (p=0.02). Weaker correlations have been found with cathepsin K, matrix metalloproteinase 9, and interleukin 18 gene expression.

The use of statins in atherosclerosis is not uncommon. In addition to the FDG-PET gene expression correlation, this technique, coupled with MRI, may be useful in monitoring anti-inflammatory effects of statins over time [Fayad ZA et al. *J Am Coll Cardiol* 2005; Tahara N et al. *J Am Coll Cardiol* 2006]. Using MRI and FDG-PET as evaluation tools, Dr. Fayad is currently assessing the efficacy of a drug on atherosclerotic plaque in an ongoing multicenter Phase II trial, the results of which are still pending.

In December 2009, the merging of imaging techniques was realized. The first whole-body multimodality scanner was introduced at the Mt. Sinai Medical School of Medicine. This technology allows CT, PET, and MRI to occur in the same setting. Although the cost of such technology may be an issue at the moment, Dr. Fayad explained that the benefit is significant, and as with many new technologies, the cost often decreases over time, especially once it enters mainstream clinical medicine.

Figure 1. PET/CT Detection of Plaque.



The Future of Intervention: Where Are We Now and Where Are We Going?

Interventional strategies have evolved over the past decade, and determining an optimal approach depends on many factors. Samin Sharma, MD, FACC, Mt. Sinai Medical Center, New York, NY, discussed the latest developments in cardiac intervention.

Left ventricular assist device (LVAD) support may be indicated for high-risk percutaneous coronary intervention (PCI) cases in the presence of severe left ventricular (LV) dysfunction (ejection fraction [EF] <30%), complex lesions in which transient closure may be catastrophic, large myocardial infarction (MI) with hemodynamic instability, or cardiogenic shock. The ongoing PROTECT II trial is evaluating the Impella Recover 2.5 system compared with a traditional intra-aorta balloon pump (IABP) during high-risk elective PCI procedures. A total of 654 elderly patients with triple vessel disease (mean age 69 years and mean EF 26.1±6%) will be randomized as part of this prospective, multicenter trial. The Impella system is a miniaturized LVAD system that is placed percutaneously via the femoral artery and actively unloads the ventricle, providing up to 2.5 L/min of flow with support up to 5 days. This device decreases myocardial O₂ demand and thus augments coronary and end-organ perfusion. The primary outcome is the composite rate of intraprocedural and postprocedural major events, including death, MI, stroke, transient ischemic attack, target vessel revascularization, coronary artery bypass grafting (CABG), acute renal failure, and severe hypotension [Sharma S. TCT 2009]. Secondary outcomes include maximum cardiac power output decrease from baseline and the rate of in-hospital major cardiac events (MACE) for Impella compared with IABP. Thus far, the rate of successful implantation for the Impella system is 100%, with 80% freedom from 1-year MACE for the first 20 consecutive elderly patients. Of these 20 patients, 40% required rotational atherectomy (n=8). Further results for the PROTECT II trial are pending.

The Coronary Sinus Reducer Stent, a percutaneous implantable device that is designed to narrow the coronary sinus and elevate coronary sinus pressure, may be a future option for patients with refractory angina who are not good candidates for conventional revascularization procedures. The first-in-man study of 15 patients showed that the Coronary Sinus Reducer Stent is safe and feasible for the treatment of refractory angina when conventional revascularization