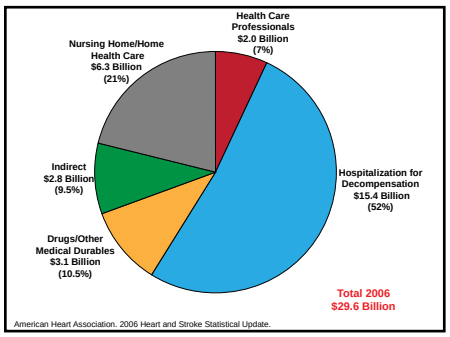
Devices in Heart Failure: Update 2009

Professor Pangiotis Vardas, MD, Heraklion University Hospital, Crete, Greece, discussed some of the open issues in implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT). Commenting on the concern about the high number of patients who must be treated (NNT) to save 1 life with ICD implantation and CRT, Prof. Vardas reminded the audience that "this number is highly dependent on the time window over which the benefit is assessed." Pointing to the MADIT-II trial, he noted that while the NNT in Year 1 was 133 patients, it was only 17 in Year 2 and 11 in Year 3. Another important issue for ICDs and CRT therapy is the criteria for patient evaluation, which Prof. Vardas believes should be updated with a particular need for additional, more reliable markers. Technical issues that he believes need to be addressed include device longevity, inappropriate shocks, lead reliability, and follow-up for ICDs and lead stability, easier device programming, and follow-up for CRT. In concluding, Prof. Vardas suggested that existing guidelines need to be modified, particularly for patients with mild heart failure (HF), in light of the recent study results.

HF is the most common cause of hospitalization due to cardiovascular disease in patients aged over 65 years, and it has a considerable impact on health care costs (Figure 1) [AHA. *Heart and Stroke Statistical Update* 2006], noted Professor Luigi Tavazzi, MD, GVM Care and Research, Cotignola, Italy.

Figure 1. Impact of HF Hospitalizations in Patients Aged Over 65 Years on Health Care Costs.



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Prof. Tavazzi discussed some of the recent technological advancements that raise the possibility that remotely acquired physiological data from permanently implanted CRT/ICD devices may contribute to the management of HF patients by allowing for timely treatment. Several devices are currently being tested in clinical trials, including the PARADYM™-8770 sonR™ cardiac resynchronization therapy defibrillator (CRT-D), which is designed to adjust CRT delivery based on hemodynamic response. Another device in testing is the InSync Sentry, a CRT-D device with automatic intrathoracic fluid status monitoring (OptiVol™ Fluid Status Monitoring) that assesses a patient's fluid status by measuring, tracking, and reporting intrathoracic impedance. Prof. Tavazzi said that the combination of multiple diagnostics is feasible and may increase the clinical utility of device monitoring.

Results from the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy; NCT00180271) study, presented by Arthur J. Moss, MD, University of Rochester, Rochester, NY, showed that asymptomatic or mildly symptomatic cardiac patients who are treated with CRT-D have a significant 34% (p=0.001) lower risk of HF or death than those who receive a standard ICD only.

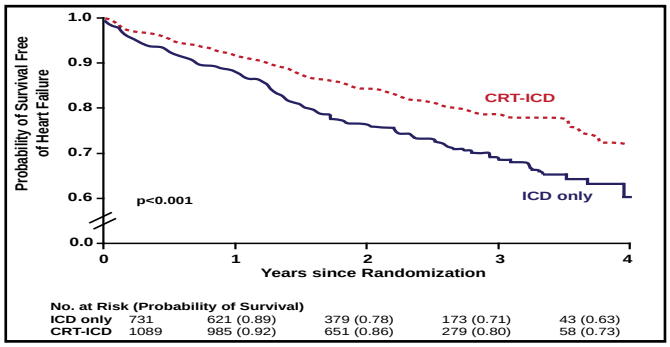
MADIT-CRT was a randomized, multicenter, international trial that comprised 1820 patients (~53% aged ≥65 years; 75% men) with New York Heart Association Class I or II (no or mild symptoms) who had either ischemic or nonischemic heart disease with LVEF <30% and QRS duration of >130 ms on ECG. Subjects were randomized to receive either CRT-D (n=1089) or ICD (n=731) along with optimal medical therapy. Subjects were followed for an average of 24 months. The primary study endpoint was all-cause mortality or an HF event, whichever occurred first.

Highlights from the

Barcelona ESC Congress 2009

CRT-D therapy was superior on the primary endpoint (Figure 2) and in all patient subgroups. The benefit was driven by a 41% reduction in HF events. CRT-D was more effective in women (HR, 0.37; 95% CI, 0.22 to 0.61) versus men (HR, 0.76; 95% CI, 0.59 to 0.97) and in subjects who had wider (HR, 0.48; 95% CI, 0.37 to 0.64) versus narrower (HR, 1.06; 95% CI, 0.74 to 1.52) QRS complexes. Full article: http://content.nejm.org/cgi/content/full/NEJMoa0906431v1.

Figure 2. Kaplan-Meier Estimates of the Probability of Survival Free of HF.



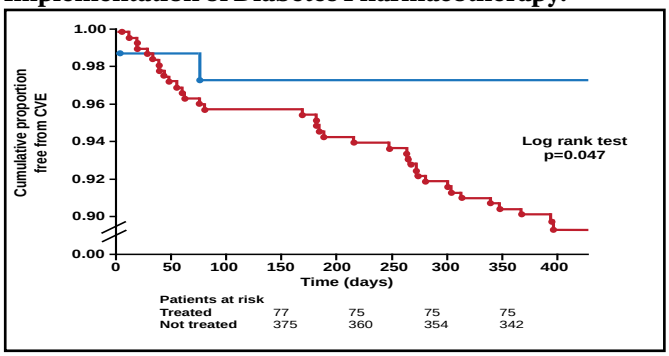
Diabetes and the Heart

Hyperglycemia is common but often undiagnosed in patients with coronary artery disease (CAD) in Europe and Asia; yet, patients with abnormal glucose tolerance have a significantly (p=0.002) higher probability of having a cardiovascular (CV) event compared with those with normal glucose tolerance [Bartnik M et al. *Eur Heart J* 2004]. This risk can be significantly (p=0.041) reduced with glucose-lowering drugs (Figure 1) [Anselmino M et al. *Eur Heart J* 2008]. In a study that assessed the relationship between impaired fasting glucose and impaired glucose tolerance, as well as diabetes mellitus (DM) and all-cause and cardiovascular disease (CVD) mortality, 65% of patients who died of CVD had known DM, newly diagnosed DM, impaired fasting glucose, or impaired glucose tolerance at baseline.

Professor Linda Mellbin, MD, Karolinska Institute, Stockholm, Sweden, discussed the therapeutic challenges that are associated with the combination of CAD and DM. She said that a possible link between CAD and dysglycemia is that the release of stress hormones and peptides due to a myocardial infarction is associated with insulin resistance and increased glucose or free fatty acid levels. They may induce oxidative stress and endothelial dysfunction, which in turn lead to inflammation, thrombus formation, and ischemia. The use of beta-blockers and glucose-lowering agents in the acute setting may limit these harmful reactions.

Data have shown that intensive multifactorial therapy, in a long-term perspective, with glucose regulation and the use of renin-angiotensin system blockers, aspirin, and lipid-lowering agents is associated with a lower risk of death from CV causes (HR, 0.43; 95% CI, 0.19 to 0.94; p=0.04) and of cardiovascular events (HR, 0.41; 95% CI, 0.25 to 0.67; p<0.001) [Gaede P et al. *N Engl J Med* 2008].

Figure 1. Euro Heart Survey: Improved CV Outcomes in Patients with Newly Detected Diabetes and Implementation of Diabetes Pharmacotherapy.



Anselmino M et al. *Eur Heart J* 2008;29:177-184. By permission of Oxford University Press.

Prof. Mellbin stressed the need for aggressive, guideline-based treatment to control blood pressure, lower serum cholesterol, and abolish cigarette smoking for diabetic patients with CAD.

Professor Lars Ryden, MD, Karolinska University Hospital, Stockholm, Sweden, listed the following 10 most important recommendations from the guidelines, jointly issued by the European Society of Cardiology and European Association for the Study of Diabetes, for adult patients with diabetes, prediabetes, and CAD (full-text document freely available at http://wwwescardio.org or http://www.easd.org):

1. To reach all treatment targets, including glycemic control
2. To screen for DM and impaired glucose tolerance by means of an OGTT in all patients with CAD and other high-risk individuals
3. To see lifestyle counseling as a cornerstone in preventing DM and CVD
4. To offer patients with DM and acute coronary syndrome standard, guideline-based treatment and early angiographic and mechanical revascularization
5. To apply strict, when needed insulin-based, glucose control in acutely ill DM patients.
6. To favor coronary artery bypass graft over percutaneous coronary intervention (PCI) when revascularizing DM patients
7. To use drug-eluting stents in PCI with stent implantation
8. To include investigations for cardiac autonomic dysfunction, heart failure, arrhythmias, hypotension, peripheral vascular disease (Doppler index), and (micro)albuminuria in routine follow-up
9. To use a multifactorial (no smoking; tight glucose, blood pressure, and lipid control; and antiplatelet therapy) approach
10. To establish collaboration between cardiologists and diabetologists in the management team