

ing drugs with a variety of proposed mechanisms for reducing infarct size, none of which have come to fruition.

"I caution us with the following: Despite great biological belief and promise and preclinical work that suggested upwards of 50% reduction in infarct size in animal models and then in early human experiments, absolutely no benefit has been seen for these [earlier] agents in clinical trials enrolling more than 100,000 patients," stressed Dr. Harrington, professor of medicine at Duke University, Durham, N.C., and director of the Duke Clinical Research Institute.

Contemporary guideline-driven therapy

for acute MI is so effective that a ceiling may be near. The way to make a major difference in MI today is not by focusing on shaving a sliver off 30-day mortality or final infarct size, but by preventing MI from occurring in the first place, he argued.

Dr. Harrington pointed to the landmark INTERHEART study led by Dr. Salim Yusuf of McMaster University, Hamilton, Ont., which has convincingly shown that 90% of the population-attributable risk for first-time MI worldwide is contained in familiar risk factors such as smoking, hypertension and hyperlipidemia (Lancet 2004; 364[9437]: 937-52). ■

High LVEF Hikes Risk in Older Women With ACS

BY BRUCE JANCIN
Denver Bureau

CHICAGO — Sometimes a woman's heart can be too strong for her own good.

Data from the Global Registry of Acute Coronary Events (GRACE) indicate that elderly women with supernormal left ventricular systolic function as defined by an

ejection fraction (EF) greater than 65% at the time they present with an acute coronary syndrome (ACS) have a twofold greater mortality risk than those presenting with a normal EF, Dr. Fadi A. Saab reported at the annual scientific sessions of the American Heart Association.

The highest mortality of all in the GRACE analysis was seen in elderly women with an EF below 55%, as would be expected. Depressed left ventricular systolic function complicating ACS is well established as the most powerful predictor of poor outcome, both during acute hospitalization and at 6 months.

However, the elevated risk associated with supernormal EFs came as a surprise to the investigators. A plot of in-hospital mortality against EF deciles in the more



'This is the first time this J-shaped association [between mortality and EF deciles] has been described.'

DR. SAAB

than 5,100 women over age 65 with ACS in GRACE describes a J-shaped curve with a nadir at an EF of 60%-69%. "We believe this is the first time this J-shaped association has been described," noted Dr. Saab of the University of Michigan, Ann Arbor.

GRACE is an ongoing Sanofi-Aventis-sponsored observational study at 112 hospitals in 14 countries. An EF below 55% was present in 2,987 elderly female ACS patients in GRACE, a normal EF of 55%-65% in 1,483, and a supernormal EF in 657.

In a multivariate logistic regression analysis adjusted for age, medical history, Killip class at presentation, in-hospital complications such as heart failure or atrial fibrillation, in-hospital management, and medical therapies, an EF greater than 65% was an independent predictor of poor outcomes. It was linked to a 2.4-fold greater risk of in-hospital mortality than in patients with a normal EF, a 2.0-fold greater 6-month mortality, and a 2.5-fold increased risk of cardiac arrest/ventricular fibrillation.

Dr. Saab said one possible explanation for the observed association between supernormal EF and poor outcomes is that elderly women with a hypertrophic heart and a very high EF may be particularly susceptible to oxygen supply-mediated myocardial ischemia, with resultant QT prolongation and an increase in serious arrhythmias, although he was quick to add that this is speculation.

Session cochair Dr. Galen S. Wagner noted that the GRACE investigators haven't looked at elderly male ACS patients with supernormal EFs. "We know that elderly women do badly if their hearts are too strong, but we really don't know what it means when elderly men have hearts that are too strong," observed Dr. Wagner of Duke University, Durham, N.C. ■

Brought to you by

sanofi aventis

INCREASED ACTIVITY OF THE ENDOCANNABINOID SYSTEM (ECS) IS ASSOCIATED WITH INCREASED WAIST CIRCUMFERENCE^{1,2}

INCREASED WAIST CIRCUMFERENCE, A MARKER FOR IAA, IS AN ESTABLISHED CARDIOMETABOLIC RISK FACTOR³

- Significantly increases the risk of myocardial infarction, death from cardiovascular disease, and all-cause mortality⁴
- Has been found to be an independent predictor of type 2 diabetes⁵

ADIPOSE TISSUE IS A HIGHLY ACTIVE ENDOCRINE ORGAN⁶

- Fat cells (adipocytes) produce adiponectin⁶
 - In type 2 diabetes and obesity, adiponectin levels are reduced⁶

TARGETING THE ECS MAY PLAY A POTENTIAL ROLE IN THE CONTROL OF MAJOR CARDIOMETABOLIC RISK FACTORS SUCH AS IAA*

IF YOU ARE INTERESTED IN LEARNING MORE ABOUT THE ECS, PLEASE CALL 1-800-815-0298 TO RECEIVE A MONOGRAPH.

References

1. DiMarzo V, Matias I. Endocannabinoid control of food intake and energy balance. *Nat Neurosci.* 2005;8:585-589.
2. Cota D, Marsicano G, Tschöp M, et al. The endogenous cannabinoid system affects energy balance via central orexigenic drive and peripheral lipogenesis. *J Clin Invest.* 2003;112:423-431.
3. National Heart, Lung, and Blood Institute. National Cholesterol Education Program. *ATP III Guidelines At-A-Glance: Quick Desk Reference.* Bethesda, Md: National Institutes of Health; May 2001.
4. Dagenais GR, Yi Q, Mann JFE, et al. Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. *Am Heart J.* 2005;149:54-60.
5. Carey VJ, Walters EE, Colditz GA, et al. Body fat distribution and risk of non-insulin-dependent diabetes mellitus in women: the Nurses' Health Study. *Am J Epidemiol.* 1997;145:614-619.
6. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab.* 2004;89:2548-2556.