

Benefit of Revascularization in Women Questioned

BY BRUCE JANCIN
Denver Bureau

VIENNA — Women with non-ST-elevation acute coronary syndrome don't show the same clear benefit as men do in response to a routine invasive management strategy, Dr. Eva Swahn reported at the annual congress of the European Society of Cardiology.

In fact, her new meta-analysis raises the possibility that women with non-ST-elevation acute coronary syndrome (NSTE ACS) are more likely to be harmed than helped by such an approach.

"The results of our study, taken together with the results of previous larger trials, suggest that the results from men do not necessarily apply to women and that large-scale randomized trials in women are needed to determine the optimal strategy in NSTE ACS," said Dr. Swahn, a cardiologist at Linköping (Sweden) University Hospital.

She presented the findings of the OASIS (Organization to Assess Strategies in Acute Ischemic Syndromes) 5 Women's Substudy, involving 184 women with NSTE ACS, 80% of whom had elevated cardiac damage biomarkers. Participants were randomized either to a routine invasive strategy involving catheterization followed by percutaneous coronary intervention or coronary artery bypass surgery within 7 days, or to a selective invasive strategy in which catheterization was reserved for those women with evidence of recurrent symptoms or severe ischemia despite intensive management with anti-ischemic and antithrombotic medications.

During 2 years of follow-up, 8 of 92 women in the routine invasive management arm died, compared with 2 of 92 assigned to a selective invasive strategy. Similarly, major bleeding occurred in nine patients in the routine invasive arm, compared with two in the selective invasive arm.

The OASIS 5 Women's Substudy was undertaken because the earlier landmark clinical trials, heralded as establishing the value of a routine early invasive management strategy in NSTE ACS, demonstrated a clear advantage of such an approach only in men. The results in women were equivocal, she continued.

The original plan was for the OASIS 5 substudy to enroll 1,600 women with NSTE ACS, which statisticians considered sufficient to provide definitive answers. However, recruitment in the multinational trial occurred at a glacial pace. Most physicians declined to participate, having already made up their minds that a routine invasive strategy is best for all—including women, Dr. Swahn explained.

Recognizing that the OASIS 5 substudy was small and underpowered, she performed a meta-analysis of outcomes in women from OASIS 5 and the three earlier, larger trials that compared a routine early invasive treatment strategy to a selective one. Those studies were the FRISC



The results in men do not necessarily apply to women. Large-scale trials in women are needed, said Dr. Eva Swahn.

(Fast Revascularization During Instability in Coronary Artery Disease) II trial, the RITA-2 (second Randomized Intervention Treatment of Angina) trial, and the TACTICS-TIMI-18 (Treat Angina With Aggrastat and Determine Cost of Therapy With an Invasive or Conservative Strategy—Thrombolysis In Myocardial Infarction-18) trial.

The mortality difference between the routine and selective invasive treatment groups was striking. There were 55 deaths among 1,185 women randomized to routine invasive treatment, compared with 35 in 1,187 women assigned to selective invasive management, for an odds ratio of 1.5.

The explanation for the worse outcomes in women un-

dergoing routine invasive management is unclear. Dr. Swahn had hypothesized that excess bleeding would prove to be the culprit, but that's not the case.

Discussant Dr. Annika Rosengren cited a number of differences in ACS between men and women that may be relevant to the gender-based disparity in outcomes with routine invasive therapy. Onset of ACS in women occurs later in life. They have more comorbidities. The pathophysiology is different: They are more likely than are men with ACS to have normal or near-normal coronary angiograms, and less likely to have two- or three-vessel disease. And women typically have more bleeding complications in conjunction with revascularization procedures.

Plus, women with ACS have an intrinsically better prognosis. This was evident in the FRISC II trial, which showed a "quite impressive" benefit for the early invasive strategy in men, whereas women—whether they underwent coronary intervention or not—had a prognosis similar to that of men in the early invasive group, noted Dr. Rosengren of Sahlgrenska University Hospital, Gothenburg, Sweden.

The meta-analysis highlights the need for all future interventional cardiology trials to include gender-specific analysis of outcomes, something that until now has generally not been done, she added.

Dr. Christian W. Hamm said in an interview that the questions raised by the new data can be resolved only by large studies done in women.

"It's a Catch-22 situation. I think women have very often been undertreated in the past, but it looks as though if you treat them they have worse outcomes," observed Dr. Hamm, cochairperson of the recently released European Society of Cardiology guidelines on the diagnosis and treatment on NSTE ACS (Euro. Heart J. 2007;28:1598-660).

Dr. Freek W.A. Verheugt said that most Dutch cardiologists never bought into the routine early invasive intervention strategy. Instead, they receive aggressive in-hospital therapy with a four-drug regimen consisting of clopidogrel, aspirin, a high-dose statin, and enoxaparin. Those who have recurrent ischemia despite this intensive medical management go to catheterization, explained Dr. Verheugt, professor and chairman of the department of cardiology at Radboud University Medical Center, Nijmegen, the Netherlands. ■

Silent Heart Ischemia Appears Reversible in Type 2 Diabetes

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Nearly 80% of patients with type 2 diabetes who had silent myocardial ischemia revealed by stress myocardial perfusion imaging had a reversal of exercise-induced myocardial perfusion abnormalities when they were retested 3 years later.

The unexpected finding suggests that a substantial proportion of patients with type 2 diabetes and silent myocardial ischemia have the potential for improvement of stress myocardial perfusion imaging abnormalities with medical management, Dr. Frans J.T. Wackers said at the annual meeting of the American Society of Nuclear Cardiology.

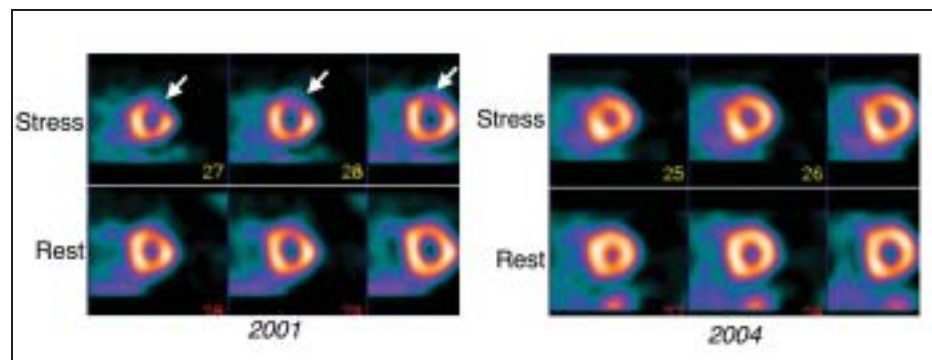
"It is conceivable that this [result] is due to aggressive treatment of cardiovascular risk factors," said Dr. Wackers, director of the cardiovascular nuclear imaging and stress laboratories at Yale University, New Haven, Conn. "These results are consistent with the INSPIRE study and the COURAGE trial, which found that aggressive and optimal treatment can reverse

myocardial perfusion abnormalities."

The study was a follow-up to the Detection of Ischemia in Asymptomatic Diabetics (DIAD)-1 study, which documented a 22% prevalence of silent myocardial ischemia during adenosine stress testing with sestamibi single-photon emission computed tomography myocardial perfusion imaging.

In the current study, known as DIAD-2, Dr. Wackers and his associates performed repeat stress myocardial perfusion imaging in DIAD-1 study participants after 3 years to evaluate for progression of silent myocardial ischemia. Initial myocardial perfusion imaging was performed in 2003, and repeat myocardial perfusion imaging was performed in 2006. Of the initial 522 patients, 356 underwent repeat myocardial perfusion imaging, 70 of whom had previously documented silent myocardial ischemia in DIAD-1. The mean age of the 356 patients was 61 years, and 44% were women.

Repeat myocardial perfusion imaging could not be performed in 166 patients. The initial and repeat DIAD studies were read by the same blinded panel of experts and included computer quantification of de-



At baseline, this 59-year-old asymptomatic man had a small reversible defect in the anterior wall (arrows). Three years later, the images have normalized.

fect size, said Dr. Wackers, who is also a professor of diagnostic radiology and medicine at Yale.

The overall prevalence of silent myocardial ischemia in DIAD-2 was 12%, which is 10% lower than the overall prevalence in DIAD-1.

In addition, of the 286 patients who had normal DIAD-1 studies, 90% remained normal in DIAD-2, whereas 10% developed new myocardial ischemia.

Of the 71 patients who had abnormal DIAD-1 studies, 56 (79%) showed resolu-

tion of inducible ischemia, and 15 (21%) remained abnormal.

When the researchers compared patients who had resolution of ischemia with those who developed new inducible ischemia, they observed no significant baseline differences.

Dr. Wackers disclosed that he has received research honoraria from Bristol-Myers Squibb, Astellas, and General Electric, and that he is a scientific adviser for General Electric and King Pharmaceuticals. ■