# Aggressive Revascularization in ACS Fails Women

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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. 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 (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–Thrombosis 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 undergoing 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 interventional cardiology trials to include gender-specific analysis of outcomes, she added.

"Right now 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. Christian W. Hamm, cochair of the recently released European Society of Cardiology guidelines on the diagnosis and treatment of NSTE ACS (Euro. Heart J. 2007;28:1598-660).

Dr. Freek W.A. Verheugt said that a national Dutch trial—ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes)—failed to show persuasive evidence of benefit for the invasive approach.

The strategy widely followed in the Netherlands is to provide aggressive in-hospital therapy with clopidogrel, aspirin, a high-dose statin, and enoxaparin. Patients with recurrent ischemia despite medical management go to catheterization, explained Dr. Verheugt, professor and chairman of the department of cardiology at Radboud University Medical Center, Nijmegen, the Netherlands. ■

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**The beneficial results for men with non–ST-elevation acute coronary syndrome do not necessarily apply to women, Dr. Eva Swahn said.**