Arteries Show Signs of Early Aging in Young PCOS Patients

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — Young women with polycystic ovary syndrome have evidence of endothelial dysfunction and low-grade, chronic inflammatory markers characteristic of much older patients, researchers reported at the annual meeting of the Endocrine Society.

Dr. Eleanthia Diamanti-Kandarakis and associates at Laiko Hospital of the University of Athens compared endothelial function and inflammatory cytokines in 25 women with PCOS and 20 age-matched controls with similar body mass index (BMI) measurements and waist-hip ratios. The women were in their mid-to-late 20s and had BMI’s of about 26-29 kg/m².

Endothelial function was assessed by flow-mediated dilatation of the brachial artery on ultrasound, plus plasma endothelin-1. Numerous cytokines were measured to assess arterial inflammation.

Subjects with PCOS had significantly lower percentages of flow-mediated dilatation than controls (3.47% vs 9.26%). Nitrate-induced dilatation, measured to exclude smooth muscle cell injury, was not significantly different in the two groups.

Significantly higher levels of endothelin-1, intracellular adhesion molecules, vascular cell adhesion molecules, and C-reactive protein were found in PCOS subjects, compared with controls.

In PCOS “the lining of the arteries is affected and at the same time, the molecules are sticking to each other and to the vessel wall, leading to a compromised circulation as would be seen in a woman much older” than these subjects, Dr. Diamanti-Kandarakis said at a press conference during the meeting.

As expected, testosterone levels were significantly elevated in women with PCOS. When asked to advise clinicians on how to use the information, she pointed out that a multiple regression analysis determined that the best predictor of endothelial damage in PCOS subjects were elevated levels of testosterone and CRP.

Young PCOS patients with high levels of both should be closely followed for cardiovascular consequences of the syndrome, particularly if they are obese.

“If they are obese, this risk is multiplied,” she said. “We cannot assume that all women with PCOS have [endothelial dysfunction]. There are different subtypes of the disease,” she said.

Either cholesterol or inflammatory markers would be useful in determining the risk, she said.

The authors determined that the best predictors of endothelial damage in PCOS patients were elevated levels of testosterone and CRP.

“Simvastatin improved a clinical end point of treatment of polycystic ovary syndrome/hirsutism,” Dr. Duleba, the lead investigator, said in an interview.

The data were presented by another investigator in the study, Dr. Beata Banaszewska, at the joint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society.

Oral contraceptive pills “do reduce testosterone levels, but in this crossover study, we can appreciate that statins have a greater power to this effect,” Dr. Ba-
naszewska, of Poznan University of Medical Sciences in Poland, said at the meeting.

“We still don’t have satisfactory medical treatments for PCOS; symptomatic treatments only partly improve the situation, and long term, these patients are at increased risk of cardiovascular problems,” he said.

The study randomized 48 PCOS patients (mean age 24 years) into two treatment groups. One group received oral contraceptive pills (OCP) alone (20 mcg ethinyl estradiol and 110 mcg desogestrel); for 12 weeks, after which 20 mg simvastatin was added to their regimen daily for 12 more weeks. The other group first received the combined drug regimen for 12 weeks and then were given OCP alone for 12 weeks. Clinical, endocrine, and metabolic evaluations were performed at baseline, at crossover (12 weeks), and at 24 weeks.

“Simvastatin induced a decrease of total testosterone by 18% below the effect of OCP,” Dr. Duleba said. “This effect was paralleled by a 16% decrease of free testosterone below the effect of OCP. We also found that the hirsutism declined, and there was a strong trend toward an improvement in PCOS.

A simvastatin attributable decline of hirsutism was modestly but significantly greater than with OCP alone; this 4% difference was statistically significant.

‘This is the first report that simvastatin improves a clinical end point of treatment of PCOS/hirsutism.’

Dr. DULEBA

‘Fitness is more important than the presence or absence of the metabolic syndrome.’

Dr. GULATI

Fitness Attenuates Metabolic Syndrome Mortality in Women

BY BETSY BATES
Los Angeles Bureau

DALLAS — Physical fitness cancels out the excess mortality risk associated with the metabolic syndrome in asymptomatic women, Dr. Martha Gulati, said at the annual scientific sessions of the American Heart Association.

This finding from the large observational St. James project on women Take Heart Project has important clinical implications: It suggests that as part of a primary cardiovascular prevention strategy, physicians ought to routinely assess cardiorespiratory fitness in asymptomatic women who meet criteria for the metabolic syndrome (MS). If risk is stratified in this manner, the unfit can be targeted for more aggressive interventions, explained Dr. Gulati of Northwestern University, Chicago.

She reported on 5,721 asymptomatic women age 35-86 years who participates in the St. James Project, a prospective observational study whose primary purpose was to assess the value of exercise stress testing in asymptomatic women.

The mean age of participants was 52 years. Thirty percent met National Cholesterol Education Program (NCEP) criteria for the MS. The MS has been shown to confer at least a two-fold increased risk of all-cause and cardiovascular mortality. That’s why the condition received prominent attention in the NCEP Adult Treatment Panel III guidelines. The impetus for Dr. Gulati’s study was a recognition that the impact of physical fitness upon this mortality risk hadn’t previously been studied in women.

In 1992, participants underwent a symptom limited Bruce protocol exercise stress test; then were followed prospectively through 2000. During a mean 8.4 years of follow-up, 180 women died, with one-third of the deaths being due to cardiac causes.

An unadjusted analysis showed that women with the MS were at least 1.5 times more likely to die from any cause, compared with those without it, and at least twice as likely to die from cardiac causes. Upon adjustment of the data for cardiorespiratory fitness, however, the MS was no longer an independent risk factor for mortality. What this actually means is that fitness is more important than the presence or absence of the metabolic syndrome,” Dr. Gulati said.