Hypogonadism Red Flags Cardiac Risks in Elderly

BY NANCY WALSH
New York Bureau

MONTREAL — Hypogonadism should be considered a risk factor for cardiovascular disease in older men, Dr. Andre T. Guay said at a congress sponsored by the Canadian Society for the Study of the Aging Male.

He based that conclusion on an analysis of testosterone levels in 154 men (average age of 53.5) seen at the erectile dysfunction (ED) clinic of the Lahey Clinic Medical Center, Peabody, Mass., where Dr. Guay is an endocrinologist.

Overall, 25% of the men had hypogonadism, defined as a free testosterone level below 10 pg/mL. Among men with low testosterone, 92.3% had insulin resistance, compared with 25.2% of those without low testosterone levels. High rates of metabolic syndrome also were seen among hypogonadal men, using both the National Cholesterol Education Program (NCEP) criteria and the more stringent World Health Organization criteria for metabolic syndrome. (See box.)
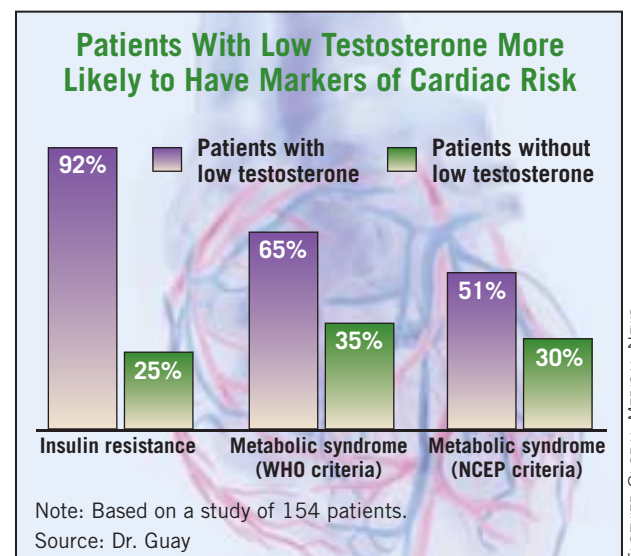
In a previous study, 91% of the cohort of men seen in the ED clinic had cardiac risk factors. A total of 43% had hypertension, 73% had dyslipidemia, and 85% had a body mass index greater than 25 kg/m^2, Dr. Guay said.

Also, 43% of the men had metabolic syndrome, according to the NCEP criteria, compared with 24% of the general population. Insulin resistance was found in 79%, compared with a 25% incidence in the general population. These findings suggest that ED may be an early warning sign of cardiac disease, he said.

The new findings on hypogonadism go beyond this link to suggest that low testosterone also may be associated with underlying cardiovascular disease, according to Dr. Guay.

Several large reviews have indicated that men with low testosterone have increased cardiovascular risks, with a high incidence of metabolic syndrome and insulin resistance. "There are associations, but that doesn't necessarily prove cause and effect," Dr. Guay said in an interview. "However, we know that testosterone can positively affect endothelial function, increasing blood flow, and we know that even acute stimulation of testosterone can decrease insulin resistance, which is the basis of the metabolic syndrome and many chronic diseases. Testosterone must therefore have a protective effect on the vascular lining where atherosclerosis begins."

The study findings suggest that "when patients present with ED, you should immediately look for major cardiac

Patients With Low Testosterone More Likely to Have Markers of Cardiac Risk

Patients with low testosterone
Patients without low testosterone

92% 25% Insulin resistance
65% 35% Metabolic syndrome (WHO criteria)
51% 30% Metabolic syndrome (NCEP criteria)

Note: Based on a study of 154 patients.
Source: Dr. Guay

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risks and either treat or refer for treatment. It also may be that we should be checking the testosterone level in every man with ED," he said at the meeting, which was cosponsored by the International Society for the Study of the Aging Male. ■

Algorithm Refines Cardiac Risk Assessment in Women

BY MARY ANN MOON
Contributing Writer

A new, much more accurate clinical algorithm for predicting cardiovascular risk in women has been developed and validated by investigators in the Women's Health Study.

The new method reclassified approximately half of women who had been previously categorized as intermediate risk into either low-risk or high-risk categories. If the new algorithm were applied to a representative population of 100,000 U.S. women who are now considered to be at intermediate risk, it would recategorize 13,500 of them as low risk, 48,500 as low to moderate risk, 32,500 as moderate to high risk, and 5,400 as high risk, researchers reported.

"As 8-10 million U.S. women have an estimated 1-year risk between 5% and 20%, application of these data could have an immediate effect on cardiovascular prevention," allowing more accurate targeting of statin and other therapies, wrote Dr. Paul M. Ridker of Brigham and Women's Hospital, Boston, and his associates in the WHS.

The investigators used data on a subgroup of 16,400 healthy WHS subjects to assess which of 35 possible risk markers would best predict CV risk, then developed a model (model A) that included the nine most valuable predictors. Next, they modified the model to create a simplified version (model B) that would be more practical for clinical use. They tested the validity of both models in another subgroup of 8,158 WHS subjects.

During a median follow-up of 10 years, 504 CV events occurred in the first cohort and 262 occurred in the validation cohort.

With model A, 43% of women who had been classified as being at intermediate risk by traditional criteria were reclassified as being at either lower or higher risk. Of these 681 reclassified subjects, all but 93 were placed into more accurate risk categories, based on their 10-year clinical outcomes.

Among subjects who did not have diabetes, approximately 50% who had been classified as being at intermediate risk by traditional criteria were reclassified as being at either lower or higher risk. Of these 722 reclassified subjects, all but 2 were placed into more accurate risk categories (JAMA 2007;297:611-9).

Similar results were obtained using the simplified model B, which the researchers have termed the Reynolds Risk Score. For the 647 subjects without diabetes who were reclassified using model B, all but 6 were placed into more accurate risk categories, they said.

The Reynolds Risk Score uses these eight clinical markers to predict risk: age, systolic blood pressure, hemoglobin A$_{1c}$ if the patient is diabetic, current smoking status, total and HDL cholesterol levels, high-sensitivity C-reactive protein, and parental history of MI before the age of 60.

"A user-friendly calculator for the Reynolds Risk Score can be freely accessed at www.reynoldsriskscore.org," the investigators added.

Homocysteine, fibrinogen, soluble intercellular adhesion molecule 1, and creatinine measures did not add to the accuracy of risk prediction, nor did body mass index or exercise frequency, Dr. Ridker and his associates said.

The researchers cautioned that since the study subjects were predominantly white, well-educated women, these findings may not be generalizable to other populations. ■

Link Between Metabolic Syndrome, Heart Disease Is Weak in Women

BY PATRICE WENDLING
Chicago Bureau

NEW ORLEANS — Despite having a higher incidence of metabolic syndrome, women had less obstructive coronary artery disease in a study of 468 patients who presented for elective cardiac catheterization.

Nondiabetic women were significantly more likely to have metabolic syndrome than were their nondiabetic male counterparts (52% vs. 28%), although nondiabetic men had a significantly greater percentage of coronary artery disease (CAD) (42% vs. 18%). Dr. Andrew Weissman and colleagues from Lenox Hill Hospital in New York City reported their findings in a poster at the Southern regional meeting of the American Federation for Medical Research.

The results call into question whether lower cutoffs should be used to identify metabolic syndrome in women or whether the presence of metabolic syndrome itself is truly a risk factor for coronary artery disease, Dr. Weissman said in an interview.

"The goal of identifying metabolic syndrome is to try and pick out those people with a higher risk for coronary artery disease and it doesn't seem to be doing that in nondiabetic females according to the results of our study," he said.

The study included 277 men (mean age 60 years) and 191 women (mean age 63 years) with no known history of CAD. Metabolic syndrome was evaluated using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria.

The NCEP criteria recommend that metabolic syndrome be identified if three or more of the following risk factors are present: waist circumference of 102 cm or more in men and 88 cm or more in women; elevated triglyceride level of 150 mg/dL or greater; reduced HDL cholesterol level of less than 40 mg/dL in men and less than 50 mg/dL in women; elevated blood pressure of 135/85 mm Hg or greater; and an elevated fasting glucose of 110 mg/dL or greater.

Diabetes mellitus was present in 79 men (28.5%) and 49 women (25.6%), a difference that was not statistically significant.

Metabolic syndrome was present in 233 of 468 patients and was found in a significantly higher percentage of women (62%) than men (41%).

CAD, defined as the presence of 70% or greater stenosis in one of the three major coronary vessels or 50% stenosis in the left main coronary artery, was present in 48 (25%) women and in 132 (48%) men.

There was no significant difference between patients with and without metabolic syndrome with regard to mean Framingham risk score or for age, tobacco use, or family history of CAD, said Dr. Weissman, a third-year cardiology fellow at Lenox Hill Hospital.

However, both men and women with diabetes were significantly more likely to have CAD than were their nondiabetic counterparts.

There was no significant difference in percentage of CAD between men and women with diabetes (62% vs. 45%). There was a trend toward women with diabetes being more likely to have metabolic syndrome than were men with diabetes (90% vs. 75%), but it was not statistically significant, the authors wrote.

Although diabetes is considered a coronary risk equivalent, the independent significance of metabolic syndrome in practice remains controversial.

"The clinical implication is that our study results do not support the use of metabolic syndrome as a useful risk stratifier for coronary artery disease," Dr. Weissman said. ■