

Obesity-Preeclampsia Linkage May Be Vascular

ARTICLES BY
MITCHEL L. ZOLER
Philadelphia Bureau

LISBON — Neutrophil infiltration and vascular inflammation were substantially more prevalent and severe in blood vessels from overweight and obese women than in vessels taken from normal-weight women in a study of 22 women.

"The data indicate that the vasculature of obese women is inflamed and susceptible to developing hypertension," Scott W. Walsh, Ph.D., said at the 15th World Congress of the International Society for the Study of Hypertension in Pregnancy.

"We speculate that neutrophil infiltration and vascular inflammation puts obese women at risk for preeclampsia" through the release of reactive oxygen species and immunostimulants. This may explain why obesity is a risk factor for preeclampsia.

Until now, the pathophysiologic link between obesity and preeclampsia has been unclear, said Dr. Walsh, a professor of ob.gyn. at Virginia Commonwealth University in Richmond.

Dr. Walsh and his associates assessed neutrophil infiltration and vascular inflammation in the blood vessels of adipose tissue biopsies taken from volunteers. Participating women were divided into three groups based on their body mass index. Five normal-weight women had a BMI of less than 25 kg/m², 7 overweight women had a BMI of 25-29.9 kg/m², and 10 obese women had a BMI of at least 30 kg/m².

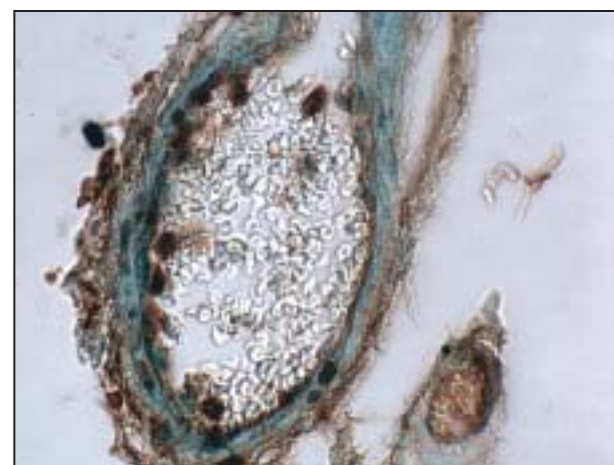
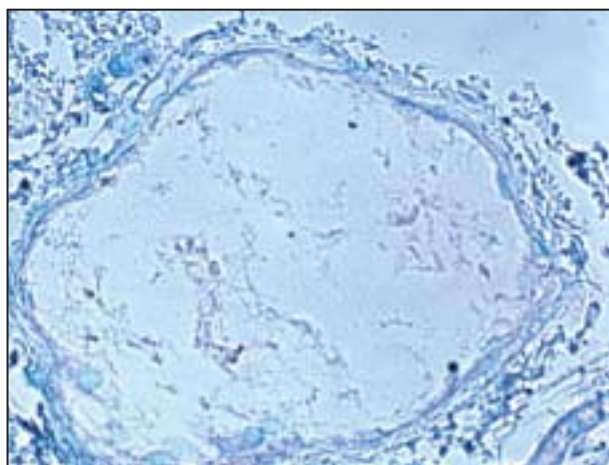
Neutrophil infiltration was measured using a monoclonal-antibody stain against CD66b, a granulocyte membrane antigen (about 96% of granulocytes in blood vessels are neutrophils). Inflammation was measured with monoclonal-antibody stains against two markers of inflammation, nuclear factor (NF)-κB and cyclooxygenase (COX)-2. The extent of vessel staining with these reagents was gauged in fixed, adipose tissue specimens by two measures: a visual score scale of 0-3 and stained vessels as a percent of all vessels examined.

By both measurements, all three stains were significantly increased in both overweight and obese women,

compared with the normal-weight controls. The greatest staining was in the vessels from obese women.

For example, for NF-κB staining, the visual score was about 0.3 in biopsies from normal-weight women, about 1.1 in overweight women, and about 2.6 in obese women. The percent of vessels stained was about 28%, 60%, and 90%, respectively. Similar results were obtained with the stains for neutrophils and for COX-2.

The patterns seen in adipose tissue are likely to be representative of the entire vasculature in each woman. In fact, inflammation may be even more extensive in certain other vascular beds in each woman, Dr. Walsh said. ■



The images show blood vessels in fixed, adipose-tissue biopsies that were stained for the cytokine NF-κB, a marker for vascular inflammation. The control specimen (left) is from a normal-weight woman and shows no NF-κB staining. The specimen on the right, from a woman with a BMI of at least 30 kg/m², shows heavy staining.

PHOTOS COURTESY DR. SCOTT W. WALSH

Long-Term CV Mortality Risk Up After Severe Preeclampsia

LISBON — The high long-term death rates in women who have had one episode of severe preeclampsia suggest a strong link with cardiovascular disease in an analysis of more than 600,000 Norwegian women.

Integrating data from the Norwegian national registries for birth and for death showed that women who had one case of severe preeclampsia were nearly three times more likely to die in the long term and eight times more likely to die from cardiovascular disease, compared with women who had a term delivery and no preeclampsia, Dr. Rolv T. Lie reported at the 15th World Congress of the International Society for the Study of Hypertension in Pregnancy.

The eightfold increased risk of cardiovascular disease death was "stunning," said Dr. Lie, an epidemiologist at the University of Bergen (Norway). It suggests that both preeclampsia and cardiovascular disease occur because of a single underlying predisposition, or that serious preeclampsia results in long-term cardiovascular complications. "They're not independent. There has to be a common pathophysiology," he said.

His initial analysis dealt with the 626,000 women who had their first delivery during 1967-1992. Subsequent mortality and cause of death were tracked through 1992.

During follow-up of up to 25 years, women who had a term delivery and no preeclampsia had a 0.8% mortality rate. Those who had preeclampsia and a preterm delivery (a marker for early and more severe preeclampsia) had a 2.3% mortality rate. When adjusted for the

women's ages and the calendar year they gave birth, severe preeclampsia was linked with a statistically significant, 2.7-fold increased risk of death.

In addition to the much higher rate of cardiovascular death, women with severe preeclampsia also had a five-fold increased risk of death from stroke.

A more recent analysis used data collected through 2004, which allowed for up to 35 years of follow-up. It also allowed death rates to be analyzed for the first 10 years after delivery and for the subsequent 10 years, which gives some insight into the persistence of the mortality effect of severe preeclampsia.

The analysis showed that the women who had experienced serious preeclampsia had a lower mortality risk in the period 10-20 years after the episode, compared with during the initial 10 years following the pregnancy. This may mean that mortality risk from severe preeclampsia diminishes with time, or it may just mean that deaths due to other causes were diluting the effect, Dr. Lie said. ■

The eightfold increased risk of CV disease death was 'stunning' and suggests a single underlying predisposition.

U.S., Canada Need Narrower Severe Preeclampsia Definition

LISBON — The definition of severe preeclampsia that's been adopted by the U.S. National High Blood Pressure Education Program contains some criteria that did not lead to adverse maternal outcomes in an analysis of 657 patients.

Based on these findings, a narrower definition of severe preeclampsia is warranted, with a narrower list of criteria used to justify delivery for maternal indications, Dr. Peter von Dadelszen and his associates reported in a poster at the 15th World Congress of the International Society for the Study of Hypertension in Pregnancy.

Three criteria that did not shake out as adverse-outcome predictors from the list of the National High Blood Pressure Education Program (NHBPEP) were proteinuria, persistent headache or other cerebral or visual disturbances, and persistent epigastric pain, reported the poster's authors, including Dr. Dadelszen, an ob.gyn. at the University of British Columbia, Vancouver. The NHBPEP Working Group on High Blood Pressure in Pregnancy published its revised recommendations in 2000.

The researchers found that the severe preeclampsia criteria of the Canadian Hypertension Society also included several diagnostic markers that weren't associated with adverse outcomes in the current study, including proteinuria, low serum albumin, severe nausea, intrauterine growth restriction, oligohydramnios, headache, and right upper quadrant pain.

The study was done at six hospitals in Canada, the United Kingdom, and New Zealand during September 2003 to May 2006. It included 657 women who were diagnosed with preeclampsia, superimposed preeclampsia, or HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets). For this study, preeclampsia was defined as a blood pressure of at least 140/90 mm Hg and proteinuria or hyperuricemia.

The researchers identified the clinical markers that were statistically significant predictors of adverse maternal outcomes in this group. The adverse outcomes included death, hepatic dysfunction, acute renal failure, eclampsia, pulmonary edema, and need for any transfusion.

The multivariate analysis identified these factors as independent predictors of adverse outcomes: blood pressure at or above 160/110 mm Hg, platelets less than 100 x 10⁹/L, creatinine more than 100 μmol/L, elevated liver enzymes, HELLP syndrome, chest pain or dyspnea, and placental abruption.

All of these conditions are diagnostic criteria in both the NHBPEP and Canadian Hypertension Society guidelines, except chest pain or dyspnea and placental abruption, which don't appear in the NHBPEP definition of severe preeclampsia, the researchers said. However, the researchers did not suggest that the NHBPEP needed to expand its criteria to match the Canadian guidelines. ■