

Aortic Calcification Linked to Hip Fracture Risk

BY NANCY WALSH
New York Bureau

TORONTO — Aortic calcification was found to be an independent predictor of accelerated bone loss and hip fracture among postmenopausal women in a prospective epidemiologic study, Dr. Laszlo B. Tanko said at a world congress on osteoporosis.

Epidemiologic studies have suggested a link between cardiovascular disease and osteoporosis, two conditions that clearly are major contributors to morbidity and mortality in the elderly, but whether atherosclerosis is an independent contributor to fracture risk had not yet been determined, Dr. Tanko said. In the first long-term study addressing the questions of whether the severity and progression of aortic calcification might be associated with bone loss and fracture risk, Dr. Tanko and his colleagues from the Center for Clinical and Basic Research, Ballerup, Denmark, analyzed data from the Danish Prospective Epidemiological Risk Factors study.

In this study of 2,662 postmenopausal women, investigators identified classic cardiovascular risk factors in a baseline interview. They assessed aortic calcification using lateral x-rays and scored any calcification according to the Framingham system. Lumbar spine and total hip bone mineral density (BMD) were measured by dual-energy x-ray absorptiometry.

A total of 1,877 patients had normal aortic calcification scores (below 3) at baseline, while 785 had scores of 3 or higher. Mean score among those in the group with low-

er scores was 0.4, compared with 6.5 among those in the higher-scores group.

Those with advanced aortic calcification at baseline subsequently had annual rates of progression of atherosclerotic burden that were approximately 2.5 higher than did those with normal calcification at baseline, Dr. Tanko said at the meeting, which was sponsored by the International Osteoporosis Foundation.

BMD scores at baseline for lumbar spine and hip were significantly lower among women with advanced atherosclerosis, with means of 0.84 g/cm² and 0.80 g/cm², respectively. The corresponding scores among women with normal aortic calcification at baseline were 0.87 g/cm² and 0.82 g/cm², respectively.

These differences were independent of age and body mass index, he said.

Accelerated subsequent rates of bone loss were seen among women with advanced atherosclerosis but not among those who were normal at baseline.

But at the lumbar spine, increases in BMD, rather than decreases, were seen among the advanced atherosclerosis group. An explanation for this may lie in the fact that the local blood supply to the proximal femur is unilateral, delicate, and more vulnerable to impaired blood flow than is blood supply to the vertebrae. Vertebral blood supply is bilateral and more advanced in terms of compensating for arterial obstruction, Dr. Tanko said.

During the study follow-up period, which averaged 7.5 years, there were 431 incident vertebral fractures and 37 incident



Heavy calcification of the aortic wall (red arrows) at its site of bifurcation.

COURTESY DR. LASZLO B. TANKO

hip fractures. There also were 113 acute cardiovascular events.

On multivariate regression analysis, there was a slightly increased but not statistically significant risk (relative risk 1.2) of vertebral fractures among those with advanced aortic calcification at baseline. Hip fracture risk, however, was 2.3-fold increased among those with higher calcification, compared with those whose calcification scores were normal at baseline. Regression analysis also showed that women with higher calcification also had a 2.5-fold increased risk of a cardiovascular event.

“We can say that aortic calcification is an independent predictor of accelerated bone loss and incident fracture at the hip but not at the vertebra. We are tempted to speculate that antiatherogenic measures might help decrease not only cardiovascular disease but also might help prevent fractures,” Dr. Tanko said.

In the question and answer session following Dr. Tanko’s presentation, an audience member asked if he had considered the possibility that both atherosclerosis and bone loss are associated with a single common factor such as a cytokine cascade, or whether the bone loss might be causing atherosclerosis.

Dr. Tanko acknowledged that although he could not exclude systemic factors such as the impact of proinflammatory cytokines, he believed that his findings more clearly demonstrate the direct impact of ischemic atherosclerotic vascular disease on local bone metabolism.

He recently wrote that the underlying mechanism linking osteoporosis and cardiovascular disease is not yet fully understood, but “it seems reasonable to presume that the independent association reflects either a direct contribution of ischemic vascular disease to bone turnover or common pathomechanisms acting simultaneously on both bone and vascular cells. As for the latter option, proinflammatory cytokines such as IL-6 and TNF- α are known to exert proatherogenic effects, but they may also enhance osteoclastogenesis and consequently increased bone resorption” (J. Intern. Med. 2006;259:598-605). ■

Type 1, 2 Distinctions Blurry in Children

BY KATE JOHNSON
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COPENHAGEN — Type 1 diabetes, traditionally considered a disease of wasting, is now frequently diagnosed in children who are overweight, according to a new study.

That means that determining which pediatric patient has type 1 diabetes and which has type 2 is getting harder, said Dr. Ingrid M. Libman, assistant professor of pediatric endocrinology at the University of Pittsburgh.

“The problem now is that the lines are blurred between what we thought was clearly defined as type 1 and 2 diabetes,” Dr. Libman said in an interview. “The distinction can no longer be made based on phenotype.”

Data she presented at the annual meeting of the European Association for the Study of Diabetes showed that over 23 years of observation (1979-2002), the overall prevalence of overweight and obesity in children with newly diagnosed insulin-treated diabetes (traditionally considered type 1 disease) has more than tripled—doubling in African American children (from 30% to 62%) and quadrupling in white children (from 6% to 26%).

“In some cases we now have no clear way of distinguishing what kind of di-

abetes someone has based on how they look,” she said, adding that acanthosis nigricans, traditionally associated with type 2 diabetes, is now commonly found in overweight patients with type 1 disease as well.

Subjects diagnosed in period I (1979-1989) and period II (1990-98) were tested for beta-cell autoimmunity. In those with autoimmune positivity (known as diabetes type 1a), there was a similar increase in the prevalence of obesity between periods I and II: 6% to 21% among whites and 22% to 43% among African Americans. For period III (1999-2002), autoimmune antibodies are still being measured, she said. Autoimmune-negative subjects in the study may have had type 2 diabetes or type 1b—an insulin-dependent, nonautoimmune form of the disorder.

Dr. Libman said physicians might frequently face a new presentation of diabetes in which patients may actually have a confusing combination of characteristics.

“What we argue is that some kids may have characteristics of both type 1 and type 2 disease processes going on. If they are autoimmune positive, they have type 1a diabetes; however, if they are also overweight and have acanthosis nigricans, you could argue that they may also be insulin resistant.”

Although establishing a clear diagnosis may often seem essential to physicians, Dr. Libman said that in the end, it might not be so important.

“If the child is really sick, does it matter if they have type 1 or 2? You will need to treat them with insulin. If they are overweight, not sick, and diagnosed randomly, you can likely control their blood sugars with lifestyle and metformin. If their antibodies come back positive, it doesn’t mean you should start insulin—but you may need to monitor them more carefully and you may have a lower threshold for starting it.”

Overweight in children may not only make them more susceptible to developing type 2 disease, but in those who are genetically susceptible, it may also increase their risk or accelerate the development of type 1 disease—the concept of “double diabetes,” she said.

“Genetically, they have the genes to develop diabetes at some point (or not), but if they become overweight, they may have more chance. Weight makes the beta cell work harder and may trigger an increased immune response—this is known as the ‘accelerator hypothesis,’” she said, adding that first-degree relatives of patients with type 1 diabetes have a 1 in 20 chance of developing the disorder, making overweight particularly dangerous in this group. ■

Annual Celiac Disease Test Urged in Type 1

COPENHAGEN — Children who are newly diagnosed with type 1 diabetes should be screened annually for celiac disease for at least 3 years and not just at diagnosis, according to Dr. Karin Larsson of Kristianstad (Sweden) Hospital.

Study findings, which were presented at annual meeting of the European Association for the Study of Diabetes, were based on 300 patients under age 20 (mean age 10 years) who were newly diagnosed with type 1 diabetes at six different pediatric diabetes centers in Sweden. Serum IgA-antiendomysium antibody (EMA) testing was done at baseline to screen for celiac disease and, if negative, testing was repeated annually for 5 years. Patients with a positive blood screening test then underwent intestinal biopsy to confirm celiac disease.

At the end of the 5-year study, 29 diabetes patients (10%) had been diagnosed with celiac disease after their diagnosis of diabetes. Two had preexisting celiac disease before their diagnosis of diabetes—one patient 2 years earlier; the other, 10 years earlier. Twelve patients had a positive EMA test at the time of their diabetes diagnosis followed by biopsy confirmation of celiac disease. In the first year after the diabetes diagnosis, another 10 patients were diagnosed with celiac disease; another 5 were diagnosed in the second year. One more patient was diagnosed in year 3 and a final one in the fifth year. Of those diagnosed with celiac disease, 59% had no symptoms.

—Kate Johnson