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## New Predictor of Coronary Calcification Identified in Dialysis Patients

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Medscape Medical News 2007. © 2007 Medscape

June 26, 2007 (Barcelona) — Decreased osteoid surface may join age, diabetes, and dialysis duration as an independent predictor of coronary artery calcification (CAC) and heart disease in patients with end-stage renal disease.

In the largest study of its kind to date, patients with the most severe CAC, defined as a CAC score of 400 or more, had a significantly lower percentage of osteoid surface (immature bone that is not yet calcified) than patients with no CAC at all ( $P < .05$ ), reported Gulay Asci, MD, at the 44th European Renal Association–European Dialysis and Transplantation Association Congress. Osteoclast surface was also significantly lower in patients with CAC scores greater than 1000 ( $P < .05$ ).

CAC was identified in 2003 as a cardiovascular disease risk factor and an independent predictor of mortality. Investigators have known since at least 1996 that CAC is from 2 to 5 times more extensive in people on hemodialysis than in people with coronary artery disease but not kidney disease, said Dr. Asci, a nephrologist at the Ege University School of Medicine in Izmir, Turkey. Subsequent studies have shown an association between CAC and left ventricular hypertrophy and coronary abnormalities, including atherosclerosis, stiffness, and perfusion problems. In their study, Dr. Asci and colleagues investigated the relationship between CAC and renal bone disease, as shown on bone biopsy, in 224 prevalent hemodialysis patients recruited from 8 centers operated by Fresenius Medical Care, which supported the study.

The patients underwent a variety of examinations, including bone histomorphometry, computed tomography to determine CAC score, echocardiography, carotid ultrasonography, and pulse wave analysis to determine pulse wave velocity and augmentation index, both of which are measures of systemic arterial stiffness.

Low-turnover bone disease (LT) was much more common in the study group (168 patients [75%]). In addition, the patients with LT had higher CAC scores and were more likely to be male, to have diabetes, and to have spent less time on dialysis, but these differences were not significant. Patients with LT had a mean age of 60 years compared with 49 years among patients with high-turnover disease (HT;  $P < .01$ ). The mean parathyroid hormone level among patients with LT was 160 pg/mL compared with a mean of 343 pg/mL in those with HT ( $P < .001$ ), and their mean calcium level was 9.2 mg/dL vs 8.9 mg/dL in patients with HT ( $P < .05$ ). There were no other significant differences in any of the lipid or mineral parameters measured. Both groups also had received similar doses of elemental calcium and calcium-based phosphate binder within the previous 2 years.

Regarding cardiovascular parameters, patients with LT had significantly greater carotid intima media thickness ( $P < .01$ ) and higher plaque frequency ( $P < .05$ ). “Nevertheless, [LT] was not an independent predictor for any of them,” Dr. Asci noted. There also were no differences found in pulse wave velocity or augmentation index.

The investigators found significant correlations between CAC and age, duration of dialysis, carotid intimal media thickness, and left ventricular mass. Several bone parameters correlated negatively with CAC, including osteoid surface ( $P < .001$ ), number and size of osteoblasts and osteoclasts ( $P < .05$ ), and activation frequency, which is a measure of bone remodeling activity. On multiple regression linear analysis, the inverse correlation between

osteoid surface and CAC score persisted. "Besides age, dialysis, and diabetes duration, lower osteoid surface seems to be an independent predictive factor for coronary artery calcification," Dr. Asci concluded.

Andrezj Wiecek, MD, who cochaired the session at which these data were presented, noted that there was no mention of the criteria used to define LT. "I think this is fundamental, because then you can select patients for long-term protocols," said Dr. Wiecek, head of the Department of Nephrology, Endocrinology, and Metabolic Diseases at Silesian University School of Medicine in Katowice, Poland. He was not involved in the study.

Hartmut Malluche, MD, a study coauthor and chief of the Division of Nephrology, Bone, and Mineral Metabolism at the University of Kentucky Medical Center in Lexington, replied that activation frequency, which the investigators did measure, is the best reflection of bone turnover because it accounts for bone resorption and formation time.

Dr. Wiecek reports no relevant financial relationships.

European Renal Association–European Dialysis and Transplantation Association 44th Congress: Abstract SaO012. Presented June 23, 2007.

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