Bone Hormone May Predict Mortality in HF

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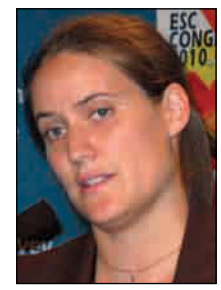
STOCKHOLM – Higher blood levels of the bone hormone osteoprotegerin are linked with a higher long-term risk of death in patients with chronic heart failure, reported Dr. Ragnhild R. Roysland.

The relationship between osteoprotegerin (OPG) and mortality in heart failure is independent of the conventional cardiovascular risk factors, based on a secondary analysis of results of the Italian GISSI-Heart Failure trial.

Osteoprotegerin, a cytokine that's a member of the tumor necrosis factor superfamily, is drawing increasing attention among cardiovascular researchers as a likely key player in what's known as "the calcification paradox." In animal studies, low levels of OPG are associated with decreased skeletal calcification, osteoporosis, and increased calcification of the major arteries. But in recent human studies, increased OPG levels have been linked to a greater atherosclerotic burden; an increased risk of death following acute MI; and now, in GISSI-HF, to increased mortality in the setting of chronic HF, Dr. Roysland said at the congress.

The GISSI-HF study was a randomized clinical trial in which 6,975 Italian patients with chronic heart failure were assigned to rosuvastatin, fish oil, or placebo and followed up for a median of 3.9 years (Lancet 2008;372:1223-30;1231-9). Dr. Roysland presented a new substudy involving 1,229 GISSI-HF participants for whom baseline OPG levels were available.

The aim was to see if baseline OPG was predictive of all-cause mortality. This indeed proved to be the case. During follow-up 332 patients died. The mortality rate was 20% in those in the bottom tertile for baseline OPG with a value less than 1,210 ng/L, and more than twice as great at 45% in patients in the highest tertile, with an OPG of at least 1,923 ng/L. Patients with an intermediate-tertile baseline OPG of 1,210-1,922 ng/L split the difference in terms of mortality, said Dr. Roysland of Akershus University Hospital, Lørenskog, Norway.



Mortality for patients with high OPG levels, at 45%, was more than twice that in patients with low levels, at 20%.

DR. ROYSLAND

Treatment assignment in GISSI-HF did not affect OPG levels. However, if a medication could be identified that reduces OPG levels and attenuates the risk associated with high OPG, then OPG could become an important marker to use in managing chronic HF in clinical practice. There is early evidence that treatments for osteoporosis reduce OPG levels in a non-HF population, but no studies have been done in patients with chronic HF, she said.

Dr. Marco Metra, a member of the ESC congress scientific program committee, said he'd reviewed all the HF studies being presented at the meeting. Two studies in addition to Dr. Roysland's consistently showed that HF patients with high levels of OPG have a poor prognosis. "We know that patients with heart failure have low levels of vitamin D and increased rates of osteoporosis and bone fractures. So the bone is in some way a target of heart failure," said Dr. Metra of the University of Brescia (Italy). ■

Disclosures: *Dr. Roysland said she had no financial conflicts.*