In this subgroup, the MI rate ran 2.5% in women randomized to calcium supplement treatment, and 2.0% among women in the placebo arm, a 22% relative increased MI rate with the calcium supplement that was statistically significant. The rate of MI or stroke ran a relative 16% higher among the women taking the calcium supplement, which was also statistically significant. The results showed no significant effect of calcium supplementation on stroke rate. "We saw the same effect as in the meta-analysis," Dr. Reid said.

But if Dr. Reid's analysis did not start with a prior hypothesis, this finding can only be considered hypothesis generating, not hypothesis testing, Dr. Manson said in an interview. "Many subgroups were tested in the WHI, and some would be expected to show significant effect modification by chance," she pointed out. In addition, randomization made background levels of calcium use similar in the two treatment arms and thereby neutralized background calcium use as a possible confounder. Dr. Manson also noted that if supplemental calcium posed a risk, the event rates should have been highest among women taking both the study calcium dose and an additional dose on their own.

The evidence for an increased MI risk is stronger than the evidence that supplements prevent bone fractures.

DR. REID

When the Auckland researchers added the results from the WHI subanalysis to their previously reported meta-analysis, they "just reinforced the trends and made them more significant," Dr. Reid said in an interview.

When data from the WHI subgroup that did not use personal calcium supplements at baseline were added to the meta-analysis, the results showed that those who did take supplements had a 24% relative excess of MIs, a 15% relative excess of stroke, and a 16% relative excess of MI or stroke, he reported.

There are concerns about 'whether omitting the subgroups with favorable results is appropriate.'

DR. MANSON

"What we now have is six or seven very large trials, and [the results they show] for myocardial infarction all line up very consistently, without significant heterogeneity. When you look at risk vs. benefit, the evidence for an increased risk of myocardial infarction is stronger than the evidence that calcium supplements prevent bone fractures. It's hard to justify continuing calcium supplements," Dr. Reid said. ■

Bone Changes Precede RA Symptoms

Bone metabolism appears to change before patients show clinical signs of rheumatoid arthritis and could ultimately serve as an early marker of disease, based on a study of 79 patients.

"There appears to be an alteration in bone metabolism parallel to inflammation and autoimmunity in the asymptomatic preclinical phase of RA, which may reflect the beginning of joint destruction," according to Dr. Dirkjan van Schaardenburg, a rheumatologist at Jan van Breemen Institute in Amsterdam, and his coinvestigators.

They found significantly increased average levels of only P1NP (procollagen type I intact N-terminal propeptide) and osteoprotegerin in the group of preclinical RA patients, compared with a control group of healthy individuals. Specifically, P1NP increased by 5 ng/mL and osteoprotegerin increased by 4 pmol/L (Ann. Rheum. Dis. 2010 Oct. 18 [doi:10.1136/ard.2010.135723]).

Three blood samples taken 1, 2, and 5 years prior to the onset of symptoms were identified for 47 patients with RA; two samples were collected from 18 patients and one sample was collected from 14 patients. The individuals had been blood donors prior to developing the disease.

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–Kerri Wachter