CORONARY ARTERY DISEASE

Biological ageing—a potentially modifiable risk factor for CAD?

Research conducted in patients with coronary heart disease suggests that increasing dietary intake of marine omega-3 fatty acids could slow cellular ageing. The longitudinal study by Ramin Farzaneh-Far—from the University of California, San Francisco, USA—and colleagues was published in the *Journal of the American Medical Association*.

In eukaryotic cells, the ends of each chromosome are formed of tandem repeat DNA sequences known as telomeres. These structures stabilize the chromosomes and protect them from degradation during cell division. Sections of telomere are progressively lost with each DNA replication; telomere shortening is thus associated with cellular ageing and apoptosis. Other processes, such as inflammation and oxidative stress, have also been proposed to lead to telomere shortening. Telomere length could, therefore, be a marker of biological age, which is different from and independent of chronological age and has previously been associated with cardiovascular morbidity and mortality. “Biological ageing could be understood as a potentially modifiable risk factor” explains Farzaneh-Far. “The next natural step was to study the dynamics of telomere length over time to determine which, if any, factors may be able to halt or slow the process of telomere shortening.

Among [those] considered were omega-3 fatty acids, which have been shown to be effective in secondary prevention [of cardiovascular disease].”

Omega-3 fatty acids have been associated with beneficial effects on lipid levels and blood pressure, as well as the mediation of inflammation and thrombosis. Epidemiological studies indicate that these nutrients also reduce cardiovascular morbidity and mortality. The precise cardioprotective mechanisms of omega-3 fatty acids are not fully understood, but are likely to be multifactorial. The report by Farzaneh-Far *et al.* demonstrates that the rate of telomere shortening is reduced in the presence of high levels of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), suggesting a novel antiageing mechanism for omega-3.

The researchers studied 608 participants of the Heart and Soul Study, which was an investigation of psychosocial risk factors in coronary heart disease. All patients enrolled in the study had evidence of exercise-induced ischemia, a history of myocardial infarction, $\geq 50\%$ stenosis on angiography, or had previously undergone coronary revascularization. Telomere length (from peripheral blood leukocytes) was measured at baseline and at 5-year follow-up. Baseline blood levels of DHA and EPA were also recorded. The mean age of participants was 66 years and 82% were male.

At the time of enrollment, there was no significant correlation between telomere length and omega-3 levels, which tended to be higher among older, better educated, white individuals. By contrast, patients with diabetes mellitus, a history of myocardial infarction, current smokers, and those with elevated triglyceride levels had the lowest levels of DHA and EPA. The rate of telomere shortening over 5 years was significantly faster among individuals in the lowest omega-3 quartile when compared with the highest quartile. The

odds of telomere shortening was reduced by 19% for each individual standard deviation increase in log DHA and EPA levels. This association persisted, and increased to 32%, after adjustment for confounding variables related to the other biological effects of omega-3, “suggesting that one or more novel pathways may be involved” says Farzaneh-Far. Interestingly, patients with the longest telomeres at baseline seemed to ‘benefit’ the most from high levels of omega-3.

The investigators postulate that the link between increased levels of omega-3 and the reduced rate of telomere shortening could result from attenuation of oxidative stress, increased expression of telomerase—the enzyme that forms and maintains telomeres after DNA replication—or both.

The observational design of this study precludes the investigators from drawing any conclusions about whether increased levels of omega-3 actually cause deceleration in the rate of telomere shortening and their findings should, therefore, be considered as hypothesis generating rather than definitive. Farzaneh-Far comments that “a double-blind, randomized, placebo-controlled trial will be necessary [to establish causality]” and this is something that the research group is interested in pursuing.

Although promising, Farzaneh-Far cautions that the findings do not provide the impetus for changing the treatment or advice given to patients with coronary heart disease. He believes that physicians should continue to follow the AHA’s recommendation that “patients with established coronary artery disease should take 1 g of omega-3 fatty acids daily, either through diet or supplements.”

Alexandra King

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