Association of Marine Omega-3 Fatty Acid Levels With Telomeric Aging in Patients With Coronary Heart Disease

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NOTE FROM DAN MURPHY:
Elizabeth Blackburn, from the Department of Biochemistry and Biophysics, University of California, San Francisco, was awarded the Nobel Prize in Medicine/Physiology, October 2009, for her work pertaining to telomeres.

FROM ABSTRACT:

Context—Increased dietary intake of marine omega-3 fatty acids is associated with prolonged survival in patients with coronary heart disease. However, the mechanisms underlying this protective effect are poorly understood.

Objective—To investigate the association of omega-3 fatty acid blood levels with temporal changes in telomere length, an emerging marker of biological age.

Design, Setting, and Participants—Prospective cohort study of 608 ambulatory outpatients in California with stable coronary artery disease recruited from the Heart and Soul Study between September 2000 and December 2002 and followed up to January 2009 (median, 6.0 years; range, 5.0-8.1 years).

Main Outcome Measures—We measured leukocyte telomere length at baseline and again after 5 years of follow-up. Multivariable linear and logistic regression models were used to investigate the association of baseline levels of omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) with subsequent change in telomere length.

Results—Individuals in the lowest quartile of DHA+EPA experienced the fastest rate of telomere shortening, whereas those in the highest quartile experienced the slowest rate of telomere shortening.

Levels of DHA+EPA were associated with less telomere shortening before and after sequential adjustment for established risk factors and potential confounders.

Each 1-SD(standard deviation) increase in DHA+EPA levels was associated with a 32% reduction in the odds of telomere shortening.

Conclusion—Among this cohort of patients with coronary artery disease, there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years.

THESE AUTHORS ALSO NOTE:

"Multiple epidemiologic studies, including several large randomized controlled trials, have demonstrated higher survival rates among individuals with high dietary intake of marine omega-3 fatty acids and established cardiovascular disease."

"The American Heart Association recommends increased oily fish intake and the use of omega-3 fatty acid supplements for the primary and secondary prevention of coronary heart disease."

Omega-3 fatty acids are cardio-protective for several reasons, including:

A)) Anti-inflammatory
B)) Anti-platelet
C)) Anti-hypertensive
D)) Anti-arrhythmic
E)) Triglyceride-lowering
F)) Telomere lengthening

Telomeres are tandem repeat DNA sequences (TTAGGG) that form a protective cap at the ends of chromosomes. During somatic cell division there is a progressive loss of telomeric repeats. "This process may eventually result in cellular senescence [state of being old; the process of becoming old] or apoptosis [cell death]."

Telomere length is emerging as a marker of biological age, integrating the "cumulative lifetime burden of genetic factors and environmental stressors independent of chronological age."

It is known that telomeres may lengthen as well as shorten.

RESULTS

Each 1-SD increase in omega-3 fatty acid levels was associated with a 32% decrease in the odds of telomere shortening. This was independent of sex, race/ethnicity, smoking, income, education, or type 2 diabetes.

COMMENT FROM AUTHORS

"Leukocyte telomere length is an emerging marker of biological age that independently predicts morbidity and mortality."

"Baseline levels of marine omega-3 fatty acids were associated with decelerated telomere attrition over 5 years. The association was linear and persisted after adjustment for potential confounders. These findings raise the possibility that omega-3 fatty acids may protect against cellular aging in patients with coronary heart disease."

Longer telomeres are also linked to taking nutritional supplements, including multivitamins, vitamin C, vitamin D, vitamin E, and folic acid.

"Omega-3 fatty acids exert direct effects on aging and age-related diseases."

Omega-3 fatty acid supplementation:
A)) Reduces vascular stiffness
B)) Slows age-related cognitive decline
C)) Reduces age-related macular degeneration

In animals, "dietary enrichment with omega-3 fatty acids prolongs life span by approximately one-third."

"The present findings identify deceleration of telomere attrition as a potentially novel pathway for the anti-aging effects of marine omega-3 fatty acids."

Oxidative stress is a powerful driver of telomere shortening and aging.

Supplementation with omega-3 fatty acids has been associated with lower levels of systemic oxidative stress, and with higher levels of the antioxidant enzymes catalase and superoxide dismutase.

Omega-3 fatty acid levels may decelerate telomere attrition by increasing activity of the enzyme telomerase. "Daily supplementation with 3 g of omega-3 fish oil was associated with a significant increase in telomerase activity."

Other factors that cumulatively determine telomere length throughout life include:
A)) Systemic inflammation
B)) Obesity
C)) Oxidative stress
D)) Lack of physical activity

"In summary, among patients with stable coronary artery disease, there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years."

KEY POINTS FROM DAN MURPHY
BACKGROUND FROM DAN MURPHY

In 1953, Leonard Hayflick, PhD from the University of California, San Francisco, discovered that human cells divided about 50 times, and then die. This is known as the *Hayflick limit*. Dr. Hayflick continues to research and publish on human aging and longevity.

About 30 years ago, scientists discovered the reason for the *Hayflick limit* was *telomeres*. *Telomeres* are short caps of DNA on the ends of chromosomes. Each time the cell divides, the *telomere* shortens a little. When most of the *telomere* disappears, the cell dies. Consequently, *telomere* length has been proposed as a marker of biological aging.

1) Telomeres are tandem repeat DNA sequences (TTAGGG) that form a protective cap at the ends of chromosomes. During somatic cell division there is a progressive loss of telomeric repeats. "This process may eventually result in cellular senescence [state of being old; the process of becoming old] or apoptosis [cell death]."

2) Telomere length is emerging as a marker of biological age, integrating the "cumulative lifetime burden of genetic factors and environmental stressors independent of chronological age."

3) "Telomere length is an emerging marker of biological age that independently predicts morbidity and mortality."

4) "Increased dietary intake of marine omega-3 fatty acids is associated with prolonged survival in patients with coronary heart disease."

5) "Multiple epidemiologic studies, including several large randomized controlled trials, have demonstrated higher survival rates among individuals with high dietary intake of marine omega-3 fatty acids and established cardiovascular disease."

6) "The American Heart Association recommends increased oily fish intake and the use of omega-3 fatty acid supplements for the primary and secondary prevention of coronary heart disease."

7) Omega-3 fatty acids are cardio-protective for several reasons, including:

A)) Anti-inflammatory
B)) Anti-platelet
C)) Anti-hypertensive
D)) Anti-arrhythmic
E)) Triglyceride-lowering
F)) Telomere lengthening

8) For each 1-Standard Deviation increase in omega-3 fatty acid levels there was an associated 32% increase in the telomeres.

9) "Baseline levels of marine omega-3 fatty acids were associated with decelerated telomere attrition over 5 years. The association was linear and persisted after adjustment for potential confounders. These findings raise the possibility that omega-3 fatty acids may protect against cellular aging in patients with coronary heart disease."

10) Longer telomeres are also linked to taking nutritional supplements, including multivitamins, vitamin C, vitamin D, vitamin E, and folic acid.

11) "Omega-3 fatty acids exert direct effects on aging and age-related diseases."

12) Omega-3 fatty acid supplementation:

A)) Reduces vascular stiffness
B)) Slows age-related cognitive decline
C)) Reduces age-related macular degeneration

13) In animals, "dietary enrichment with omega-3 fatty acids prolongs life span by approximately one-third."

14) "The present findings identify deceleration of telomere attrition as a potentially novel pathway for the anti-aging effects of marine omega-3 fatty acids."

15) Oxidative stress is a powerful driver of telomere shortening and aging.

16) Supplementation with omega-3 fatty acids has been associated with lower levels of systemic oxidative stress, and with higher levels of the antioxidant enzymes catalase and superoxide dismutase.

17) Omega-3 fatty acid levels may decelerate telomere attrition by increasing activity of the enzyme telomerase. "Daily supplementation with 3 g of omega-3 fish oil was associated with a significant increase in telomerase activity."

18) Other factors that cumulatively determine telomere length throughout life include:

A)) Systemic inflammation
B)) Obesity
C)) Oxidative stress
D)) Lack of physical activity

19) "In summary, among patients with stable coronary artery disease, there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years."