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THE ASSOCIATION BETWEEN LOWER LEVELS OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL AND CANCER PREDATES THE DIAGNOSIS OF CANCER BY 18 YEARS

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Background: We recently reported, in a meta-analysis of statin trials, a strong association between low concentrations of low-density lipoprotein cholesterol (LDL-C) and incident cancer risk. Interpretation of these data has been a point of significant debate. At issue is whether low LDL-C concentration signifies a predisposition to cancer development, or rather results from the presence of even a subclinical neoplastic process (reverse causality). Of pivotal importance to this debate is the duration of low LDL-C levels prior to cancer diagnosis. We explored this controversy using data from the Framingham Heart Study Offspring Cohort to assess the trend of LDL-C for an extended period prior to cancer diagnosis.

Methods: Incident cancer cases and control subjects (propensity score matched for age, gender, diabetes, tobacco use, blood pressure, and body mass index) without history of lipid-lowering therapy, were followed for 4 time points prior to cancer diagnosis. Linear mixed model regression analyses delineated the relationship of LDL-C between cancer and cancer-free participants over time.

Results: 201 incident cancer cases and 402 matched controls were identified. LDL-C values were lower in cancer subjects than matched controls at each point of assessment throughout an average of 18.7 years prior to diagnosis (F = 4.32, p = .038). The trend for lower LDL-C in cancer patients compared with control subjects was consistent throughout the duration of the study (F = .14, p = .968 for differences between time points). These findings did not change when controlling for high-density lipoprotein cholesterol levels.

Conclusion: Our analysis demonstrates an inverse association between LDL-C and cancer extending over 18 years prior to diagnosis. This is inconsistent with the reverse causality hypothesis, but rather supports that low levels of LDL-C can predate cancer diagnosis by decades. While not itself indicative of an etiologic role for LDL-C in predisposition to cancer, these findings underscore the need for further study in this area, particularly in light of current LDL-C lowering guidelines.