Letter to the Editor

Cancer Epidemiology, Biomarkers & Prevention

Telomere Length and Pancreatic Cancer Risk—Reply

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Our report (1) showed that genetic risk scores computed from polymorphic variants previously associated with interindividual variation in leukocyte telomere length (2–4) are not associated with risk of pancreatic cancer (pancreatic ductal adenocarcinoma). Consistent with our finding, a recent meta-analysis that used methods similar to ours (published while our manuscript was under review) found no association between genetically predicted telomere length and pancreatic cancer risk (5). We are not aware of any other published reports on the association between genetically predicted telomere length and pancreatic cancer risk.

The author referred to a study by Lynch and colleagues (6) and others (7, 8) and concluded that longer telomere length is associated with an increase in risk of pancreatic cancer. We would like to point out that while Lynch and colleagues directly measured leukocyte telomere length using monochrome quantitative multiplex PCR (6), we used genotypes to predict telomere length, as has been done by others (5, 9). Therefore, the two studies are not directly comparable. Measured telomere length reflects inherited genetic factors, aging, lifestyle (e.g., tobacco smoking), and chronic conditions, such as diabetes mellitus (10). Our study sought to delineate the role of the genetic component alone, which is estimated to account for up to 80% of interindividual differences in telomere length (10). The study by Lynch and colleagues would have reflected the genetic and the environmental components, age-related telomere attrition, and effect of other exposures that influence telomere length. It should be noted, however, that results from studies involving measured leukocyte telomere length have varied widely.

In contrast to Lynch and colleagues, who studied Finnish males who smoked five or more cigarettes a day (6), Bao and colleagues recently performed a pooled analysis of five prospective studies in the United States and found that short, rather than long, leukocyte telomere length is associated with an increase in risk of pancreatic cancer in a dose–response fashion (11). Furthermore, a prospective cohort study in China found a "U-shaped" association between leukocyte telomere length and pancreatic cancer risk (12), as did a clinic-based case–control in the United States (13). A study of the European Prospective Investigation into Cancer and Nutrition (EPIC) found no significant association between leukocyte telomere length and pancreatic cancer; however, in a secondary analysis using cubic spline regression, the investigators found evidence for a nonlinear relationship (14).

Although it is plausible that leukocyte telomere length represents an integrative molecular marker of exposure to risk factors for pancreatic cancer, the current evidence precludes definitive conclusions. Potential reasons for the discrepancy in study findings have been discussed (1). We agree that the potential roles of telomerase and survivin in telomere lengthening and inhibition of apoptosis to promote carcinogenesis should be explored further in both tumor- and blood-based studies for new insights into telomere dynamics in pancreatic cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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