Sender's message: Long telomeres increase the risk of cancer as determined by measuring telomere lengths

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1. Carcinogenesis. 2017 Apr 1;38(4):439-446. doi: 10.1093/carcin/bgx021.

Prospective and longitudinal evaluations of telomere length of circulating DNA as a risk predictor of hepatocellular carcinoma in HBV patients.

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Abstract

Prospective and longitudinal epidemiological evidence is needed to assess the association between telomere length and risk of hepatocellular carcinoma (HCC). In 323 cancer-free Korean-American HBV patients with 1-year exclusion window (followed for >1 year and did not develop HCC within 1 year), we measured the relative telomere length (RTL) in baseline serum DNAs and conducted extensive prospective and longitudinal analyses to assess RTL-HCC relationship. We found that long baseline RTL conferred an increased HCC risk compared to short RTL [hazard ratio (HR) = 4.93, P = 0.0005). The association remained prominent when the analysis was restricted to patients with a more stringent 5-year exclusion window (HR = 7.51, P = 0.012), indicating that the association was unlikely due to including undetected HCC patients in the cohort, thus minimizing the reverse-causation limitation in most retrospective studies. Adding baseline RTL to demographic variables increased the discrimination accuracy of the time-dependent receiver operating characteristic analysis from 0.769 to 0.868 (P = 1.0 × 10-5). In a nested longitudinal subcohort of 16 matched cases-control pairs, using a mixed effects model, we observed a trend of increased RTL in cases and decreased RTL in controls along 5 years of follow-up, with a significant interaction of case/control status with time (P for interaction=0.002) and confirmed the association between long RTL and HCC risk [odds ratio [OR] = 3.63, P = 0.016]. In summary, serum DNA RTL may be a novel non-invasive prospective marker of HBV-related HCC. Independent studies are necessary to validate and generalize this finding in diverse populations and assess the clinical applicability of RTL in HCC prediction.

PMID: 28334112 [Indexed for MEDLINE]

Similar articles

2. Carcinogenesis. 2015 Nov;36(11):1327-32. doi: 10.1093/carcin/bgv133. Epub 2015 Sep 18.

Association of leukocyte telomere length in peripheral blood leukocytes with endometrial cancer risk in Caucasian Americans.

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Abstract

Telomeres are the protective structure at the ends of each chromosome and play an important role in maintaining genomic integrity. Interindividual variation of telomere length in peripheral blood leukocytes has been associated with the risks of developing many human diseases including several cancers. The association between leukocyte telomere length (LTL) and endometrial cancer risk is still inconsistent. Using a case-control study of endometrial cancer patients (n = 139) and control subjects (n = 139) in a Caucasian population, we assessed the association of relative LTL with the risk of endometrial cancer. We calculated odds ratios and 95% confidence intervals using multivariate logistic regression. We also determined the joint effects of LTL with established risk factors of endometrial cancer. The normalized LTL was significantly longer in endometrial cancer cases (median, 0.93; range, 0.19-1.62) than in controls (median, 0.70; range, 0.03-2.14) ($P < 0.001$). When individuals were dichotomized into long and short groups based on the median LTL value in the controls, individuals with long LTL had a significantly increased risk of endometrial cancer (adjusted OR, 3.84; 95%CI, 2.16-6.85; $P < 0.001$) compared to those with short LTL. When individuals were categorized into three groups or four groups according to tertile or quartile LTL value in the controls, there was a significant dose-response association between LTL and the risk of endometrial cancer ($P < 0.001$). Joint effects between LTL and smoking status, body mass index and a history of hypertension or diabetes in elevating endometrial cancer risk were observed. Long telomere length in peripheral blood leukocytes is associated with a significantly increased risk of endometrial cancer.

PMID: 26385889 [Indexed for MEDLINE]
Similar articles

3. Carcinogenesis. 2015 Nov;36(11):1284-90. doi: 10.1093/carcin/bgv121. Epub 2015 Sep 5.

Strong association between long and heterogeneous telomere length in blood lymphocytes and bladder cancer risk in

Egyptian.

Wang H[1], Wang Y[2], Kota KK[2], Kallakury B[3], Mikhail NN[4], Sayed D[4], Mokhtar A[4], Maximous D[4], Yassin EH[4], Gouda I[5], Sobitan A[2], Sun B[2], Loffredo CA[6], Zheng YL[7].

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Abstract

Although it is widely recognized that telomere dysfunction plays an important role in cancer, the relationship between telomere function and bladder cancer risk is not well defined. In a case-control study of bladder cancer in Egypt, we examined relationships between two telomere features and bladder cancer risk. Telomere fluorescent in situ hybridization was used to measure telomere features using short-term cultured blood lymphocytes. Logistic regression was used to estimate the strength of association between telomere features and the risk of urothelial carcinoma of the bladder. High telomere length variation (TLV) across all chromosomal ends was significantly associated with an increased risk of bladder cancer [adjusted odds ratios (OR) = 2.22, 95% confidence interval (CI) = 1.48-3.35], as was long average telomere length (OR = 3.19, 95% CI = 2.07, 4.91). Further, TLV and average telomere length jointly affected bladder cancer risk: when comparing individuals with long telomere length and high TLV to those with short telomere length and low TLV, the adjusted OR was 14.68 (95% CI: 6.74-31.98). These associations were stronger among individuals who are 60 years of age or younger. In summary, long and heterogeneous telomere length in blood lymphocytes was strongly associated with an increased bladder cancer risk in Egyptian and the association was modulated by age.

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4. Br J Cancer. 2015 Feb 17;112(4):769-76. doi: 10.1038/bjc.2014.640. Epub 2015 Jan 6.

Circulating leukocyte telomere length and risk of overall and aggressive prostate cancer.

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Abstract

BACKGROUND:

Recent large-scale prospective studies suggest that long telomeres are associated with an increase cancer risk, counter to conventional wisdom.

METHODS:

To further clarify the association between leukocyte telomere length (LTL) and prostate cancer, and assess genetic variability in relation to both LTL and prostate cancer, we performed a nested case-control study (922 cases and 935 controls). The participants provided blood in 1993-1995 and were followed through August 2004 (prostate cancer incidence) or until 28 February 2013 (lethal or fatal prostate cancer). Relative LTL was measured by quantitative PCR and was calculated as the ratio of telomere repeat copy number to a single gene (36B4) copy number (T/S). Genotyping was performed using the TaqMan OpenArray SNP Genotyping Platform. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of all prostate cancer and subtypes defined by Gleason grade, stage and lethality (metastasis or death).

RESULTS:

We observed a positive association between each s.d. increase in LTL and all (multivariable-adjusted OR 1.11, 95% CI: 1.01-1.22), low-grade (OR 1.13, 95% CI:1.01-1.27), and localised (OR 1.12, 95% CI:1.01-1.24) prostate cancer. Associations for other subtypes were similar, but did not reach statistical significance. In subgroup analyses, associations for high grade and advanced stage (OR=2.04, 95% CI 1.00-4.17; Pinteraction=0.06) or lethal disease (OR=2.37, 95% CI 1.19-4.72; Pinteraction=0.01) were stronger in men with a family history of the disease compared with those without. The minor allele of SNP, rs7726159, which has previously been shown to be positively associated with LTL, showed an inverse association with all prostate cancer risk after correction for multiple testing (P=0.0005).

CONCLUSION:

In this prospective study, longer LTL was modestly associated with higher risk of prostate cancer. A stronger association for more aggressive cancer in men with a family history of the

disease needs to be confirmed in larger studies.

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