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Sender's message: Short Telomeres Increase the Risk of Cancer as determined by measurement of telomere lengths.

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42 selected items

PubMed Results

Items 1 -42 of 42 (Display the 42 citations in PubMed)

1. Am J Epidemiol. 2017 Apr 28:1-10. doi: 10.1093/aje/kww210. [Epub ahead of print]

Leukocyte Telomere Length and All-Cause, Cardiovascular Disease, and Cancer Mortality: Results From Individual-Participant-Data Meta-Analysis of 2 Large Prospective Cohort Studies.

Mons U, Müezzinler A, Schöttker B, Dieffenbach AK, Butterbach K, Schick M, Peasey A, De Vivo I, Trichopoulou A, Boffetta P, Brenner H.

Abstract

We studied the associations of leukocyte telomere length (LTL) with all-cause, cardiovascular disease, and cancer mortality in 12,199 adults participating in 2 population-based prospective cohort studies from Europe (ESTHER) and the United States (Nurses' Health Study). Blood samples were collected in 1989-1990 (Nurses' Health Study) and 2000-2002 (ESTHER). LTL was measured by quantitative polymerase chain reaction. We calculated z scores for LTL to standardize LTL measurements across the cohorts. Cox proportional hazards regression models were used to calculate relative mortality according to continuous levels and quintiles of LTL z scores. The hazard ratios obtained from each cohort were subsequently pooled by meta-analysis. Overall, 2,882 deaths were recorded during follow-up (Nurses' Health Study, 1989-2010; ESTHER, 2000-2015). LTL was inversely associated with age in both cohorts. After adjustment for age, a significant inverse trend of LTL with all-cause mortality was observed in both cohorts. In random-effects meta-analysis, age-adjusted hazard ratios for the shortest LTL quintile compared with the longest were 1.23 (95% confidence interval (CI): 1.04, 1.46) for all-cause mortality, 1.29 (95% CI: 0.83, 2.00) for cardiovascular mortality, and 1.10 (95% CI: 0.88, 1.37) for cancer mortality. In this study population with an age range of 43-75 years, we corroborated previous evidence suggesting that LTL predicts all-cause mortality beyond its association with age.

PMID: 28459963
Similar articles

2. Oncotarget. 2017 Mar 28;8(13):21472-21482. doi: 10.18632/oncotarget.15592.

Critically short telomeres and toxicity of chemotherapy in early breast cancer.

Quintela-Fandino M[1], Soberon N[2], Lluch A[3], Manso L[4], Calvo I[5], Cortes J[6,7], Moreno-Antón F[8], Gil-Gil M[9], Martinez-Jánez N[7], Gonzalez-Martin A[10], Adrover E[11], de Andres R[12], Viñas G[13], Llombart-Cussac A[14], Alba E[15], Mouron S[1], Guerra J[16], Bermejo B[3], Zamora E[6], García-Saenz JA[8], Simon SP[9], Carrasco E[17], Escudero MJ[17], Campo R[17], Colomer R[18], Blasco MA[2].

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Abstract

Cumulative toxicity from weekly paclitaxel (myalgia, peripheral neuropathy, fatigue) compromises long-term administration. Preclinical data suggest that the burden of critically short telomeres (< 3 kilobases, CSTs), but not average telomere length by itself, accounts for limited tissue renewal and turnover capacity. The impact of this parameter (which can be modified with different therapies) in chemotherapy-derived toxicity has not been studied.Blood from 115 treatment-naive patients from a clinical trial in early HER2-negative breast cancer that received weekly paclitaxel (80 mg/m2 for 12 weeks) either alone or in combination with nintedanib and from 85 healthy controls was prospectively obtained and individual CSTs and average telomere lenght were determined by HT Q-FISH (high-throughput quantitative FISH). Toxicity was graded according to NCI common toxicity criteria for adverse events (NCI CTCAE V.4.0). The variable under study was "number of toxic episodes" during the 12 weeks of therapy.The percentage of CSTs ranged from 6.5%-49.4% and was directly associated with the number of toxic events ($R2 = 0.333$; $P < 0.001$). According to a linear regression model, each 18% increase in the percentage of CSTs was associated to one additional toxic episode during the paclitaxel cycles; this effect was independent of the age or treatment arm. Patients in the upper quartile (> 21.9% CSTs) had 2-fold higher number of neuropathy ($P = 0.04$) or fatigue ($P = 0.019$) episodes and >3-fold higher number of myalgia episodes ($P = 0.005$). The average telomere length was unrelated to the incidence of side effects.The percentage of CSTs, but not the average telomere size, is associated with weekly paclitaxel-derived toxicity.

PMCID: PMC5400599 **Free PMC Article**
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3. PLoS One. 2017 Mar 31;12(3):e0174833. doi: 10.1371/journal.pone.0174833. eCollection 2017.

Extensive telomere erosion is consistent with localised clonal expansions in Barrett's metaplasia.

Letsolo BT[1], Jones RE[1], Rowson J[1], Grimstead JW[1], Keith WN[2], Jenkins GJ[3], Baird DM[1].

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Abstract

Barrett's oesophagus is a premalignant metaplastic condition that predisposes patients to the development of oesophageal adenocarcinoma. However, only a minor fraction of Barrett's oesophagus patients progress to adenocarcinoma and it is thus essential to determine bio-molecular markers that can predict the progression of this condition. Telomere dysfunction is considered to drive clonal evolution in several tumour types and telomere length analysis provides clinically relevant prognostic and predictive information. The aim of this work was to use high-resolution telomere analysis to examine telomere dynamics in Barrett's oesophagus. Telomere length analysis of XpYp, 17p, 11q and 9p, chromosome arms that contain key cancer related genes that are known to be subjected to copy number changes in Barrett's metaplasia, revealed similar profiles at each chromosome end, indicating that no one specific telomere is likely to suffer preferential telomere erosion. Analysis of patient matched tissues (233 samples from 32 patients) sampled from normal squamous oesophagus, Z-line, and 2 cm intervals within Barrett's metaplasia, plus oesophago-gastric junction, gastric body and antrum, revealed extensive telomere erosion in Barrett's metaplasia to within the length ranges at which telomere fusion is detected in other tumour types. Telomere erosion was not uniform, with distinct zones displaying more extensive erosion and more homogenous telomere length profiles. These data are consistent with an extensive proliferative history of cells within Barrett's metaplasia and are indicative of localised clonal growth. The extent of telomere erosion highlights the potential of telomere dysfunction to drive genome instability and clonal evolution in Barrett's metaplasia.

PMCID: PMC5375150 **Free PMC Article**
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4. Cancer Epidemiol Biomarkers Prev. 2017 Feb 24. pii: cebp.0946.2016. doi: 10.1158/1055-9965.EPI-16-0946. [Epub ahead of print]

Telomere length is predictive of breast cancer risk in BRCA2 mutation carriers.

Thorvaldsdottir B[1], Aradottir M[1], Stefansson OA[1], Bodvarsdottir SK[1], Eyfjörd JE[2].

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Abstract

BACKGROUND:

Germline BRCA2 mutations increase risk of breast cancer and other malignancies. BRCA2 has been shown to play a role in telomere protection and maintenance. Telomere length (TL) has been studied as a modifying factor for various diseases, including breast cancer. Previous research on TL in BRCA mutation carriers has produced contradicting results.

METHODS:

We measured blood TL, using a high-throughput monochrome multiplex qPCR method, in a well-defined Icelandic cohort of female BRCA2 mutation carriers (n=169), sporadic breast cancer patients (n=561) and healthy controls (n=537).

RESULTS:

Breast cancer cases had significantly shorter TL than unaffected women ($p<0.0001$), both BRCA2 mutation carriers ($p=0.0097$) and non-carriers ($p=0.00006$). Using exclusively samples acquired before breast cancer diagnosis, we found that shorter telomeres were significantly associated with increased breast cancer risk in BRCA2 mutation carriers (HR = 3.60, 95% CI 1.17-11.28, $p=0.025$) but not in non-carriers (HR = 1.40, 95% CI 0.89-2.22, $p=0.15$). We found no association between TL and breast cancer specific survival.

CONCLUSIONS:

Blood TL is predictive of breast cancer risk in BRCA2 mutation carriers. Breast cancer cases have significantly shorter TL than unaffected women, regardless of BRCA2 status, indicating that samples taken after breast cancer diagnosis should not be included in evaluations of TL and breast cancer risk.

IMPACT:

Our study is built on a well-defined cohort, highly accurate methods and long follow-up and can therefore help to clarify some previously published, contradictory results. Our findings also suggest that BRCA2 has an important role in telomere maintenance, even in normal blood cells.

PMID: 28235830
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5. Cancer Epidemiol Biomarkers Prev. 2017 Mar;26(3):339-345. doi: 10.1158/1055-9965.EPI-16-0466. Epub 2017 Feb 16.

Prediagnosis Leukocyte Telomere Length and Risk of Ovarian Cancer.

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Abstract

Background: The associations between telomere length and cancer risk are equivocal, and none have examined the association between prediagnosis leukocyte telomere length (LTL) and the risk of developing ovarian cancer.**Methods:** We prospectively measured LTL collected from 442 ovarian cancer cases and 727 controls in the Nurses' Health Studies and the Northern Sweden Health and Disease Study. Cases were matched to one or two controls on age, menopausal status, and date of blood collection. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using conditional logistic regression.**Results:** LTL was measured a median of 9.5 years before ovarian cancer diagnosis among cases. We observed a decreased risk of ovarian cancer with longer LTL. In multivariable models, women in the top quartile of LTL had an OR for ovarian cancer of 0.67 (95% CI, 0.46-0.97) compared with those in the bottom quartile. Inverse associations were stronger for nonserous cases ($OR_{\text{quartile 4 vs. quartile 1 of LTL}}$ = 0.55, 95% CI, 0.33-0.94) and rapidly fatal cases (i.e., cases who died within 3 years of diagnosis; $OR_{\text{quartile 4 vs. quartile 1 of LTL}}$ = 0.55, 95% CI, 0.32-0.95).**Conclusions:** Our prospective findings suggest that longer circulating LTL may be associated with a lower ovarian cancer risk, especially for nonserous and rapidly fatal cases. The evaluation of LTL in relation to ovarian cancer risk by tumor subtypes is warranted in larger prospective studies.**Impact:** Prediagnosis LTL may reflect an early event in the ovarian cancer development and could serve as a biomarker to predict future risk. *Cancer Epidemiol Biomarkers Prev; 26(3); 339-45. ©2017 AACR.*

PMCID: PMC5336400 [Available on 2018-03-01]
PMID: 28209595
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6. Iran Biomed J. 2016 Nov 22.Pii-IBJ-A-10-2008-1. [Epub ahead of print]

Is Leukocyte Telomere Length Related with Lung Cancer Risk?: A Meta-Analysis.

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Abstract

BACKGROUND:

Epidemiological studies have probed the correlation between telomere length and the risk of lung cancer, but their findings are inconsistent in this regard. The present meta-analysis study has been carried out to demonstrate the association between relative telomere length in peripheral blood leukocytes and the risk of lung cancer using an established Q-PCR technique.

METHODS:

A systematic search was carried out using PubMed, EMBASE, and ISI before 2015. A total of 2925 cases of lung cancer and 2931 controls from 9 studies were employed to probe the relationship between lung cancer and telomere length .ORs were used at 95% CI. Random-effects models were used to investigate this relationship based on the heterogeneity test. Heterogeneity among studies was analyzed employing subgroup analysis based on type studies and the year of publication.

RESULTS:

Random-effects meta-analysis revealed that patients with lung cancer were expected to have shorter telomere length than the control (1.13, 95% CI: 0.82-1.81, P=0.46). The summary of the pooled ORs of telomere length in adenocarcinoma lung cancer patients was 1 (95%CI=0.68-1.47, I2=93%) compared to patients with squamous cell lung cancer, which was 1.78 (95% CI=1.25-2.53, I2=3.9%). The meta-regression revealed that the effect of telomere length shortening, decreased and increased with the year of publication and the age of risks to lung cancer, was clearly related to short telomeres lengths.

CONCLUSION:

Lung cancer risks clearly related with short telomeres lengths. In patients with breathing problems, lung cancer risk can be predicted by telomere length adjustment with age, sex, and smoking.

Free Article

PMID: 27874106

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7. Carcinogenesis. 2017 Jan;38(1):12-18. doi: 10.1093/carcin/bgw111. Epub 2016 Oct 24.

Short leukocyte telomere length, alone and in combination with smoking, contributes to increased risk of gastric cancer or esophageal squamous cell carcinoma.

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Abstract

In humans, telomeres shorten along with division of somatic cells. Shortened telomere length might result in genomic instability and has been associated with several malignancies. However, the findings in different populations remain conflicting. Therefore, we assessed the association of telomere length in peripheral blood leukocytes with risk of gastric cancer (GC) or esophageal squamous cell carcinoma (ESCC) in a Chinese Han population. A total of 574 GC cases, 740 ESCC cases and 774 age- and sex-matched healthy controls were included in this analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression. The GC or ESCC patients had significantly shorter relative telomere length (RTL)

(median ± SD: GC: 1.20 ± 0.42; ESCC: 1.27 ± 0.48) than controls (1.41 ± 0.58). Four-fold increased GC risk (OR = 4.10, 95% CI = 2.78-6.05, P = 1.10×10^{-12}) or 1.56-fold increased ESCC risk (95% CI = 1.12-2.18, P = 0.009) among subjects in the shortest quartile of telomere length was found compared with the highest quartile. We also observed a cumulative effect between short RTL and smoking in intensifying risk of GC (P = 4.50×10^{-9}) or ESCC (P = 5.92×10^{-33}). Moreover, there were cumulative effects between RTL, smoking and drinking in elevating risk of GC (P_{trend} = 0.001) or ESCC (P_{trend} = 1.57×10^{-32}). Interestingly, RTL-related rs621559 and rs398652 genetic variants are significantly associated with GC risk. These results indicate that short RTL is involved in susceptibility to developing GC or ESCC, alone and in a gene-environment interaction manner. Short telomere length might be a potential molecular marker, in combination with lifestyle risk factors, to identify high-risk individuals.

PMID: 27797826

Similar articles

8. Gut. 2016 Oct 21. pii: gutjnl-2016-312510. doi: 10.1136/gutjnl-2016-312510. [Epub ahead of print]

Leucocyte telomere length, genetic variants at the TERT gene region and risk of pancreatic cancer.

Bao Y[1], Prescott J[1], Yuan C[2,3], Zhang M[4], Kraft P[2,5], Babic A[3], Morales-Oyarvide V[3], Qian ZR[3], Buring JE[6,7], Cochrane BB[8], Gaziano JM[6,9], Giovannucci EL[1,2,10], Manson JE[1,2,6], Ng K[3], Ogino S[2,3,11], Rohan TE[12], Sesso HD[2,6], Stampfer MJ[1,2,10], Fuchs CS[1,3], De Vivo I[1,2], Amundadottir LT[4], Wolpin BM[3,13].

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Abstract

OBJECTIVE:

Telomere shortening occurs as an early event in pancreatic tumorigenesis, and genetic variants at the telomerase reverse transcriptase (TERT) gene region have been associated with pancreatic cancer risk. However, it is unknown whether prediagnostic leucocyte telomere length is associated with subsequent risk of pancreatic cancer.

DESIGN:

We measured prediagnostic leucocyte telomere length in 386 pancreatic cancer cases and 896 matched controls from five prospective US cohorts. ORs and 95% CIs were calculated using conditional logistic regression. Matching factors included year of birth, cohort (which also matches on sex), smoking status, fasting status and month/year of blood collection. We additionally examined single-nucleotide polymorphisms (SNPs) at the TERT region in relation to pancreatic cancer risk and leucocyte telomere length using logistic and linear regression, respectively.

RESULTS:

Shorter prediagnostic leucocyte telomere length was associated with higher risk of pancreatic cancer (comparing extreme quintiles of telomere length, OR 1.72; 95% CI 1.07 to 2.78; p_{trend}=0.048). Results remained unchanged after adjustment for diabetes, body mass index and physical activity. Three SNPs at TERT (linkage disequilibrium r^2<0.25) were associated with pancreatic cancer risk, including rs401681 (per minor allele OR 1.33; 95% CI 1.12 to 1.59; p=0.002), rs2736100 (per minor allele OR 1.36; 95% CI 1.13 to 1.63; p=0.001) and rs2736098 (per minor allele OR 0.75; 95% CI 0.63 to 0.90; p=0.002). The minor allele for rs401681 was associated with shorter telomere length (p=0.023).

CONCLUSIONS:

Prediagnostic leucocyte telomere length and genetic variants at the TERT gene region were associated with risk of pancreatic cancer.

PMID: 27797938
Similar articles

9. Tumour Biol. 2016 Sep;37(9):11917-11926. Epub 2016 Apr 12.

Shorter telomeres and high telomerase activity correlate with a highly aggressive phenotype in breast cancer cell lines.

Ceja-Rangel HA[1,2], Sánchez-Suárez P[2], Castellanos-Juárez E[2], Peñaroja-Flores R[2], Arenas-Aranda DJ[3], Gariglio P[4], Benítez-Bribiesca L[5].

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Abstract

Maintenance of telomere length is one function of human telomerase that is crucial for the survival of cancer cells and cancer progression. Both telomeres and telomerase have been proposed as possible biomarkers of cancer risk and cancer invasiveness; however, their clinical relevance is still under discussion. In order to improve our understanding of the relationship between telomere length and telomerase activity with cancer invasiveness, we studied telomere length as well as telomerase levels, activity, and intracellular localization in breast cancer cell lines with diverse invasive phenotypes. We found an apparently paradoxical coincidence of short telomeres and enhanced telomerase activity in the most invasive breast cancer cell lines. We also observed that hTERT intracellular localization could be correlated with its level of activity. There was no association between human telomerase reverse transcriptase (hTERT) protein expression levels and invasiveness. We propose that simultaneous evaluation of these two biomarkers-telomere length and telomerase activity-could be useful for the assessment of the invasive capacity and aggressiveness of tumor cells from breast cancer patients.
PMID: 27072825 [Indexed for MEDLINE]
Similar articles

10. Cancer Epidemiol Biomarkers Prev. 2017 Jan;26(1):3-10. doi: 10.1158/1055-9965.EPI-16-0343. Epub 2016 Sep 27.

Telomere Length and Breast Cancer Prognosis: A Systematic Review.

Ennour-Idrissi K[1,2,3], Maunsell E[1,2,3,4], Diorio C[5,2,3,4].

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Abstract

Telomeres ensure genome integrity during replication. Loss of telomeric function leads to cell immortalization and accumulation of genetic alterations. The association of telomere length (TL) with breast cancer prognosis is examined through a systematic review. Electronic databases (MEDLINE, EMBASE, CENTRAL), from inception to December 2015, and relevant reviews were searched. Studies that evaluated TL (blood and/or tumor) in association with breast cancer survival or prognostic factor were included. Thirty-six studies met inclusion criteria. Overall risk of bias was critical. Eight studies reported survival outcomes. Overall, there was a trend toward an association of longer telomeres with better outcomes (tumor, not blood). Of the 33 studies reporting associations with prognostic factors, nine adjusted for potential confounders. Among the latter, shorter telomeres were associated with older age (blood, not tumor), higher local recurrence rates (normal tissue), higher tumor grade (tumor), and lower physical activity (blood), which were reported in one study each. TL was not associated with molecular subtype (blood, one study), family history (tumor, one study), chemotherapy (blood, three of four studies), and stress reduction interventions (blood, two of two studies). Although major methodologic differences preclude from drawing conclusive results, TL could be a valuable breast cancer prognostic marker. Cancer Epidemiol Biomarkers Prev; 26(1); 3-10. ©2016 AACR.

PMID: 27677729
Similar articles


11. Acta Haematol. 2016;136(4):210-218. Epub 2016 Sep 16.

Telomere Length Recovery: A Strong Predictor of Overall Survival in Acute Promyelocytic Leukemia.

Baljevic M[1], Dumitriu B, Lee JW, Paietta EM, Wiernik PH, Racevskis J, Chen C, Stein EM, Gallagher RE, Rowe JM, Appelbaum FR, Powell BL, Larson RA, Coutré SE, Lancet J, Litzow MR, Luger SM, Young NS, Tallman MS.

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Abstract

Telomeres are the capping ends of chromosomes that protect the loss of genetic material and prevent chromosomal instability. In human tissue-specific stem/progenitor cells, telomere length (TL) is maintained by the telomerase complex, which consists of a reverse transcriptase catalytic subunit (TERT) and an RNA template (TERC). Very short telomeres and loss-of-function mutations in the TERT and TERC genes have been reported in acute myeloid leukemia, but the role of telomeres in acute promyelocytic leukemia (APL) has not been well established. We report the results for a large cohort of 187 PML/RARα-positive APL patients. No germline mutations in the TERT or TERC genes were identified. Codon 279 and 1062 TERT polymorphisms were present at a frequency similar to that in the general population. TL measured in blood or marrow mononuclear cells at diagnosis was significantly shorter in the APL patients than in healthy volunteers, and shorter telomeres at diagnosis were significantly associated with high-risk disease. For patients who achieved complete remission, the median increase in TL from diagnosis to remission (delta TL) was 2.0 kilobase (kb), and we found delta TL to be the most powerful predictor of overall survival when compared with well-established risk factors for poor outcomes in APL.

PMCID: PMC5198772 [Available on 2017-09-16] **Free Article**
PMID: 27632567 [Indexed for MEDLINE]

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Conflict of interest statement

of Conflicts of Interest: Authors report no conflicts of interest.

12. Leuk Res. 2016 Oct;49:62-5. doi: 10.1016/j.leukres.2016.07.013. Epub 2016 Jul 25.

Telomere length and associations with somatic mutations and clinical outcomes in acute myeloid leukemia.

Watts JM[1], Dumitriu B[2], Hilden P[3], Kishtagari A[4], Rapaport F[5], Chen C[2], Ahn J[5], Devlin SM[3], Stein EM[5], Rampal R[5], Levine RL[5], Young N[2], Tallman MS[5].

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Abstract

We examined the genetic implications and clinical impact of telomere length (TL) in 67 patients with acute myeloid leukemia (AML). There was a trend toward improved survival at 6 months in patients with longer TL. We found that patients with activating mutations, such as FLT3-ITD, had shorter TL, while those with mutations in epigenetic modifying enzymes, particularly IDH1 and IDH2, had longer TL. These are intriguing findings that warrant further investigation in larger cohorts. Our data show the potential of TL as a predictive biomarker in AML and identify genetic subsets that may be particularly vulnerable to telomere-targeted therapies.

PMID: 27568819
Similar articles

13. Oncotarget. 2016 Jun 21;7(25):38579-85. doi: 10.18632/oncotarget.9536.

Association of peripheral leukocyte telomere length and its variation with pancreatic cancer and colorectal cancer risk in Chinese population.

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Abstract

There is increasing evidence supporting the role of telomeres in cancer pathogenesis. However, limited studies have investigated the association between telomere length features and risk of pancreatic cancer and colorectal cancer (CRC), and little was conducted in Asians. To help clarify this issue, We measured relative peripheral leukocytes telomere length (LTL) and telomere length variation (TLV) in a prospective study of 900 pancreatic cancer cases, 300 CRC cases, and 900 controls. Both subjects with longer LTL (quartile 4: adjusted OR=1.51, 95% CI: 1.14-1.99, P=0.004) and shorter LTL (quartile 1: adjusted OR=3.12, 95% CI: 1.89-5.14, P=8.50x10-6) showed increased risk of pancreatic cancer. A linear increased risk was detected For TLV (adjusted OR=1.60, 95% CI: 1.14-2.24, P=0.006). We also identified significant interaction for relative LTL, TLV on pancreatic cancer risk (P interaction =0.009). Significant relationship between shorter RTL and increased CRC risk were also detected. This findings provide insights into telomere dynamics and highlight the complex relationship between relative LTL, TLV and cancer risk.

PMCID: PMC5122412 **Free PMC Article**
PMID: 27509261
Similar articles

Conflict of interest statement

The authors declare that they have no conflicts of interest.

14. Onco Targets Ther. 2016 May 4;9:2675-82. doi: 10.2147/OTT.S98488. eCollection 2016.

Shorter telomere length of T-cells in peripheral blood of patients with lung cancer.

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Abstract

PURPOSE:

Telomere shortening occurs in tumor tissues and peripheral blood lymphocytes of many common human malignancies, including lung cancer, but its variation in T-cells has never been investigated. Thus, the aim of this study was to assess telomere length in T-cells and its correlation with the clinical characteristics of patients with lung cancer.

PATIENTS AND METHODS:

A total of 40 patients with lung cancer but without prior cancer history and 25 healthy individuals were selected. T-cells were isolated and their telomere lengths were measured using quantitative real-time polymerase chain reaction methods.

RESULTS:

Telomere length in T-cells was significantly shorter in patients with lung cancer than in controls ($P<0.001$). Shorter telomere length was significantly associated with increased clinical stage ($P=0.008$) and distant metastasis ($P=0.028$). Naïve T-cells from patients with lung cancer had significantly decreased telomere length when compared with those from controls ($P=0.012$).

CONCLUSION:

The shortened telomere length in T-cells occurred in naïve T-cells and might be related to lung cancer progression.

PMCID: PMC4863689 **Free PMC Article**
PMID: 27226730
Similar articles

15. Front Med. 2016 Jun;10(2):191-203. doi: 10.1007/s11684-016-0450-2. Epub 2016 May 16.

Association between telomere length and survival in cancer patients: a meta-analysis and review of literature.

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Abstract

The relationship between telomere length and cancer survival has been widely studied. To gain a deeper insight, we reviewed the published studies. A total of 29 studies evaluated telomere length in the peripheral blood; 22 studies evaluated telomere length in the tumor tissue. First, in the peripheral blood studies, for solid tumor patients with shortened telomere length, the combined hazard ratios (HRs) for mortality and tumor progression were 1.21 (95%CI, 1.10-1.32) and 1.71 (95%CI, 1.37-2.13), respectively. Meanwhile, in hematology malignancy, the combined HRs for mortality and tumor progression were 2.83 (95%CI, 2.14-3.74) and 2.65 (95%CI, 2.18-3.22), respectively. Second, in the studies that use tumor tissue, for patients with shortened telomeres, the combined HRs for mortality and tumor progression were 1.26 (95%CI, 0.95-1.66) and 1.65 (95%CI, 1.26-2.15), respectively. In the studies that calculate the telomere length ratios of tumor tissue to adjacent normal mucosa, for patients with lower telomere length ratios, the combined HRs were 0.66 (95%CI, 0.53-0.83) and 0.74 (95%CI, 0.41-1.32) for mortality and tumor progression, respectively. In conclusion, shortened telomere in peripheral blood and tumor tissue might indicate poor survival for cancer patients. However, by calculating the telomere length ratios of tumor tissue to adjacent normal mucosa, the lower ratio might indicate better survival.

PMID: 27185042 [Indexed for MEDLINE]

Similar articles

16. Virchows Arch. 2016 Jul;469(1):19-24. doi: 10.1007/s00428-016-1948-3. Epub 2016 May 12.

Telomere length shortening in gastric mucosa is a field effect associated with increased risk of gastric cancer.

Tahara T[1], Shibata T[2], Kawamura T[2], Horiguchi N[2], Okubo M[2], Nakano N[2], Ishizuka T[2], Nagasaka M[2], Nakagawa Y[2], Ohmiya N[2].

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Abstract

Telomere shortening occurs in many organs and tissues and is accelerated by oxidative injury and rapid cell turnover. Short telomeres initiate chromosomal instability and may eventually contribute to tumorigenesis. To evaluate telomere length as potential biomarker for gastric cancer (GC) risk, we measured average telomere length using quantitative real-time PCR in GC tissues and in non-neoplastic mucosa from patients with GC and without GC. We obtained of 217 GC patients matched biopsies from the GC and adjacent tissues as well as gastric biopsies of 102 subjects without GC. Relative telomere length was measured in genomic DNA by real-time PCR. Relative telomere length decreased gradually in Helicobacter pylori (H. pylori) negative and positive gastric mucosa of GC free subjects compared with adjacent mucosa and cancer tissue from GC patients (4.03 ± 0.3 vs. 2.82 ± 0.19 vs. 0.82 ± 0.07 vs. 0.29 ± 0.09, $P < 0.0001$). In non-neoplastic mucosa of GC patients, shorter telomeres were found significantly more often than in that of GC free subjects (age, sex, and H. pylori adjusted odds ratio = 7.81, 95 % confidence interval = 4.71-12.9, $P < 0.0001$). Telomere shortening in non-neoplastic mucosa was associated with chronic inflammation ($P = 0.0018$) and intestinal metaplasia ($P < 0.0001$). No significant associations were found between relative telomere length and clinicopathological features of GC and overall survival. Telomere shortening in gastric mucosa reflects a field effect in an early stage of carcinogenesis and is associated with an increased risk of GC. Telomere length in GC is not associated with clinicopathological features or prognosis.

PMID: 27173780 [Indexed for MEDLINE]

Similar articles

17. Oncotarget. 2016 Jun 14;7(24):36474-36488. doi: 10.18632/oncotarget.9015.

Relative telomere lengths in tumor and normal mucosa are related to disease progression and chromosome instability profiles in colorectal cancer.

Suraweera N[1], Mouradov D[2,3], Li S[2], Jorissen RN[2,3], Hampson D[1], Ghosh A[1], Sengupta N[1],

Thaha M[1,4], Ahmed S[4], Kirwan M[5], Aleva F[6], Propper D[6], Feakins RM[7], Vulliamy T[8], Elwood NJ[9,10], Tian P[9,10], Ward RL[11], Hawkins NJ[12], Xu ZZ[13], Molloy PL[13], Jones IT[14,15], Croxford M[16], Gibbs P[2,3,17], Silver A[1], Sieber OM[2,3,15,18].

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Abstract

Telomeric dysfunction is linked to colorectal cancer (CRC) initiation. However, the relationship of normal tissue and tumor telomere lengths with CRC progression, molecular features and prognosis is unclear. Here, we measured relative telomere length (RTL) by real-time quantitative PCR in 90 adenomas (aRTL), 419 stage I-IV CRCs (cRTL) and adjacent normal mucosa (nRTL). Age-adjusted RTL was analyzed against germline variants in telomere biology genes, chromosome instability (CIN), microsatellite instability (MSI), CpG island methylator phenotype (CIMP), TP53, KRAS, BRAF mutations and clinical outcomes. In 509 adenoma or CRC patients, nRTL decreased with advancing age. Female gender, proximal location and the TERT rs2736100 G allele were independently associated with longer age-adjusted nRTL. Adenomas and carcinomas exhibited telomere shortening in 79% and 67% and lengthening in 7% and 15% of cases. Age-adjusted nRTL and cRTL were independently associated with tumor stage, decreasing from adenoma to stage III and leveling out or increasing from stage III to IV, respectively. Cancer MSI, CIMP, TP53, KRAS and BRAF status were not related to nRTL or cRTL. Near-tetraploid CRCs exhibited significantly longer cRTLs than CIN- and aneuploidy CRCs, while cRTL was significantly shorter in CRCs with larger numbers of chromosome breaks. Age-adjusted nRTL, cRTL or cRTL:nRTL ratios were not associated with disease-free or overall survival in stage II/III CRC. Taken together, our data show that both normal mucosa and tumor RTL are independently associated with CRC progression, and highlight divergent associations of CRC telomere length with tumor CIN profiles.

PMCID: PMC5095014 **Free PMC Article**
PMID: 27167335
Similar articles

Conflict of interest statement

No conflicts of interest to disclose.

18. Oncol Lett. 2016 Mar;11(3):2305-2309. Epub 2016 Feb 4.

Telomere length assessment in leukocytes presents potential diagnostic value in patients with breast cancer.

Barczak W[1], Rozwadowska N[2], Romaniuk A[3], Lipińska N[3], Lisiak N[3], Grodecka-Gazdecka S[4], Książek K[5], Rubiś B[3].

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Abstract

Telomere shortening is associated with cancer development, primarily through the induction of genomic instability. The majority of studies have indicated that individuals with shorter blood telomeres may be at a higher risk of developing various types of cancer. There is increasing evidence that the study of the alterations in telomere length may improve cancer prognosis. The aim of the present study was to verify the use of telomere length parameters in the diagnostics of breast cancer stage. Telomere length was analyzed in the blood leukocytes of 52 patients with breast cancer relative to 47 control subjects using quantitative polymerase chain reaction. The effects of stage, grade, estrogen receptor, progesterone receptor and human epidermal growth factor 2 (HER2) status were assessed. The current study demonstrated that the average telomeric sequence length was significantly shorter in leukocytes from individuals diagnosed with a more severe stage of breast cancer (T2N1M0) than in leukocytes in the early stages of the disease (T1N0M0) (P=0.0207). Furthermore, the data indicated that telomeres in leukocytes derived from patients with $HER2^{+}$ breast cancer were significantly longer compared with those with the $HER2^{-}$ type (P=0.0347). These results suggest that the assessment of telomeres in blood leukocytes may, at least partially, correspond with breast cancer staging and HER2 receptor status.

PMCID: PMC4774613 **Free PMC Article**
PMID: 26998167
Similar articles

19. Sci Rep. 2016 Feb 26;6:22243. doi: 10.1038/srep22243.

The association between telomere length and cancer risk in population studies.

Zhu X[1], Han W[2], Xue W[1], Zou Y[1], Xie C[1], Du J[1], Jin G[1].

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Abstract

Telomeres are crucial in the maintenance of chromosome integrity and genomic stability. A series of epidemiological studies have examined the association between telomere length and the risk of cancers, but the findings remain conflicting. We performed literature review and meta-analysis to demonstrate the relationship between telomere length and cancer risk. A total of 23,379 cases and 68,792 controls from 51 publications with 62 population studies were included in this meta-analysis to assess the association between overall cancer or cancer-specific risk and telomere length. General association and dose-response relationship were evaluated based on two and three groups, respectively. The estimates of association were evaluated with odds ratios and 95% confidence intervals by the random-effects or fixed-effects model based on heterogeneity test. We observed a non-significant association between short telomeres and overall risk of cancer. Convincing evidence was observed for the association of short telomeres with an increased risk of gastrointestinal tumor and head and neck cancer. Significant dose-response associations were also observed for gastrointestinal tumor and head and neck cancer. Our findings indicate that telomeres may play diverse roles in different cancers, and short telomeres may be risk factors for the tumors of digestive system.

PMCID: PMC4768100 **Free PMC Article**
PMID: 26915412 [Indexed for MEDLINE]
Similar articles

20. PLoS One. 2016 Feb 25;11(2):e0149626. doi: 10.1371/journal.pone.0149626. eCollection 2016.

Clinical Relevance of Telomere Status and Telomerase Activity

in Colorectal Cancer.

Fernández-Marcelo T[1,2], Sánchez-Pernaute A[3,2], Pascua I[1,2], De Juan C[1,2], Head J[1,2], Torres-García AJ[3,2], Iniesta P[1,2].

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Abstract

The role of telomeres and telomerase in colorectal cancer (CRC) is well established as the major driving force in generating chromosomal instability. However, their potential as prognostic markers remains unclear. We investigated the outcome implications of telomeres and telomerase in this tumour type. We considered telomere length (TL), ratio of telomere length in cancer to non-cancer tissue (T/N ratio), telomerase activity and TERT levels; their relation with clinical variables and their role as prognostic markers. We analyzed 132 CRCs and paired non-cancer tissues. Kaplan-Meier curves for disease-free survival were calculated for TL, T/N ratio, telomerase activity and TERT levels. Overall, tumours had shorter telomeres than non-tumour tissues ($P < 0.001$) and more than 80% of CRCs displayed telomerase activity. Telomere lengths of non-tumour tissues and CRCs were positively correlated ($P < 0.001$). Considering telomere status and clinical variables, the lowest degree of telomere shortening was shown by tumours located in the rectum ($P = 0.021$). Regarding prognosis studies, patients with tumours showing a mean TL < 6.35 Kb experienced a significantly better clinical evolution ($P < 0.001$) and none of them with the highest degree of tumour telomere shortening relapsed during the follow-up period ($P = 0.043$). The mean TL in CRCs emerged as an independent prognostic factor in the Cox analysis ($P = 0.017$). Telomerase-positive activity was identified as a marker that confers a trend toward a poor prognosis. In CRC, our results support the use of telomere status as an independent prognostic factor. Telomere status may contribute to explaining the different molecular identities of this tumour type.

PMCID: PMC4767779 **Free PMC Article**
PMID: 26913901 [Indexed for MEDLINE]
Similar articles

21. Sci Rep. 2016 Feb 9;6:20675. doi: 10.1038/srep20675.

Telomere length, genetic variants and risk of squamous cell carcinoma of the head and neck in Southeast Chinese.

Gu Y[1], Yu C[1], Miao L[2], Wang L[1], Xu C[1], Xue W[1], Du J[1], Yuan H[1,2], Dai J[1,3], Jin G[1,3], Hu Z[1,3], Ma H[1,3], Shen H[1,3].

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Abstract

Telomere dysfunction participates in malignant transformation and tumorigenesis. Previous studies have explored the associations between telomere length (TL) and cancer susceptibility; however, the findings are inconclusive. The associations between genetic variants and TL have been verified by quite a few genome-wide association studies (GWAS). Yet, to date, there was no published study on the relationship between TL, related genetic variants and susceptibility to squamous cell carcinoma of the head and neck (SCCHN) in Chinese. Hence, we detected relative telomere length (RTL) by using quantitative PCR and genotyped seven selected single nucleotide polymorphisms by TaqMan allelic discrimination assay in 510 SCCHN cases and 913 controls in southeast Chinese. The results showed that RTL was significantly associated with SCCHN risk [(adjusted odds ratio (OR) = 1.19, 95% confidence interval (CI) = 1.08-1.32, P = 0.001]. Furthermore, among seven selected SNPs, only G allele of rs2736100 related to RTL in Caucasians was significantly associated with both the decreased RTL (P = 0.002) and the increased susceptibility to SCCHN in Chinese (additive model: adjusted OR = 1.17, 95%CI = 1.00-1.38, P = 0.049). These findings provide evidence that shortened TL is a risk factor for SCCHN, and genetic variants can contribute to both TL and the susceptibility to SCCHN in southeast Chinese population.

PMCID: PMC4746643 **Free PMC Article**
PMID: 26857734 [Indexed for MEDLINE]
Similar articles

22. J Hepatobiliary Pancreat Sci. 2016 May;23(5):276-82. doi: 10.1002/jhbp.332. Epub 2016

Mar 20.

Dysfunction of subtelomeric methylation and telomere length in gallstone disease and gallbladder cancer patients of North Central India.

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Abstract

BACKGROUND:

Telomeres play an important role in cancer progression. Recently it has been shown that subtelomeric methylation negatively regulates telomere length in various diseases, including cancers. Here, we evaluated the influence of subtelomeric methylation in telomere dysfunction in gallbladder cancer (GBC), and whether this dysfunction is affected by the presence of gallstones.

METHODS:

Relative telomere length and subtelomeric methylation levels were assessed using monochrome multiplex quantitative polymerase chain reaction and bisulfite sequencing, respectively, in different gallbladder tissue types including different grades of GBC, gallstones and adjacent non-tumor.

RESULTS:

We found telomere length to shorten significantly in overall GBC, but specifically in early grade cancer. We also found D4Z4 and DNF92 subtelomeric sequences to be hypermethylated and hypomethylated, respectively, in GBC; however, their methylation levels differed significantly, only in early grade cancer. We could not find any specific correlation between subtelomeric methylation and telomere length in GBC. Interestingly, telomere length and subtelomeric methylation differed significantly in GBC without

gallstones but not in GBC with gallstones.

CONCLUSIONS:

This study, thus, suggests that telomere dysfunction and changes in methylation levels may occur earlier in the progression of GBC, while the presence of gallstones may have no influence on telomere length as well as on methylation levels.

PMID: 26856965 [Indexed for MEDLINE]
Similar articles

23. Cell Physiol Biochem. 2016;38(1):122-8. doi: 10.1159/000438614. Epub 2016 Jan 8.

Telomere Length as a Prognostic Factor for Overall Survival in Colorectal Cancer Patients.

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Abstract

BACKGROUND/AIMS:

The stabilization of telomere length has important roles in the carcinogenesis of colorectal cancer. A systemic review and meta-analysis of published studies was performed to assess the prognostic role of telomere length in colorectal cancer.

METHODS:

Pubmed and Embase were searched for eligible studies on the association between telomere length and overall survival in colorectal cancer patients. The pooled hazard ratio (HR) and corresponding 95% confidence intervals (95%CI) was calculated using fixed-effects or random-effects model according to the magnitude of between-study heterogeneity.

RESULTS:

Seven individual studies with a total of 956 colorectal cancer patients were included. Long telomere length in cancer tissues was marginally associated with poorer overall survival

(Random-effects HR = 1.85, 95% 0.90 to 3.83, P = 0.09). When using studies with adjusted estimates, long telomere length in cancer tissues was independently and significantly associated with poorer overall survival (Fixed-effects HR = 2.70, 95% 1.51 to 4.84, P = 0.001). However, short telomere length in peripheral blood leukocytes was independently and significantly associated with poorer overall survival (Fixed-effects HR = 2.01, 95% 1.46 to 2.77, P < 0.001).

CONCLUSIONS:

There is some evidence for telomere length as a prognostic factor for overall survival in colorectal cancer patients. More studies with large number of participants are needed to further assess the prognostic significance of telomere length in colorectal cancer patients.

Free Article

PMID: 26741140 [Indexed for MEDLINE]

Similar articles

24. Aging (Albany NY). 2015 Dec;7(12):1066-76.

Telomere length is a prognostic biomarker in elderly advanced ovarian cancer patients: a multicenter GINECO study.

Falandry C[1], Horard B[2], Bruyas A[3], Legouffe E[4], Cretin J[5], Meunier J[6], Alexandre J[7], Delecroix V[8], Fabbro M[9], Certain MN[10], Maraval-Gaget R[11], Pujade-Lauraine E[7], Gilson E[12], Freyer G[13].

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Abstract

PURPOSE:

Age induces a progressive decline in functional reserve and impacts cancer treatments. Telomere attrition leads to tissue senescence. We tested the hypothesis that telomere length (TL) could predict patient vulnerability and outcome with cancer treatment.

PATIENTS AND METHODS:

An ancillary study in the Elderly Women GINECO Trial 3 was performed to evaluate the impact of geriatric covariates on survival in elderly advanced ovarian cancer patients receiving six cycles of carboplatin. TL was estimated from peripheral blood at inclusion using standard procedures.

RESULTS:

TL (in base pairs) was estimated for 109/111 patients (median 6.1 kb; range [4.5-8.3 kb]). With a cut-off of 5.77 kb, TL discriminated two patient groups, long telomere (LT) and short telomeres (ST), with significantly different treatment completion rates of 0.80 (95% CI [0.71-0.89]) and 0.59 (95% CI [0.41-0.76]), respectively (odds ratio [OR]=2.8, p=0.02). ST patients were at higher risk of serious adverse events (SAE, OR=2.7; p=0.02) and had more unplanned hospital admissions (OR=2.1; p=0.08). After adjustment on FIGO stage, TL shorter than 6 kb was a risk factor of premature death (HR=1.57; p=0.06).

CONCLUSION:

This exploratory study identifies TL as predictive factor of decreased treatment completion, SAE risk, unplanned hospital admissions and OS after adjustment on FIGO stage.

PMCID: PMC4712332 **Free PMC Article**
PMID: 26638179 [Indexed for MEDLINE]
Similar articles

25. Leuk Res. 2015 Dec;39(12):1360-6. doi: 10.1016/j.leukres.2015.09.015. Epub 2015 Sep 24.

Impact of telomere length on survival in classic and variant hairy cell leukemia.

Arons E[1], Zhou H[1], Edelman DC[2], Gomez A[2], Steinberg SM[3], Petersen D[2], Wang Y[2], Meltzer PS[2], Kreitman RJ[4].

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Abstract

Telomeres, which protect the ends of chromosomes, are shortened in several hematologic malignancies, often with adverse prognostic implications, but their effect on prognosis of classic and variant hairy cell leukemia (HCL and HCLv) has not been reported. HCL/HCLv genomic DNA from 46 patients was studied by PCR to determine the ratio of telomere to single copy gene number (T/S). T/S was unrelated to diagnosis of HCL or HCLv (p=0.27), but shorter T/S was associated with unmutated immunoglobulin rearrangements (p=0.033) and age above the median at diagnosis (p=0.017). Low T/S was associated with shorter overall survival from diagnosis (OS), particularly T/S <0.655 (p=0.0064, adjusted p=0.019). Shorter OS was also associated with presence of unmutated (p<0.0001) or IGHV4-34+ (p<0.0001) rearrangements, or increasing age (p=0.0002). Multivariable analysis with Cox

modeling showed that short T/S along with either unmutated or IGHV4-34+ rearrangements remained associated with reduced OS (p=0.0071, p=0.0024, respectively) after age adjustment. While T/S is relatively long in HCL and the disease usually indolent with excellent survival, shortened telomeres in HCL/HCLv are associated with decreased survival. Shortened T/S could represent a risk factor needing further investigation/intervention to determine if non-chemotherapy treatment options, in addition to or instead of chemotherapy, might be particularly useful.

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26. Leuk Lymphoma. 2016;57(3):590-5. doi: 10.3109/10428194.2015.1076929. Epub 2015 Oct 12.

Shorter telomeres correlate with an increase in the number of uniparental disomies in patients with chronic lymphocytic leukemia.

Sellmann L[1,2], Scholtysik R[2], de Beer D[3], Eisele L[1], Klein-Hitpass L[2], Nückel H[1], Dührsen U[1], Dürig J[1], Röth A[1], Baerlocher GM[3,4].

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Abstract

This study investigated the correlation of the extent of chromosomal aberrations including uniparental disomies (UPDs) by SNP-chip analysis and FISH to telomere length in 46 patients with CLL. CLL harboring high risk aberrations, i.e. deletions of 11q22-23 or 17p13,

had significantly shorter telomeres (higher ΔTL) compared to patients with CLL without such abnormalities. Patients with high chromosomal aberration rates had a worse overall survival compared to cases with lower aberration rates. Interestingly, however, an increase was found in the number of UPDs with shorter telomeres. These findings support the idea that telomeres in CLL cells play a role in the overall chromosome stability and could be involved in the occurrence of UPDs.

PMID: 26457386 [Indexed for MEDLINE]

Similar articles

27. Oncotarget. 2015 Oct 6;6(30):29795-807. doi: 10.18632/oncotarget.5083.

Aberrant reduction of telomere repetitive sequences in plasma cell-free DNA for early breast cancer detection.

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Abstract

Excessive telomere shortening is observed in breast cancer lesions when compared to adjacent non-cancerous tissues, suggesting that telomere length may represent a key biomarker for early cancer detection. Because tumor-derived, cell-free DNA (cfDNA) is often released from cancer cells and circulates in the bloodstream, we hypothesized that breast cancer development is associated with changes in the amount of telomeric cfDNA that can be detected in the plasma. To test this hypothesis, we devised a novel, highly sensitive and specific quantitative PCR (qPCR) assay, termed telomeric cfDNA qPCR, to quantify plasma telomeric cfDNA levels. Indeed, the internal reference primers of our design correctly reflected input cfDNA amount (R(2) = 0.910, P = 7.82 × 10(-52)), implying accuracy of this assay. We found that plasma telomeric cfDNA levels decreased with age in healthy individuals (n = 42, R(2) = 0.094, P = 0.048), suggesting that cfDNA is likely derived from somatic cells in which telomere length shortens with increasing age. Our results also showed a significant decrease in telomeric cfDNA level from breast cancer patients with no prior treatment (n = 47), compared to control individuals (n = 42) (P = 4.06 × 10(-8)). The sensitivity and specificity for the telomeric cfDNA qPCR assay was 91.49% and 76.19%, respectively. Furthermore, the telomeric cfDNA level distinguished even the Ductal Carcinoma In Situ (DCIS) group (n = 7) from the healthy group (n = 42) (P = 1.51 × 10(-3)). Taken together, decreasing plasma telomeric cfDNA levels could be an informative genetic biomarker for early breast cancer detection.

PMCID: PMC4745763 **Free PMC Article**
PMID: 26356673 [Indexed for MEDLINE]
Similar articles

28. EBioMedicine. 2015 Apr 13;2(6):591-6. doi: 10.1016/j.ebiom.2015.04.008. eCollection 2015 Jun.

Blood Telomere Length Attrition and Cancer Development in the Normative Aging Study Cohort.

Hou L[1], Joyce BT[2], Gao T[3], Liu L[1], Zheng Y[4], Penedo FJ[5], Liu S[6], Zhang W[3], Bergan R[7], Dai Q[8], Vokonas P[9], Hoxha M[10], Schwartz J[11], Baccarelli A[11].

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Comment in

- Leukocyte Telomere Length and Cancer Risk: A Dynamic Problem. [EBioMedicine. 2015]

Abstract

BACKGROUND:

Accelerated telomere shortening may cause cancer via chromosomal instability, making it a potentially useful biomarker. However, publications on blood telomere length (BTL) and cancer are inconsistent. We prospectively examined BTL measures over time and cancer incidence.

METHODS:

We included 792 Normative Aging Study participants with 1-4 BTL measurements from 1999 to 2012. We used linear mixed-effects models to examine BTL attrition by cancer status (relative to increasing age and decreasing years pre-diagnosis), Cox models for time-dependent associations, and logistic regression for cancer incidence stratified by years between BTL measurement and diagnosis.

FINDINGS:

Age-related BTL attrition was faster in cancer cases pre-diagnosis than in cancer-free participants (pdifference = 0.017); all participants had similar age-adjusted BTL 8-14 years pre-diagnosis, followed by decelerated attrition in cancer cases resulting in longer BTL three ($p = 0.003$) and four ($p = 0.012$) years pre-diagnosis. Longer time-dependent BTL was associated with prostate cancer (HR = 1.79, $p = 0.03$), and longer BTL measured ≤ 4 years

pre-diagnosis with any (OR = 3.27, p < 0.001) and prostate cancers (OR = 6.87, p < 0.001).

INTERPRETATION:

Age-related BTL attrition was faster in cancer cases but their age-adjusted BTL attrition began decelerating as diagnosis approached. This may explain prior inconsistencies and help develop BTL as a cancer detection biomarker.

PMCID: PMC4535161 **Free PMC Article**
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Similar articles

29. EBioMedicine. 2015 May 9;2(6):493-4. doi: 10.1016/j.ebiom.2015.05.006. eCollection 2015 Jun.

Leukocyte Telomere Length and Cancer Risk: A Dynamic Problem.

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Comment on

- Blood Telomere Length Attrition and Cancer Development in the Normative Aging Study Cohort. [EBioMedicine. 2015]

PMCID: PMC4535164 **Free PMC Article**
PMID: 26286096 [Indexed for MEDLINE]
Similar articles

30. J Exp Clin Cancer Res. 2015 Aug 7;34:78. doi: 10.1186/s13046-015-0195-9.

Telomere length and telomerase activity in non-small cell lung cancer prognosis: clinical usefulness of a specific telomere status.

Fernández-Marcelo T[1,2], Gómez A[3,4], Pascua I[5,6], de Juan C[7,8], Head J[9,10], Hernando F[11,12], Jarabo JR[13,14], Calatayud J[15,16], Torres-García AJ[17,18], Iniesta P[19,20].

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Abstract

BACKGROUND:

Considering previous data and the need to incorporate new biomarkers for the prognosis of solid tumours into the clinic, our aim in this work consists of evaluating the potential clinical use of telomeres and telomerase in non-small cell lung cancer (NSCLC).

METHODS:

Telomere status was established by determination of telomere length using the Terminal Restriction Fragment length method, and telomerase activity by the Telomeric Repeat Amplification Protocol in 142 NSCLCs and their corresponding control samples, obtained from patients submitted to surgery. Group-oriented curves for disease-free survival were calculated according to the Kaplan-Meier method considering telomere length, T/N ratio (telomere length in tumour to control tissue) and telomerase activity.

RESULTS:

Overall, tumours had significantly shorter telomeres compared with telomeres in control tissues ($P = 0.027$). More than 80 % of NSCLCs displayed telomerase activity. Regarding

prognosis studies, patients whose tumours showed a mean telomere length (MTL) <7.29 Kb or T/N ratio <0.97 showed a significantly poor clinical evolution (P = 0.034 and P = 0.040, respectively). As result of a Cox multivariate analysis including pathologic state and lymph node dissemination, the MTL and T/N ratio emerged as independent significant prognostic factors.

CONCLUSIONS:

Telomerase activity was identified as a marker of poor prognosis. The novel finding of this study is the independent prognosis role of a specific telomere status in NSCLC patients. According to our results, telomere function may emerge as a useful molecular tool that allow to select groups of NSCLC patients with different clinical evolution, in order to establish personalized therapy protocols.

PMCID: PMC4528384 **Free PMC Article**
PMID: 26250468 [Indexed for MEDLINE]
Similar articles

31. PLoS One. 2015 Jul 15;10(7):e0133174. doi: 10.1371/journal.pone.0133174. eCollection 2015.

The Association between Telomere Length and Cancer Prognosis: Evidence from a Meta-Analysis.

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Abstract

BACKGROUND:

Telomeres are essential for chromosomal integrity and stability. Shortened telomere length (TL) has been associated with risk of cancers and aging-related diseases. Several studies have explored associations between TL and cancer prognosis, but the results are conflicting.

METHODS:

Prospective studies on the relationship between TL and cancer survival were identified by a search of PubMed up to May 25, 2015. There were no restrictions on the cancer type or DNA source. The quality of the included studies was assessed using the Newcastle-Ottawa Scale. Meta-analysis approaches were conducted to determine pooled relative risks and 95% confidence intervals.

RESULTS:

Thirty-three articles containing forty-five independent studies were ultimately involved in our meta-analysis, of which twenty-seven were about overall cancer survival and eighteen were about cancer progression. Short TL was associated with increased cancer mortality risk (RR = 1.30, 95%CI: 1.06-1.59) and poor cancer progression (RR = 1.44, 95%CI: 1.10-1.88), both with high levels of heterogeneity (I2 = 83.5%, P = 0.012for overall survival and I2 = 75.4%, P = 0.008 for progression). TL was an independent predictor of overall cancer survival and progression in chronic lymphocytic leukemia. Besides, short telomeres were also associated with increased colorectal cancer mortality and decreased overall survival of esophageal cancer, but not in other cancers. Cancer progression was associated with TL in Asian and America populations and short TL predicted poor cancer survival in older populations. Compared with tumor tissue cells, TL in blood lymphocyte cells was better for prediction. In addition, the associations remained significant when restricted to studies with adjustments for age, with larger sample sizes, measuring TL using southern blotting or estimating risk effects by hazard ratios.

CONCLUSION:

Short TL demonstrated a significant association with poor cancer survival, suggesting the potential prognostic significance of TL. Additional large well-designed studies are needed to confirm our findings.

PMCID: PMC4503690 **Free PMC Article**
PMID: 26177192 [Indexed for MEDLINE]
Similar articles

32. Oncol Rep. 2015 Aug;34(2):627-32. doi: 10.3892/or.2015.4063. Epub 2015 Jun 15.

Telomere shortening in breast cancer correlates with the pathological features of tumor progression.

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Abstract

Telomeres are involved in the maintenance of genomic stability. Telomere alteration has been observed in most human cancer types, and is known to be a feature of malignancy. The aim of the present study was to evaluate whether the telomere length of breast cancer cells correlates with TNM stage and several pathological features. We investigated a total of 44 breast cancers, including 17 scirrhous, 15 papillotubular and 12 solid-tubular carcinomas. Telomere lengths were determined by tissue quantitative fluorescence in situ hybridization (Q-FISH), and compared according to the TNM stage, histological tumor size, lymph node metastases, vascular invasion and immunohistochemical status (ER, PR, HER2 status and Ki67 labeling index). In all histological types, telomeres of cancer cells were significantly shorter than those of normal epithelial cells. Mean telomere length was significantly less in patients with TNM stage III, and in those with large tumors, lymph node metastases and vascular invasion. Our results suggest that the telomere length of cancer cells is strongly correlated with the degree of cancer progression.

PMID: 26080929 [Indexed for MEDLINE]

Similar articles

33. Tumour Biol. 2015 Nov;36(11):8317-24. doi: 10.1007/s13277-015-3556-2. Epub 2015 May 26.

Telomere shortening associated with increased genomic complexity in chronic lymphocytic leukemia.

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Abstract

Telomeric dysfunction has been proposed as an emerging prognostic factor in chronic lymphocytic leukemia (CLL). We have explored the relationship between telomere length (TL) and chromosome alterations studied by fluorescence in situ hybridization (FISH) and conventional cytogenetics in 107 newly diagnosed CLL patients; 61 normal controls were also evaluated. Results were correlated with clinical parameters and outcome. Absolute TL measurement was carried out on DNA samples by real-time quantitative PCR. A significant telomere shortening in patients compared to controls was observed ($p = 0.0001$). The analysis taking into account FISH risk groups showed shorter TLs in cases with del11q/17p compared to patients with 13q14 deletion as a single alteration ($p = 0.0037$), no alterations (NA) ($p = 0.028$), and cases with abnormal karyotypes ($p = 0.014$). In addition, a significant TL reduction in cases with two or more anomalies with respect to those with NA ($p = 0.033$) and with one alteration ($p = 0.045$), and no differences compared to cases with deletions 11q/17p were observed. Patients with only one anomaly did not show statistical differences with respect to controls; meanwhile, a significant TL reduction in cases with two or more aberrations was observed ($p = 0.025$). The shortest telomeres were associated to 11q/17p deletion with significant differences compared to the remaining groups ($p \leq 0.045$). Significantly shorter treatment free survival in patients with two or more alterations compared to those with NA plus one abnormality was observed ($p = 0.0006$). Our findings support the association between short TL and chromosome alterations in CLL and indicate

the importance of telomere dysfunction in driving genomic instability in this pathology.
PMID: 26008147 [Indexed for MEDLINE]
Similar articles


34. Prostate. 2015 Aug 1;75(11):1160-6. doi: 10.1002/pros.22997. Epub 2015 Apr 20.

Prostate stromal cell telomere shortening is associated with risk of prostate cancer in the placebo arm of the Prostate Cancer Prevention Trial.

Heaphy CM[1,2], Gaonkar G[1], Peskoe SB[3], Joshu CE[2,3], De Marzo AM[1,2,4], Lucia MS[5], Goodman PJ[6], Lippman SM[7], Thompson IM Jr[8], Platz EA[2,3,4], Meeker AK[1,2,4].

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Abstract

BACKGROUND:

Telomeres are repetitive nucleoproteins that help maintain chromosomal stability by inhibiting exonucleolytic degradation, prohibiting inappropriate homologous recombination, and preventing chromosomal fusions by suppressing double-strand break signals. We

recently observed that men treated for clinically localized prostate cancer with shorter telomeres in their cancer-associated stromal cells, in combination with greater variation in cancer cell telomere lengths, were significantly more likely to progress to distant metastases, and die from their disease. Here, we hypothesized that shorter stromal cell telomere length would be associated with prostate cancer risk at time of biopsy.

METHODS:

Telomere-specific fluorescence in situ hybridization (FISH) analysis was performed in normal-appearing stromal, basal epithelial, and luminal epithelial cells in biopsies from men randomized to the placebo arm of the Prostate Cancer Prevention Trial. Prostate cancer cases (N = 32) were either detected on a biopsy performed for cause or at the end of the study per trial protocol, and controls (N = 50), defined as negative for cancer on an end-of-study biopsy performed per trial protocol (e.g., irrespective of indication), were sampled. Logistic regression was used to estimate the association between mean telomere length of the particular cell populations, cell-to-cell telomere length variability, and risk of prostate cancer.

RESULTS:

Men with short stromal cell telomere lengths (below median) had 2.66 (95% CI 1.04-3.06; P = 0.04) times the odds of prostate cancer compared with men who had longer lengths (at or above median). Conversely, we did not observe statistically significant associations for short telomere lengths in normal-appearing basal (OR = 2.15, 95% CI 0.86-5.39; P= 0 .10) or luminal (OR = 1.15, 95% CI 0.47-2.80; P = 0.77) cells.

CONCLUSIONS:

These findings suggest that telomere shortening in normal stromal cells is associated with prostate cancer risk. It is essential to extend and validate these findings, while also identifying the cellular milieu that comprises the subset of cells with short telomeres within the prostate tumor microenvironment.

PMCID: PMC4475463 **Free PMC Article**
PMID: 25893825 [Indexed for MEDLINE]
Similar articles

35. Lung Cancer. 2015 Jun;88(3):297-303. doi: 10.1016/j.lungcan.2015.03.011. Epub 2015 Mar 20.

Telomere length variation: A potential new telomere biomarker for lung cancer risk.

Sun B[1], Wang Y[1], Kota K[1], Shi Y[1], Motlak S[1], Makambi K[2], Loffredo CA[2], Shields PG[3], Yang Q[4], Harris CC[5], Zheng YL[6].

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Abstract

OBJECTIVES:

In this report the associations between telomere length variation (TLV), mean telomere length in blood lymphocytes and lung cancer risk were examined.

MATERIALS AND METHODS:

The study design is case-control. Cases (N=191) were patients newly diagnosed with histologically confirmed non-small cell lung cancer. Controls (N=207) were healthy individuals recruited from the same counties as cases and matched to cases on age and gender. 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 lung cancer risk.

RESULTS:

Telomere length variation across all chromosomal ends was significantly associated with

lung cancer risk; adjusted odds ratios 4.67 [95% confidence interval (CI): 1.46-14.9] and 0.46 (95% CI: 0.25-0.84) for younger (age≤60) and older (age>60) individuals, respectively. TLV and mean telomere length jointly affected lung cancer risk: when comparing individuals with short telomere length and high TLV to those with long telomere length and low TLV, adjusted odd ratios were 8.21 (95% CI: 1.71-39.5) and 0.33 (95% CI: 0.15-0.72) for younger and older individuals, respectively.

CONCLUSIONS:

TLV in blood lymphocytes is significantly associated with lung cancer risk and the associations were modulated by age. TLV in combination with mean telomere length might be useful in identifying high risk population for lung cancer computerized tomography screening.

PMCID: PMC4428929 **Free PMC Article**
PMID: 25840848 [Indexed for MEDLINE]
Similar articles

36. Oncotarget. 2015 Apr 30;6(12):10617-33.

TERT promoter mutations and telomere length in adult malignant gliomas and recurrences.

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Abstract

In this report on 303 gliomas we show the highest frequency of TERT promoter mutations in gliobastomas (80%) followed by oligodendrogliomas (70%) and astrocytomas (39%). We

observed positive association between TERT promoter and IDH mutations in oligodendroglial tumors (OR = 26.3; 95% CI 2.5-250.2) and inverse association in primary glioblastomas (OR = 0.13; 95% CI 0.03-0.58). Tumors with TERT promoter mutations compared to those without showed increased TERT transcription; we also showed difference in the transcription levels due to the two main mutations. Tumors with TERT promoter mutations had shorter telomeres than those without. The patients with only TERT promoter mutations showed worst survival (median survival 14.6 months) and patients with both IDH and TERT promoter mutations showed best survival (246.5 months). In patients with astrocytoma, the TERT promoter mutations only associated with poor survival ($P < 0.0001$); IDH mutations and 1p/19q deletions associated with increased survival ($P = 0.0004$). TERT promoter mutations in low grade gliomas associated with reduced progression free survival (HR 10.2; 95% CI 1.9 - 55.9). While our data affirm the role of TERT promoter mutations in glial tumors, effects on transcription and telomere length emphasise the importance of telomere biology in disease genesis and outcome.

PMCID: PMC4496380 **Free PMC Article**
PMID: 25797251 [Indexed for MEDLINE]
Similar articles


37. Oral Oncol. 2015 May;51(5):500-7. doi: 10.1016/j.oraloncology.2015.02.100. Epub 2015 Mar 11.

Telomere shortening in mucosa surrounding the tumor: biosensor of field cancerization and prognostic marker of mucosal failure in head and neck squamous cell carcinoma.

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Abstract

OBJECTIVES:

The aim of the present study was to investigate the pattern of telomere length and telomerase expression in cancer tissues and the surrounding mucosa (SM), as markers of field cancerization and clinical outcome in patients successfully treated for with head and neck squamous cell carcinoma (HNSCC).

MATERIALS AND METHODS:

This investigation was a prospective cohort study. Telomere length and levels of telomerase reverse transcriptase (TERT) transcripts were quantified by real-time PCR in cancer tissues and SM from 139 and 90 patients with HNSCC, respectively.

RESULTS:

No correlation was found between age and telomere length in SM. Patients with short telomeres in SM had a higher risk of mucosal failure (adjusted HR=4.29). Patients with high TERT levels in cancer tissues had a higher risk of regional failure (HR=2.88), distant failure (HR=7.27), worse disease-specific survival (HR for related death=2.62) but not mucosal failure. High-risk patients having both short telomeres in SM and high levels of TERT in cancer showed a significantly lower overall survival (HR=2.46).

CONCLUSIONS:

Overall these findings suggest that telomere shortening in SM is a marker of field cancerization and may precede reactivation of TERT. Short telomeres in SM are strongly prognostic of mucosal failure, whereas TERT levels in cancer tissues increase with the aggressiveness of the disease and are prognostic of tumor spread.

PMID: 25771075 [Indexed for MEDLINE]
Similar articles

38. Gene. 2015 May 15;562(2):145-51. doi: 10.1016/j.gene.2015.02.079. Epub 2015 Mar 11.

Augmented telomerase activity, reduced telomere length and the presence of alternative lengthening of telomere in renal cell carcinoma: plausible predictive and diagnostic markers.

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Abstract

In this study, we analyzed 100 cases of renal cell carcinoma (RCC) for telomerase activity, telomere length and alternative lengthening of telomeres (ALT) using the TRAP assay, TeloTTAGGG assay kit and immunohistochemical analysis of ALT associated promyelocytic leukemia (PML) bodies respectively. A significantly higher (P=0.000) telomerase activity was observed in 81 cases of RCC which was correlated with clinicopathological features of tumor for instance, stage (P=0.008) and grades (P=0.000) but not with the subtypes of RCC (P = 0.355). Notwithstanding, no correlation was found between telomerase activity and subtypes of RCC. Strikingly, the telomere length was found to be significantly shorter in RCC (P=0.000) to that of corresponding normal renal tissues and it is well correlated with grades (P=0.016) but not with stages (P=0.202) and subtypes (P=0.669) of RCC. In this study, telomere length was also negatively correlated with the age of patients (r(2)=0.528; P=0.000) which supports the notion that it could be used as a marker for biological aging. ALT associated PML bodies containing PML protein was found in telomerase negative cases of RCC. It suggests the presence of an ALT pathway mechanism to maintain the telomere length in telomerase negative RCC tissues which was associated with high stages of RCC, suggesting a prevalent mechanism for telomere maintenance in high stages. In conclusion, the telomerase activity and telomere length can be used as a diagnostic as well as a predictive marker in RCC. The prevalence of ALT mechanism in high stages of RCC is warranted for the development of anti-ALT inhibitors along with telomerase inhibitor against RCC as a therapeutic approach.

PMID: 25769384 [Indexed for MEDLINE]

Similar articles

39. J Cancer Res Clin Oncol. 2015 Oct;141(10):1739-47. doi: 10.1007/s00432-015-1938-x. Epub 2015 Feb 22.

Leukocyte telomere length: a novel biomarker to predict the prognosis of glioma patients.

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Abstract

PURPOSE:

Epidemiological studies have demonstrated that leukocyte telomere length is associated with the developing risk of various malignancies, including glioma. However, its prognostic value in glioma patients has never been investigated.

METHODS:

Relative telomere length (RTL) of peripheral blood leukocytes from 301 glioma patients were examined using a real-time PCR-based method. Kaplan-Meier curves and Cox proportional hazards regression model were used to assess the association of RTL with clinical outcomes of patients. To explore the potential mechanism, the immune phenotype of peripheral blood mononuclear cells (PBMCs) and concentrations of several cytokines from another 20 glioma patients were detected by flow cytometry and enzyme-linked immunosorbent assay (ELISA), respectively. The relationship between RTL and immunological characteristics of PBMCs were further analyzed.

RESULTS:

Patients with short RTL showed both poorer overall survival (OS) and progression-free survival (PFS) than those with long RTL. Multivariate Cox regression analysis demonstrated that RTL was an independent prognostic factor for both OS and PFS in glioma patients. Moreover, the effects of RTL on the prognosis of patients exhibited a dose-dependent manner. Stratified analysis showed that the prognostic value of RTL was not affected by host characteristics except for age. In addition, flow cytometry and ELISA analyses indicated that

there was no significant association between RTL and frequency of different immune cell subsets or plasma cytokine concentrations.

CONCLUSIONS:

Our study for the first time demonstrates that leukocyte RTL is an independent prognostic marker for glioma patients. The potential mechanism needs further investigation.

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Similar articles

40. Mol Oncol. 2015 Mar;9(3):727-39. doi: 10.1016/j.molonc.2014.11.008. Epub 2014 Dec 3.

Short telomere length in peripheral blood leukocyte predicts poor prognosis and indicates an immunosuppressive phenotype in gastric cancer patients.

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Abstract

Compelling evidences indicate that relative telomere length (RTL) in peripheral blood leukocytes (PBLs) can predict the clinical outcome of several cancers. However, to date, the prognostic value of leukocyte RTL in gastric cancer (GC) patients has not been explored. In this study, relative telomere length (RTL) in peripheral blood leukocytes (PBLs) was measured using a real-time PCR-based method in a total of 693 GC patients receiving surgical resection. The prognostic value of leukocyte RTL was first explored in the training

set (112 patients) using Kaplan-Meier and Cox proportional hazards regression analyses. Then an independent cohort of 581 patients was used as a validation set. To explore potential mechanism, we detected the immunophenotypes of peripheral blood mononuclear cells and plasma concentrations of several cytokines in GC patients. Patients with short RTL showed significantly worse overall survival (OS) and relapse-free survival (RFS) than those with long RTL in all patient sets. Furthermore, leukocyte RTL and TNM stage exhibited a notable joint effect in prognosis prediction. Integration of TNM stage and leukocyte RTL significantly improved the prognosis prediction efficacy for GC. In addition, we found that patients with short RTL had a higher CD4(+) T cell percentage in PBMCs, CD19(+)IL-10(+) Breg percentage in B cells and plasma IL-10 concentration, indicating an enhanced immunosuppressive status with short leukocyte RTL. In conclusion, our study for the first time demonstrates that leukocyte RTL is an independent prognostic marker complementing TNM stage and associated with an immunosuppressive phenotype in the peripheral blood lymphocytes in GC patients.

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PMID: 25515040 [Indexed for MEDLINE]

Similar articles

41. Cancer Epidemiol Biomarkers Prev. 2015 Feb;24(2):336-43. doi: 10.1158/1055-9965.EPI-14-0992. Epub 2014 Nov 21.

Depressive symptoms and short telomere length are associated with increased mortality in bladder cancer patients.

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Abstract

BACKGROUND:

Depression is associated with an increased risk of mortality in patients with cancer; it has been hypothesized that depression-associated alterations in cell aging mechanisms, in particular, the telomere/telomerase maintenance system, may underlie this increased risk. We evaluated the association of depressive symptoms and telomere length to mortality and recurrence/progression in 464 patients with bladder cancer.

METHODS:

We used the Center for Epidemiologic Studies Depression Scale (CES-D) and Structured Clinical Interview for DSM-IV Disorder (SCID) to assess current depressive symptoms and lifetime major depressive disorder (MDD), respectively, and telomere length was assessed from peripheral blood lymphocytes. Multivariate Cox regression was used to assess the association of depression and telomere length to outcomes and the joint effect of both. Kaplan-Meier plots and log-rank tests were used to compare survival time of subgroups by depression variables and telomere length.

RESULTS:

Patients with depressive symptoms (CES-D $\geq$ 16) had a 1.83-fold [95% confidence interval (CI), 1.08-3.08; P = 0.024] increased risk of mortality compared with patients without depressive symptoms (CES-D < 16) and shorter disease-free survival time (P = 0.004). Patients with both depressive symptoms and lifetime history of MDD were at 4.88-fold (95% CI, 1.40-16.99; P = 0.013) increased risk compared with patients with neither condition. Compared to patients without depressive symptoms and long telomere length, patients with depressive symptoms and short telomeres exhibited a 4-fold increased risk of mortality (HR, 3.96; 95% CI, 1.86-8.41; P = 0.0003) and significantly shorter disease-free survival time (P < 0.001).

CONCLUSION:

Short telomere length and depressive symptoms are associated with bladder cancer mortality individually and jointly.

IMPACT:

Further investigation of interventions that impact depression and telomere length may be warranted in patients with cancer.

PMCID: PMC4332382 **Free PMC Article**
PMID: 25416716 [Indexed for MEDLINE]
Similar articles

42. Br J Haematol. 2017 Mar 24. doi: 10.1111/bjh.14643. [Epub ahead of print]

Telomere length is a critical determinant for survival in multiple myeloma.

Hyatt S[1], Jones RE[1], Heppel NH[1], Grimstead JW[1], Fegan C[1], Jackson GH[2], Hills R[1], Allan JM[3], Pratt G[4], Pepper C[1], Baird DM[1].

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Abstract

The variable clinical outcomes of Multiple Myeloma (MM) patients are incompletely defined by current prognostication tools. We examined the clinical utility of high-resolution telomere length analysis as a prognostic marker in MM. Cohort stratification, using a previously determined length threshold for telomere dysfunction, revealed that patients with short telomeres had a significantly shorter overall survival ($P < 0{\cdot}0001$; HR = 3·4). Multivariate modelling using forward selection identified International Staging System (ISS) stage as the most important prognostic factor, followed by age and telomere length. Importantly, each ISS prognostic subset could be further risk-stratified according to telomere length, supporting the inclusion of this parameter as a refinement of the ISS.

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