U-Shaped Association between Leukocyte Telomere Length and Mortality from Natural Causes in adults from the ELSA-Brasil cohort

Lidyane V Camelo[1], Chams B Maluf[1], Pereira A[2], **Amanda V Machado,** Luana Giatti[1], Sandhi M Barreto[1]
[1]Universidade Federal de Minas Gerais, Belo Horizonte, Brazil;
[2]Hospital das Clínicas – Universidade de São Paulo, São Paulo, Brazil.

The study results indicate that both, short and long telomeres, were associated with a higher risk of death from natural causes in Brazilian adults aged 64 years and younger. Telomere length was not associated with death in older individuals.

BACKGROUND

• Hypothesis: Shorter telomere length is associated with higher mortality risk in Brazilian adults.

Studies have demonstrated that accelerated telomere shortening is linked to age-related diseases like cardiovascular diseases (CVD), diabetes, and all-cause mortality. However, recent research indicates that the relationship between telomere length and mortality is not linear, and longer telomeres have been associated with increased mortality from certain age-related diseases, such as certain types of cancer. We examined the association between leukocyte telomere length (LTL) and mortality due to natural causes after an 8.9-year follow-up period.

METHODS

We used subsample data of 2,000 participants from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Leukocyte DNA samples were obtained and frozen at the baseline (2008-2010). LTL was measured using real-time PCR. Standardized relative LTL (T/S ratio) was used. Time to death was defined as the time elapsed between the baseline to the date of death, loss to follow-up or the final follow-up assessment, whichever occurred first. Cox proportional hazards models were used stratified by age groups (≤64 years and ≥65 years) and with cubic splines of LTL with three knots (located at the 10th, 50th, and 90th percentiles), as the association between LTL and time to death was not linear.

RESULTS

The majority of individuals included aged 64 and younger, and 47 died during the follow-up period. Cancer was the leading cause of death (40%), followed by CVD (28%).

Table 1 – Association between leukocyte telomere length (T/S ratio) percentiles and mortality after approximately 8.9 years of follow-up. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), 2008-2018, N=1988.

Percentiles of leukocyte telomere length (T/S)	Model 0		Model 1	
	Age ≤ 64 years HR (95%CI)	Age ≥ 65 years HR (95%CI)	Age ≤ 64 years HR (95%CI)	Age ≥ 65 years HR (95%CI)
5%	**1.90 (1.07-3.39)**	1.12 (0.28-4.55)	**1.99 (1.05-3.75)**	0.93 (0.22-3.95)
10%	1.32 (0.94-1.83)	1.15 (0.52-2.56)	1.33 (0.93-1.91)	1.05 (0.46-2.39)
25%	0.96 (0.86-1.08)	1.14 (0.84-1.53)	0.95 (0.85-1.07)	1.13 (0.82-1.55)
50%	Ref	Ref	Ref	Ref
75%	**1.34 (1.16-1.54)**	0.79 (0.49-1.29)	**1.40 (1.20-1.62)**	0.75 (0.43-1.30)
90%	**2.16 (1.51-3.09)**	0.57 (0.17-1.92)	**2.41 (1.66-3.52)**	0.49 (0.12-1.92)
95%	**3.27 (1.90-5.63)**	0.43 (0.07-2.72)	**3.87 (2.18-6.86)**	0.34 (0.04-2.70)

Notes: Model 0 = Adjusted for age;
Model 1 = Model 0 + gender, race/skin color, education, BMI, smoking status and excessive alcohol consumption.
HR = Hazard ratio; CI = Confidence Interval.

RESULTS

Among individuals aged 64 years and younger, shorter (5th percentile versus 50th percentile: HR=1.99; 95% CI: 1.05-3.75) and longer (95th percentile versus 50th percentile: HR=3.87; 95% CI: 2.18-6.86) telomeres increased the hazard of death, as compared to those with median telomere length. However, telomere length was not associated with mortality among older individuals.
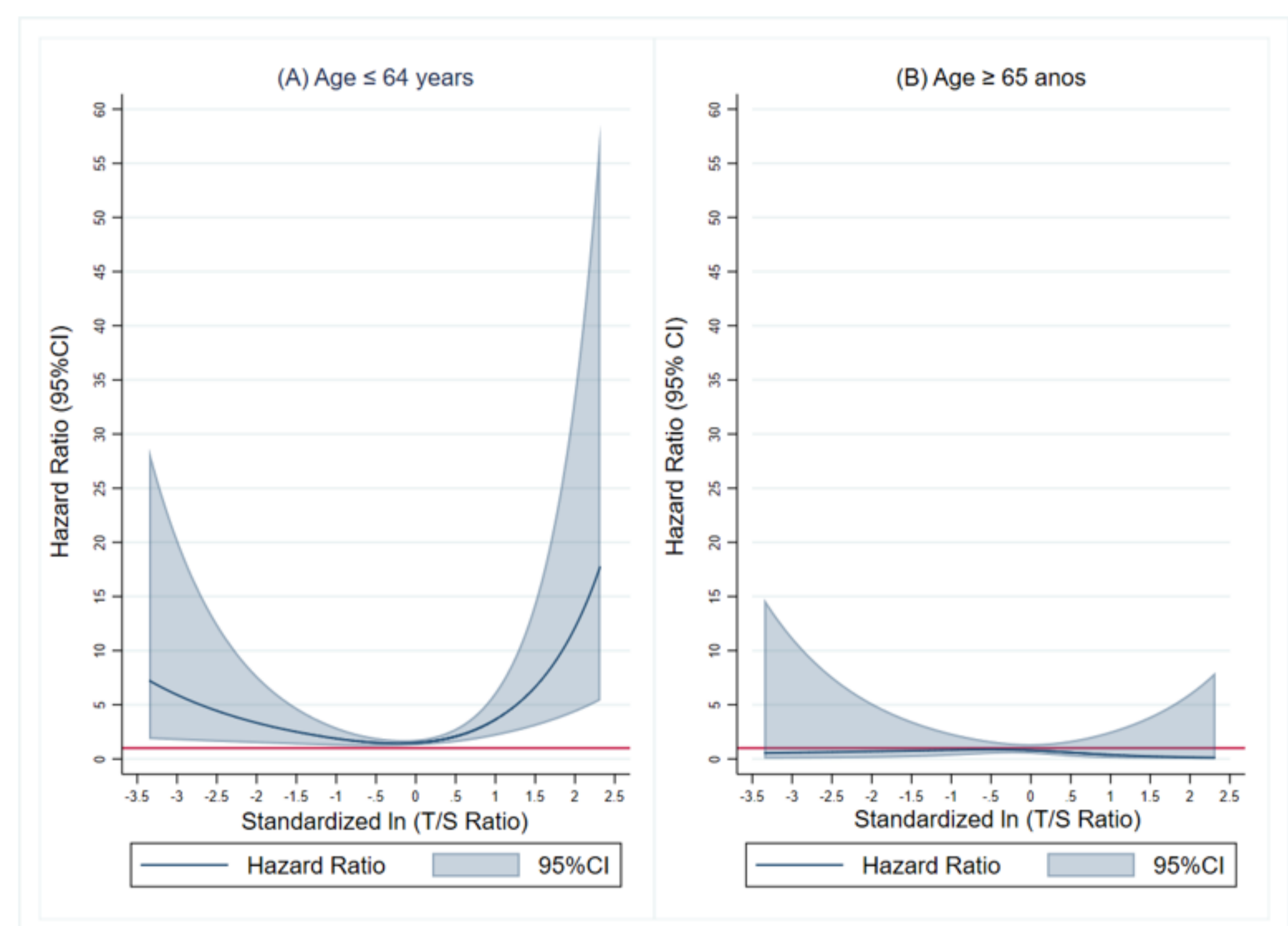

Figure 1 – Multivariate-adjusted hazard ratio for leukocyte telomere length (T/S ratio) in relation to risk of death from chronic diseases according to age groups based on fitted restricted cubic spline regression. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), 2008-2018, N=1988.

CONCLUSIONS

Results indicate higher risk of death from natural causes in adults with both shorter and long telomeres, however telomere length was not associated with death in older individuals. The U-shaped pattern of the association between LTL and mortality in younger adults might be explained by the fact that cancer and CVD were the most frequent causes of death in this study

Conflicts of interest: None.

Contact: amandavianam83@gmail.com