

Longer telomeres are not a positive indicator of extreme longevity (95+ years) in long-lived individuals

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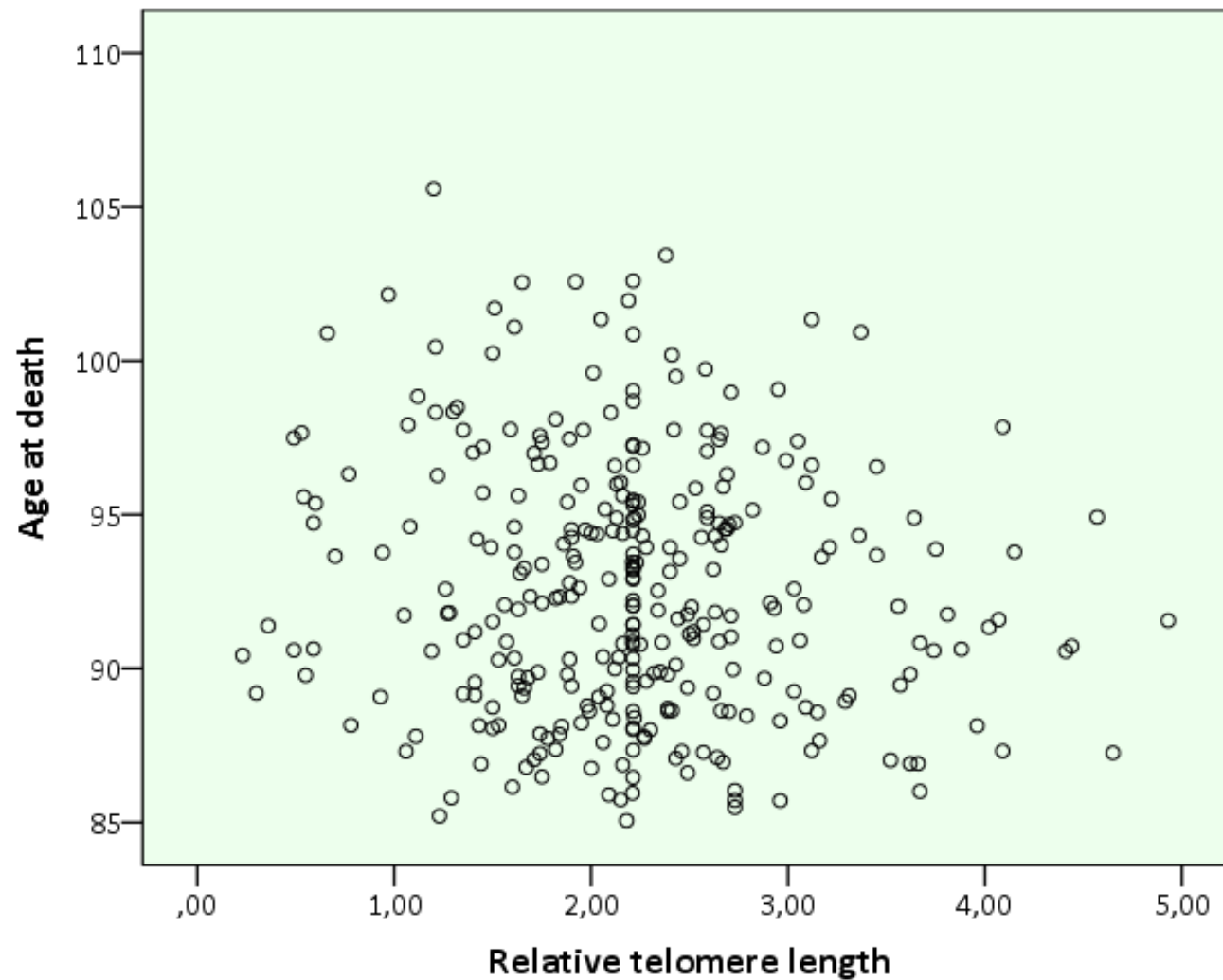


INTRODUCTION

- Telomere shortening is one of the best researched causes of cellular aging, and a positive relation of longer telomeres with human longevity is found in many studies.
- **Aim:** This study aimed to explore whether relative telomere length (RTL) is a good biomarker for extreme longevity in very old individuals (85+ years). Additionally, the relation of RTL and longevity genes is tested.

MATERIALS AND METHODS

- As the samples were collected in the period between 2007 and 2009, age at death for each individual has been determined 10 years after the initial sampling.
- RTL was determined by a quantitative polymerase chain reaction for 314 Croatian individuals aged 85 years and upwards.
- The cut-off for the high/low values of RTL was determined by its' median value.
- 42 SNPs were selected due to their prior association with human longevity and genotyped for this sample.



- In this group of elderly individuals a **negative correlation** of RTL and age at death ($r=-0.114$, $p=0.043$) is found.

Figure 1. Scatter plot of the relation between relative telomere length in very old individuals and their age at death, showing a negative trend.

Table 1. *SH2B3* rs3184504 and *LPA* rs10455872 as significant predictors of high/low relative telomere length: the selected result of the multivariate logistic regression analysis including 42 longevity loci.

Gene	SNP	Multivariate logistic regression analysis			
		Sig.	OR	95% CI for OR	
				Lower	Upper
<i>SH2B3</i>	rs3184504	0.005	2.812	1.370	5.774
<i>LPA</i>	rs10455872	0.024	4.084	1.200	13.905

Table 2. T-test of relative telomere length mean values by *SH2B3* rs3184504 and *LPA* rs10455872 genotypes.

Gene	SNP	t-test				
		Genotype	Frequency	Mean RTL	SD	p
<i>SH2B3</i>	rs3184504	TT	0.268	2.044	0.818	0.024
		CT, CC	0.732	2.274	0.789	
<i>LPA</i>	rs10455872	AA	0.933	2.163	0.713	0.048
		GA, GG	0.067	2.487	0.849	

RESULTS

- Binary logistic regression indicates **longer RTL as a negative predictor** (OR=0.684, 95% CI 0.492-0.951, $p=0.024$) for reaching 95 years of age.
- The multivariate logistic regression analysis showed that 42 selected longevity genes' loci explained 33.9% of RTL variance.
- It also pointed to ***SH2B3* rs3184504** ($p=0.005$) and ***LPA* rs10455872** ($p=0.024$) being significantly related to RTL. This relation was confirmed by t-test showing significant differences in mean RTL among genotypes: both the TT homozygote of rs3184504 and AA homozygote of rs10455872 were related with shorter RTL.

CONCLUSION

- For long-lived individuals telomere length is not a positive predictor for the age of death, especially for the oldest old category.
- Further studies are needed to explore the impact of various longevity genes on RTL in elderly individuals.

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