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Anemia in old age

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Telomere length and anemia in old age. Results from the Newcastle 85-plus Study and the Leiden 85-plus Study

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Submitted

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ABSTRACT

Background Blood cell telomere length has been correlated with a number of major age-related diseases. It is yet unknown whether telomere length is also associated with anemia in older individuals in the general population, because the results from earlier studies investigating this association are inconsistent. Therefore, we investigated the relation between telomere length and the presence of anemia in two population-based studies of individuals aged 85 years and over.

Methods The present cross-sectional study is embedded in the Newcastle 85-plus Study and the Leiden 85-plus Study, two population-based prospective follow-up studies of inhabitants of Newcastle and North Tyneside, UK (n=749) and Leiden, the Netherlands (n=658) aged 85 years and over. High molecular weight DNA was isolated from full fresh blood samples (Newcastle 85-plus Study) and from PBMC samples stored at -80ºC (Leiden 85-plus Study). Telomere length was measured as abundance of telomeric template versus a single gene by quantitative real-time PCR. Anemia was defined according to World Health Organization criteria.

Results In both studies, no differences in median telomere length were observed between participants with anemia and participants without anemia (Newcastle 85-plus Study: 2846 bp [IQR 2433-3630] vs. 2920 bp [IQR 2425-3570], p=0.63; Leiden 85-plus Study: 4136 bp [IQR 3879-4428] vs. 4167 bp [IQR 3893-4501], p=0.41). Telomere length also did not correlate with any other hematological parameter in both men and women.

Conclusion In contrast to other age-related diseases, telomere length is not associated with anemia or any other hematological parameter in older individuals in the general population.

INTRODUCTION

Anemia is very common in older people.[1] Blood loss, iron deficiency, chronic disease, inflammation, renal failure, and deficiencies in vitamin B12 and folic acid are common causes of anemia, but in approximately one third of patients the anemia remains unexplained.[1] Since older subjects with unexplained anemia often present with low leukocyte counts,[2;3] myelodysplastic syndromes or other types of bone marrow failure may be the underlying diagnosis for unexplained anemia.[1;3-5]

Telomeres are DNA-protein complexes at the ends of chromosomes. Telomeres are critical for chromosome stability and function, since they protect chromosome ends against fusion, degradation and recombination. In somatic and hematopoietic cells, telomeres shorten with every cell division as a result of the end-replication problem (i.e. the inability of the DNA replication machinery to replicate the lagging DNA strand after removal of the RNA primer) and oxidative damage.[6] Telomerase can preserve telomere length by adding de novo tandem repeats at chromosome ends, but its activity in somatic cells and hematopoietic progenitor cells is very low. Consequently, mean somatic cell and peripheral blood mononuclear cell (PBMC) telomere length shortens with age.[6] When telomere length falls below a critical level, replicative senescence (permanent growth arrest) is induced.[7;8]

Telomere length is considered a marker of biological and cellular aging and it has been correlated with a number of major age-related diseases such as dementia,[9-12] myocardial infarction,[13] heart failure,[14] atherosclerosis,[15] and solid tissue tumours.[16] However, it is yet unknown whether telomere length is associated with anemia in older persons in the general population, because the results from earlier studies investigating this association are inconsistent.[17-19] Therefore, we investigated the relation between telomere length and the presence of anemia, and unexplained anemia in particular, in two population-based studies of individuals aged 85 years and over.

METHODS

Study population and procedures

Newcastle 85-plus Study

The Newcastle 85-plus Study is a population-based study of 85-year-old inhabitants of Newcastle and North Tyneside, United Kingdom. The study protocol and baseline findings have been described in detail elsewhere.[20;21] In short, all individuals who turned 85 during the year 2006 (i.e. born in 1921) and who were registered with any Newcastle or North Tyneside Primary Care Trust general practice were eligible for study participation (n=1453). 1042 persons agreed to participate (response 71.7%); 778 participants agreed to blood sampling. For the present analyses, data from 749 participants with complete hemoglobin and telomere data were included.

From every participant an informed consent was obtained. If the individual was not able to give informed consent due to cognitive impairment, assent was sought by a caregiver, according to the UK Mental Capacity Act 2005.[22] The study was approved by the Newcastle & North Tyneside Local Research Ethics Committee.

At baseline, all information was obtained during three home visits at the participant's place of residence. During these visits, several questionnaires on socio-economic status (income, level of education) and lifestyle were completed, and a number of measurements and function tests were performed (e.g. Mini Mental State Examination). One additional visit was made to collect fasting blood samples. The participants' GP records were reviewed to obtain information about medical history.

Leiden 85-plus Study

The Leiden 85-plus Study is a population-based prospective study of inhabitants of Leiden, the Netherlands, aged 85 years and over. For the present analyses we made use of the first cohort enrolled between December 1986 and March 1988. A detailed description of the study procedures can be found elsewhere.[23] In short, on December 1, 1986, the community of Leiden in the Netherlands had 105 000 inhabitants, of whom 1258 (1%) were 85 years and over. During the enrolment period from December 1, 1986, to March 1, 1988, 221 participants died before they could be visited. Of the remaining 1037 people that were eligible for the study, 977 (94%) agreed to participate. Blood was taken from 905 subjects. The present study includes data from 658 participants for whom complete data on telomere length and hematological parameters were available.

The Medical Ethical Committee of the Leiden University Medical Center approved the study, and informed consent was obtained from all subjects or their guardian in case of cognitively impaired subjects. During two home visits, participants were interviewed and blood samples were taken according to predefined protocols under non-fasting conditions. The medical history was obtained from the participants and in memory-impaired subjects from partners and carers.

Main laboratory measurements

Routine hematology was performed on anti-coagulated whole blood samples (EDTA-coated tubes) using standard automated analysis systems. Anemia was defined according to WHO criteria (Hb <12 g/dL for women and Hb <13 g/dL for men).[24]

In the Newcastle 85-plus Study, DNA was extracted from full fresh blood (white blood cells, i.e. granulocytes and PBMC) with the QiaAmp DNA Maxi kit (Qiagen Ltd, Crawley, UK). In the Leiden 85-plus Study, DNA was extracted from PBMC samples stored at -80ºC using the QiaAmp DNA Mini kit (Qiagen Ltd, Crawley, UK). DNA concentration and quality were monitored by agarose gel

electrophoresis. Samples were discarded if DNA degradation (smear below 20 kb) was visible. Telomere length was measured as the ratio of the starting quantity for telomeres versus the starting quantity for the single copy gene of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (as control) by quantitative real-time PCR[25] with modifications as described previously.[26] Measurements were performed in quadruplicates. Three DNA samples with known telomere lengths (3.0, 5.5 and 9.5 kbp) were run as internal standards together with each batch of 16 study samples to convert the ratios of starting quality into telomere lengths in base pairs.

Additional laboratory measurements

Additional laboratory measurements were performed in the Newcastle 85-plus Study. Ferritin levels were determined by ADVIA Centaur chemiluminescence immunoassay in serum samples. A chemiluminescence microparticle immunoassay on an Abbott ARCHITECT analyzer was used to determine vitamin B12 in plasma and red cell folate levels from EDTA anti-coagulated blood samples. Serum creatinine levels were measured as a proxy of renal function on an Olympus AU640 system. Serum high-sensitivity C-reactive protein (CRP) levels were determined as an indicator of inflammatory status by the Dade Behring CardioPhase hsCRP immunoassay.

Data analysis

In both studies, differences in telomere length between participants with and without anemia were tested with Mann-Whitney U tests. The relation between telomere length and hemoglobin levels was displayed in scatter plots with superimposed regression lines, stratified by gender, and analyzed with linear regression analysis. Differences in hematological characteristics between quintiles of telomere length were tested with Chi-square tests (categorical data) or Jonkheere-Terpstra tests (continuous data), for men and women separately.

In the Newcastle 85-plus Study, telomere length was also compared between participants with RBC, platelets and WBC in the lowest (gender-dependent) quartile and participants with RBC, platelets and WBC in the highest (gender-dependent) quartile. In addition, we used Mann-Whitney U tests to analyze differences in telomere length between participants with explained and unexplained anemia. Explained anemia was defined as the presence of anemia and one or more of the following: ferritin concentration <15 μg/L, vitamin B12 concentration <170 pg/mL, red cell folate concentration <160 μg/L, C-reactive protein concentration >5 mg/L and/or creatinine concentration >155 μmol/L. Unexplained anemia was defined as the presence of anemia with normal ferritin, vitamin B12, red cell folate, CRP and creatinine concentrations. Furthermore, we compared telomere length between participants with unexplained anemia and participants without anemia and normal ferritin, vitamin B12, red cell folate, CRP and creatinine concentrations.

Data analyses were performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL).

Table 1. Socio-demographic and hematological characteristics of the study populations

	Newcastle 85-plus Study N=749	Leiden 85-plus Study N=658
Socio-demographics		
Age, years	85	89 (88-92)
Men	295 (39.3%)	176 (26.7%)
Institutionalization	62 (8.3%)	354 (53.8%)
Current smoking	42 (5.6%)	102 (15.5%)
Hematological characteristics		
Hemoglobin, g/dL	13.1 (12.1-14.1)	13.4 (12.3-14.2)
Hematocrit, %	0.40 (0.37-0.43)	0.41 (0.38-0.43)
MCV, fL	94 (90-97)	91 (88-94)
Anemia*	222 (29.6%)	127 (19.3%)
Microcytic anemia (MCV<80 fL)	9 (4.1%)	13 (10.2%)
Normocytic anemia (MCV 80-100 fL)	190 (85.6%)	104 (81.9%)
Macrocytic anemia (MCV>100 fL)	23 (10.4%)	10 (7.9%)
RBC, x 10^9/L	4.3 (3.9-4.6)	4.5 (4.2-4.8)
Platelets, x 10^9/L	249 (209-297)	NA
WBC, x 10^9/L	6.4 (5.4-7.6)	6.1 (5.2-7.3)
Telomere length, bp	2889 (2427-3589)	4163 (3885-4495)
Men	3005 (2517-3832)	4277 (3972-4684)
Women	2797 (2356-3418)	4113 (3849-4425)
Other clinical characteristics		
MMSE, points	28 (25-29)	26 (20-29)
Ferritin, µg/L	59 (28-121)	NA
Vitamin B12, pg/mL	313 (230-437)	NA
Red cell folate, µg/L	383 (271-565)	NA
Creatinine, µmol/L	99 (86-119)	NA
C-reactive protein, mg/L	2.6 (1.2-5.9)	NA
Comorbidity		
Stroke	100 (13.4%)	20 (3.0%)
Myocardial infarction	110 (14.7%)	49 (7.4%)
Dementia	52 (7.0%)	50 (7.6%)
Diabetes mellitus	103 (13.8%)	82 (12.5%)
Malignancy	184 (24.6%)	106 (16.1%)

Categorical data are presented as N (%). Continuous data are presented as median (interquartile range). IQR = interquartile range, MCV = mean cell volume, RBC = red blood cell count, WBC = white blood cell count, MMSE = Mini Mental State Examination

* Hemoglobin <12 g/dL for women and <13 g/dL for men

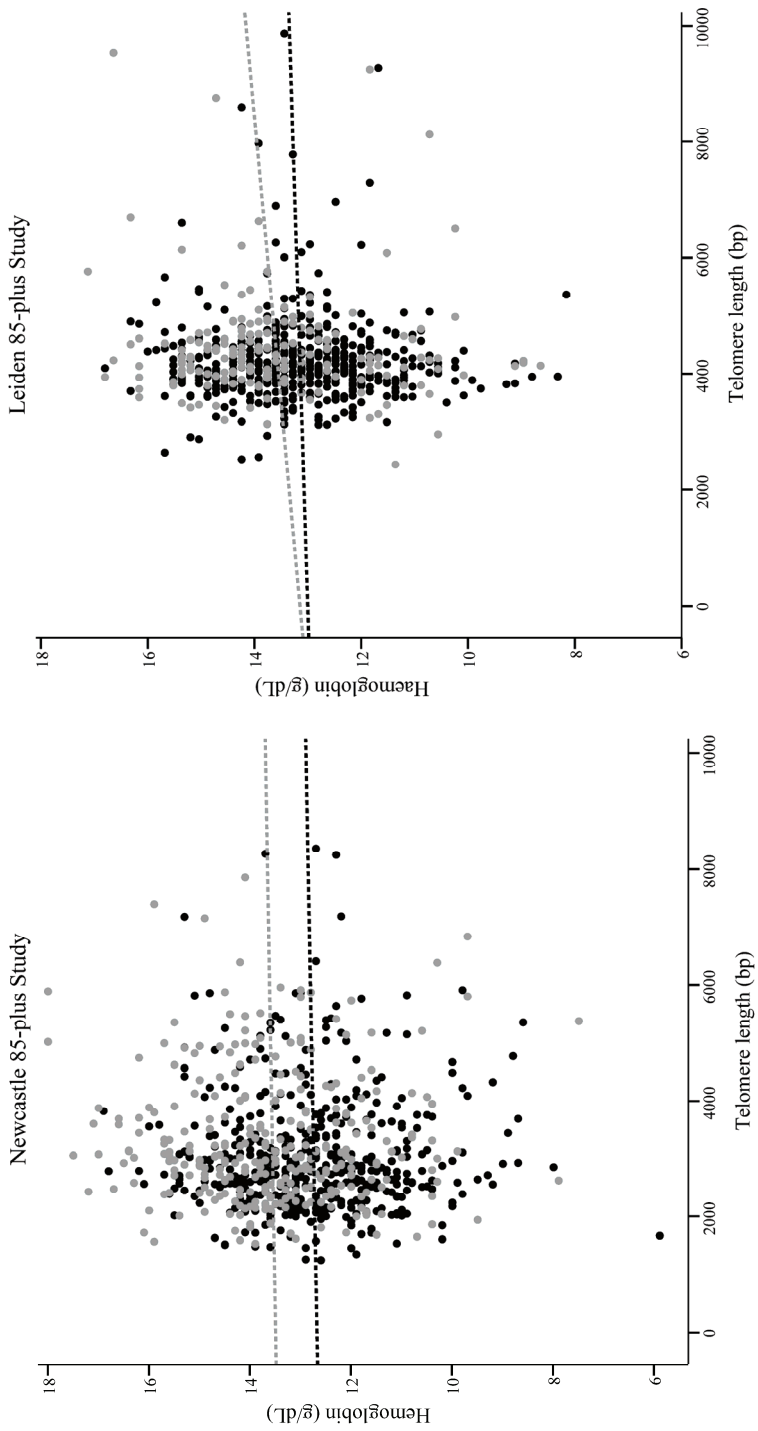

Figure 1. Scatter plots with superimposed regression lines of hemoglobin levels (*y*-axis) against telomere length (*x*-axis) in the Newcastle 85-plus Study (n=749) and Leiden 85-plus Study (n=658). Legend: ● men, ● women

RESULTS

Table 1 describes the socio-demographic and hematological characteristics of both study populations. All participants in the Newcastle 85-plus Study were aged 85 years. The median age of the cohort from Leiden was 89 years (IQR 88-92). The prevalence of anemia was 29.6% (n=222/749) in the Newcastle 85-plus Study and 19.3% (n=127/658) in the Leiden 85-plus Study. In both studies, women had shorter telomeres than men (Mann-Whitney U test $p<0.01$) and the prevalence of anemia was higher in men than in women (Newcastle 85-plus Study: men 33.2% (98/295) vs. women 27.3% (124/454), Chi-square test p=0.08; Leiden 85-plus Study: men 26.7% (47/176) vs. women 16.6% (80/482), $p<0.01$)

Figure 1 depicts two scatter plots with superimposed regression lines of hemoglobin levels (*y*-axis) against telomere length (*x*-axis) for men and women separately. There was no relation between telomere length and hemoglobin levels in either men or women in both studies (linear regression analyses, $p>0.40$).

No differences in median telomere length were observed between participants with anemia and participants without anemia (Table 2, Newcastle 85-plus Study: 2846 bp [IQR 2433-3630] vs. 2920 bp [IQR 2425-3570], p=0.63; Leiden 85-plus Study: 4136 bp [IQR 3879-4428] vs. 4167 bp [IQR 3893-4501], p=0.41). Similar results were found when we stratified on gender or when we restricted the analysis in the Leiden 85-plus Study to participants aged 85 through 89 years (n=384).

Table 2. Telomere length in base pairs depending on the presence of anemia in participants aged 85 years and over

	Anemia*		No anemia		P
	n	Median (IQR)	n	Median (IQR)	
Newcastle 85-plus Study					
Total population	222	2846 (2433-3630)	527	2920 (2425-3570)	0.63
Men	98	2994 (2518-3789)	197	3025 (2513-3899)	0.71
Women	124	2782 (2341-3536)	330	2816 (2362-3399)	0.54
Leiden 85-plus Study					
Total population	127	4136 (3879-4428)	531	4167 (3893-4501)	0.41
Men	47	4194 (3955-4585)	129	4329 (3982-4701)	0.26
Women	80	4085 (3877-4360)	402	4121 (3844-4443)	0.51

Data are presented as median (interquartile range). P-values were obtained by Mann-Whitney U tests.
* Hemoglobin <12 g/dL for women and <13 g/dL for men

Table 3. Hematological characteristics for quintiles of telomere length in men

	Quintile					
	1	2	3	4	5	P
Newcastle 85-plus Study						
N	59	59	59	59	59	
Range telomere length, bp	1527-2410	2416-2836	2840-3217	3219-4138	4141-7855	
Age	85	85	85	85	85	
Hemoglobin, g/dL	13.6 (12.5-14.3)	13.4 (12.5-14.5)	13.8 (12.5-15.0)	13.8 (12.3-15.1)	13.5 (12.5-14.5)	0.49
Anemia*	19 (32.2%)	22 (37.3%)	18 (30.0%)	22 (37.3%)	17 (28.8%)	0.79
Hematocrit, %	0.41 (0.38-0.44)	0.40 (0.37-0.44)	0.42 (0.37-0.46)	0.42 (0.38-0.46)	0.42 (0.38-0.45)	0.11
MCV, fL	95 (92-98)	95 (92-97)	96 (9-98)	94 (90-97)	94 (9-96)	0.22
RBC, x 10^9/L	4.3 (4.0-4.6)	4.3 (3.9-4.6)	4.4 (3.9-4.9)	4.5 (4.0-4.8)	4.4 (4.1-4.8)	0.05
Platelets, x 10^9/L	239 (200-277)	239 (205-287)	218 (179-269)	227 (168-269)	217 (184-250)	0.01
WBC, x 10^9/L	6.2 (5.4-7.8)	6.7 (5.7-8.1)	6.7 (5.6-7.3)	6.5 (5.8-7.5)	6.5 (5.2-7.6)	0.88
Leiden 85-plus Study						
N	35	35	36	35	35	
Range telomere length, bp	2435-3909	3914-4148	4150-4426	4428-4770	4779-9526	
Age	88 (88-92)	90 (88-93)	89 (88-91)	89 (87-92)	90 (88-92)	0.63
Hemoglobin, g/dL	13.9 (12.0-14.7)	13.8 (12.5-14.7)	14.1 (12.2-14.8)	13.9 (12.8-14.7)	13.8 (13.0-14.2)	0.96
Anemia*	11 (31.4%)	10 (28.6%)	10 (27.8%)	9 (25.7%)	7 (20.0%)	0.86
Hematocrit, %	0.42 (0.36-0.44)	0.42 (0.36-0.44)	0.42 (0.39-0.44)	0.42 (0.39-0.45)	0.42 (0.40-0.44)	0.84
MCV, fL	91 (89-97)	94 (90-97)	91 (88-95)	91 (89-94)	92 (89-96)	0.51
RBC, x 10^9/L	4.4 (4.2-4.9)	4.5 (4.2-4.7)	4.7 (4.2-4.9)	4.7 (4.3-4.9)	4.6 (4.1-4.9)	0.43
WBC, x 10^9/L	6.1 (5.4-7.8)	6.7 (5.8-7.6)	6.1 (5.3-7.8)	6.2 (5.2-6.8)	6.7 (5.6-7.4)	0.80

Categorical data are presented as N (%). Continuous data are presented as median (interquartile range).
P-values obtained by Chi-square tests (categorical data) or Jonkheere-Terpstra tests (continuous data).
MCV = mean cell volume, RBC = red blood cell count, WBC = white blood cell count.
* Hemoglobin <13 g/dL

Table 4. Hematological characteristics for quintiles of telomere length in women

	Quintile					
	1	2	3	4	5	P
Newcastle 85-plus Study						
N	90	91	91	91	91	
Range telomere length, bp	1245-2243	2245-2628	2632-2994	3010-3667	3672-8359	
Age	85	85	85	85	85	
Hemoglobin, g/dL	12.7 (11.8-13.4)	12.9 (11.7-14.0)	12.9 (11.8-13.7)	12.9 (12.3-14.0)	12.6 (11.7-13.7)	0.55
Anemia*	26 (28.9%)	28 (30.8%)	26 (28.6%)	17 (18.7%)	27 (29.7%)	0.35
Hematocrit, %	0.39 (0.36-0.41)	0.39 (0.36-0.43)	0.39 (0.36-0.42)	0.40 (0.37-0.43)	0.38 (0.36-0.42)	0.67
MCV, fL	94 (89-97)	93 (90-95.2)	94 (90-97)	92 (87-97)	93 (89-96)	0.30
RBC, x 10^9/L	4.1 (3.9-4.4)	4.2 (3.8-4.7)	4.2 (3.9-4.5)	4.3 (4.0-4.7)	4.1 (3.9-4.5)	0.40
Platelets, x 10^9/L	253 (208-295)	268 (231-326)	271 (227-309)	256 (218-303)	270 (216-317)	0.72
WBC, x 10^9/L	6.3 (5.3-7.3)	6.4 (5.4-7.6)	6.3 (5.3-7.9)	6.4 (5.3-7.5)	6.4 (5.4-8.0)	0.51
Leiden 85-plus Study						
N	96	97	96	97	96	
Range telomere length, bp	2527-3790	3791-4023	4026-4225	4226-4529	4537-10698	
Age	90 (88-93)	89 (88-92)	89 (88-92)	89 (87-91)	90 (88-91)	0.14
Hemoglobin, g/dL	13.4 (12.5-14.4)	13.0 (11.9-13.8)	13.3 (12.4-13.9)	13.1 (12.3-14.1)	13.3 (12.5-13.8)	0.93
Anema*	13 (13.5%)	24 (24.7%)	14 (14.6%)	14 (14.4%)	15 (15.6%)	0.20
Hematocrit, %	0.41 (0.38-0.44)	0.39 (0.37-0.42)	0.40 (0.38-0.43)	0.40 (0.38-0.43)	0.40 (0.38-0.43)	0.95
MCV, fL	91 (88-94)	89 (87-93)	90 (87-93)	90 (87-93)	90 (87-94)	0.74
RBC, x 10^9/L	4.5 (4.1-4.8)	4.5 (4.0-4.9)	4.5 (4.2-4.8)	4.5 (4.2-4.8)	4.5 (4.2-4.8)	0.70
WBC, x 10^9/L	6.0 (5.2-7.1)	6.2 (5.4-7.2)	5.7 (4.9-7.4)	6.4 (5.2-7.7)	5.9 (5.0-7.2)	0.64

Categorical data are presented as N (%). Continuous data are presented as median (interquartile range).
P-values obtained by Chi-square tests (categorical data) or Jonkheere-Terpstra tests (continuous data).
MCV = mean cell volume, RBC = red blood cell count, WBC = white blood cell count.
* Hemoglobin <12 g/dL

Tables 3 and 4 show the hematological characteristics depending on quintiles of telomere length for men and women, respectively. In both men and women, telomere length was not associated with any of the hematological parameters, either in the Newcastle 85-plus Study, or in the Leiden 85-plus Study. We did find a p-value below 0.05 for the association between telomere length and platelets for men in the Newcastle 85-plus Study, but this may be considered a chance finding as there was not a clear dose-dependent relation between telomere length and platelet count.

In the Newcastle 85-plus Study, no differences in telomere length were found between participants with RBC, platelets and WBC in the lowest gender-dependent quartile (n=30) and participants with RBC, platelets and WBC in the highest gender-dependent quartile (n=14) (2771 bp [IQR 2127-3099] vs. 3024 bp [IQR 2654-3724], p=0.18). In addition, we did not find any differences in median telomere length between participants with unexplained anemia (n=79) and participants with explained anemia (n=143): 2809 bp (IQR 2278-3491) vs. 2880 bp (IQR 2494-3759), p=0.40. Furthermore, no differences in median telomere length were found between participants with unexplained anemia (n=79) and participants without anemia and normal ferritin, vitamin B12, red cell folate, CRP and creatinine concentrations (n=318) (2809 bp [IQR 2278-3491] vs. 2932 bp (IQR 2405-3574) respectively, p=0.35).

DISCUSSION

We examined the relationship between telomere length and anemia in two independent population-based studies of older individuals. We found no association between telomere length and hemoglobin concentration or any other hematological parameter. Neither did participants with unexplained anemia have shorter telomeres than participants without anemia.

The lack of association between telomere length and anemia was unexpected. First, telomere length has been correlated with many other major age-related diseases.[9-16] Second, myelodysplastic syndromes or other types of bone marrow failure are thought to explain the increased frequency of (unexplained) anemia in older individuals.[1;3-5] Adult hematopoietic stem cells show a severe loss of telomeric DNA compared to cells from fetal liver or umbilical cord blood[27] and aged mice have a decreased capacity to replace blood cells during hematopoietic stress compared to younger mice,[4;28-30] indicating a loss of replicative potential for bone marrow stem cells with age[27;31] and a possible incapacity to react to the physiologic demand for blood cell replenishment with age.[4;5;29] Since the results of earlier studies indicate that patients with myelodysplastic syndromes or other types of bone marrow failure syndromes have shortened telomeres,[32-36] shorter telomere length has been associated with an increased risk of anemia in chronic heart failure patients[17] and shorter telomere length was an independent predictor of lower red blood cell counts in a study of middle-aged subjects (aged 35-55 years),[18] we

hypothesized that telomere length is a marker of hematopoietic ageing and bone marrow failure, and as a result, would be associated with anemia in older individuals in the general population. The results of this study, however, do not support this hypothesis.

One possible explanation for the lack of association between telomere length and anemia in our study may be that telomere length in WBC in old age is very unstable and does not have enough predictive power for age-related morbidity and mortality at ages over 85 years.[37] This explanation, however, seems unlikely, because we recently found a strong and significant relation between telomere length and left ventricular function in the pilot study of the Newcastle 85-plus Study (n=89, aged 85 years).[14] Another explanation for the lack of association between telomere length and anemia may be that, despite the results from earlier studies suggesting otherwise,[17;18] there in fact is no association between telomere length and bone marrow failure, or bone marrow failure and anemia, in the general population of older individuals. This explanation is supported by the results from a study by Mollica and colleagues in which no correlation was found between telomere length and blood counts in a population-based sample of 717 women aged 38-100 years (median 72 years).[19]

Our findings do not preclude that short telomeres may drive aplastic syndromes. However, the repetitive negative findings presented here suggest that in the population at large, a myelodysplastic syndrome per se is an unlikely explanation for the presence of anemia in older people. Similar discrepancies between studies in selected populations and population-based studies have been reported previously. For instance, Cherkas et al. found an association between socio-economic status and telomere length in female twins aged 18-75 years,[38] but no such association was found by Adams et al. in an unselected cohort of 50-year-olds.[39]

We observed a large difference in median telomere length between the two cohorts. Participants in the Newcastle 85-plus Study had shorter telomeres than participants in the Leiden 85-plus Study. The fact that DNA samples were derived from WBC in the Newcastle 85-plus Study and from PBMC in the Leiden 85-plus Study is unlikely to explain this difference in telomere length. Granulocytes tend to have longer telomeres than lymphocytes.[40;41] The difference in telomere length between these two cell populations increases with age,[40;41] which would have led us to expect longer median telomere length in the cohort from Newcastle. The difference in telomere length between the populations is as yet unexplained; possible factors include differences in disease incidence, dietary patterns, or socio-economic status.

A limitation of the present study is its cross-sectional design, which restricts our capacity to draw conclusions about causal relations. Another limitation is that in neither of the studies bone marrow biopsies were available to confirm the diagnosis

of myelodysplasia or bone marrow failure.[4] We are therefore limited in studying the relationships between telomere length and bone marrow failure, and bone marrow failure and unexplained anemia.

A strength of our analysis is that we made use of data from two large studies of individuals aged 85 years and over, giving us a unique opportunity to cross-validate our negative findings, especially since in both studies telomere length was measured in the same laboratory using the same validated technique.[26;37] Another strong point of the present study is the population-based nature of both cohorts, allowing us to generalize our results to the population of older people at large.

In conclusion, in contrast to other age-related diseases, telomere length is not associated with anemia or any other hematological parameter in older individuals in the general population, despite the plausible biological mechanism underlying this association. To further investigate this intriguing matter, studies incorporating bone marrow biopsies will be needed.

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