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The combined effect of anemia and dynapenia on mortality risk in older adults: 10-Year evidence from the ELSA cohort study

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ABSTRACT

Background/Objective: Anemia and dynapenia can occur simultaneously. Separately, both conditions increase the mortality risk with advancing age. However, there is no epidemiological evidence on the combined effect of these conditions on mortality in older adults. We investigated whether combined anemia and dynapenia increase the mortality risk, and whether there are gender differences.

Methods: A 10-year follow-up study was conducted involving 5,310 older adults from the English Longitudinal Study of Ageing (ELSA). According to the diagnosis of anemia (hemoglobin concentration < 13.0 g/dL in men and < 12.0 g/dL in women) and dynapenia (grip strength < 26 kg for men and < 16 kg for women), individuals at baseline were categorized as "non-anemic/non-dynapenic", "dynapenic", "anemic" and "anemic/dynapenic". The outcome was all-cause mortality during the follow-up period.

Results: A total of 984 deaths were computed during the follow-up (63.7% in non-anemic/non-dynapenic, 22.8% in dynapenic, 7.5% in anemic and 6.0% in anemic/dynapenic). Adjusted Cox proportional hazard models stratified by sex showed that anemia and dynapenia combined was associated with an increased mortality risk in men (HR: 1.64; 95% IC 1.08 – 2.50) and women (HR: 2.17; 95% CI 1.44 – 3.26). Anemia in men (HR: 1.68; 95% CI 1.22 – 2.32) and dynapenia in women (HR: 1.37; 95% CI 1.09 – 1.72) were also risk factors for mortality.

Conclusions: The coexistence of anemia and dynapenia increases the mortality risk, highlighting the need for early identification, prevention, and treatment of these conditions to reduce their complications and the mortality risk.

1. Introduction

Anemia is defined as a reduction in the number of red blood cells and oxygen-carrying capacity, compromising the ability to meet the body's physiologic demands (World Health Organization, 2011). This condition affects approximately 12% of older adults, and its prevalence can reach 25% at 85 years of age (Gaskell et al., 2008; World Health Organization, 2008) due to a reduced erythropoietin secretion and inadequate erythropoiesis, nutritional deficiencies (iron, folic acid, and vitamin B12), inflammaging, or arising from adjacent conditions, which promotes

Abbreviation: A/D, anemic/dynapenic; BADL, Basic Activities of Daily Living; BMI, Body Mass Index; CES-D, The Center for Epidemiologic Studies Depression Scale; ELSA, English Longitudinal Study of Ageing; HGS, Handgrip Strength; IADL, Instrumental Activities of Daily Living; NA/ND, non-anemic/non-dynapenic.

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greater activation of macrophages with sequestration of circulating iron (Girelli et al., 2018; Nemeth & Ganz, 2014).

Anemia is an important predictor of adverse outcomes later in life, such as falls, disability, hospitalization, and death (Penninx et al., 2004, 2005, 2006; Zakai et al., 2005). Penninx et al., 2006 and Zakai et al., 2005 in studies with 4 and 11-year of follow-up, respectively, demonstrated that anemic individuals have a mortality risk higher than 50% compared to non-anemic in a population of older American adults. This risk could be attributed to an inefficient oxygen supply to the tissues, which can cause organ damages and complications in vital functions, increasing the mortality risk (Girelli et al., 2018; Silverberg et al., 2001).

There is a growing number of cross-section evidence pointing to a relationship between anemia and functional outcomes in older adults (Cesari et al., 2004; Hirani et al., 2016; Penninx et al., 2004; Pires Corona et al., 2014), such as dynapenia, defined by the decline in muscle strength with aging (Clark & Manini, 2012). Alexandre et al., (2018) identified that anemia is an associated factor with dynapenia in a population of older Brazilian adults, and Cesari et al., (2004) found that, anemic individuals have a weaker ankle extension strength than those non-anemic in a population of older Italian adults. Similarly, Gi et al., (2020) and Jang et al., (2022) in a population of older Korean adults also shown that individuals with anemia are more likely to have dynapenia than non-anemic, and this association is more pronounced in men than in women. The reduced oxygen supply to tissues due to anemia also affects musculoskeletal structures, representing one of the possible mechanisms of decreased strength and muscle performance in these individuals (Dodd et al., 1993).

Like anemia, dynapenia is associated with mortality. Alexandre et al., (2014) demonstrated that older Brazilian adults with dynapenia had a higher mortality risk in 10-year of follow-up compared to non-dynapenic. Furthermore, Al Snih et al., (2002) found a higher mortality risk in older Mexican American adults with dynapenia compared to non-dynapenic after 5-year of follow-up, with a greater risk in men than women.

Based on the available evidence and the possibility of anemia and dynapenia occurring simultaneously with advancing age, there is still a gap in the literature regarding the effect of coexistence of both conditions on mortality. Therefore, our aims were to investigate whether the combined effect of anemia and dynapenia is associated with an increased mortality risk in older English adults over a 10-year follow-up period, and to examine whether there are gender differences.

2. Methods

2.1. Study population

The English Longitudinal Study of Ageing (ELSA) is an ongoing prospective observational study of community-dwelling people aged 50 years and older in England that commenced in 2002 and was designed to be nationally representative. The ELSA follow-up interviews occur every two years and health examinations (i.e. nurse visits), carried out for the first time in 2004, every four years, where blood samples and anthropometric data were assessed. A detailed description of the study can be found elsewhere (Steptoe et al., 2013). All ELSA participants gave written informed consent. The National Research and Ethics Committee granted Ethical approval for all the ELSA waves (MREC/01/2/91).

The baseline of this study is Wave 2 (2004-2005), composed of 8,780 individuals, of which 7,666 were eligible for a nurse visit. Among them, blood collection was obtained only in 7,364 and hemoglobin levels were ascertained in 5,841 (Banks & Institute for Fiscal Studies, 2006). Another 531 individuals were excluded due to the lack of information on the covariates, resulting in a final analytical sample comprised of 5,310 individuals. **Fig. 1.** presents the selection of individuals at baseline.

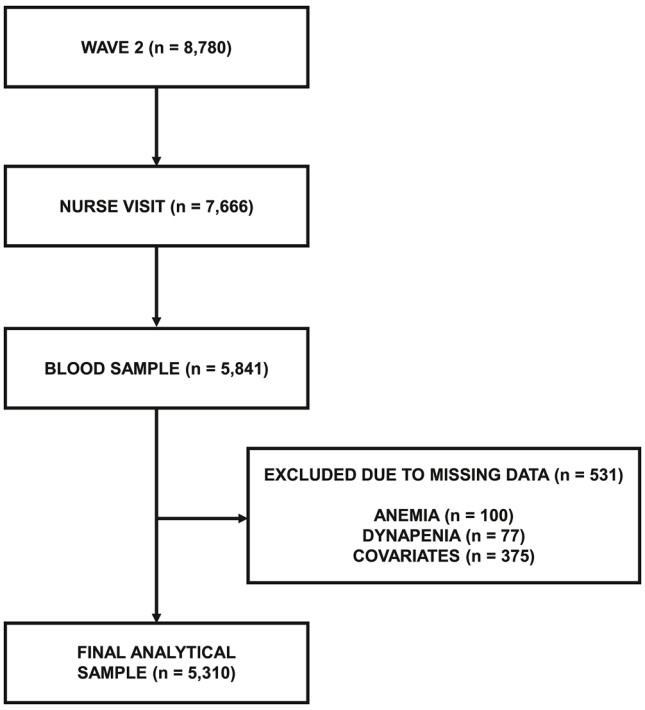

Figure 1. Selection of individuals at baseline.

2.2. Anemia

Blood samples were not taken from who had a clotting or bleeding disorder, had ever had a fit, were currently on anticoagulant drugs, or were did not give their consent in writing. Hemoglobin levels were measured with two Abbott Diagnostic Cell-Dyn 4000 analyzers and carried out at the Royal Victoria Infirmary (Newcastle-upon-Tyne, UK) (Craig et al., 2006). Anemia was defined by hemoglobin levels < 13.0 g/dL in men, and < 12.0 g/dL in women (World Health Organization, 2011).

2.3. Dynapenia

Dynapenia was based on handgrip strength (HGS), measured using a dynamometer Smedley with a scale of 0–100 kg and adjusted to the participant's hand. Maximum strength tests were performed three times in each hand, with 1 minute rest period between trials. The highest strength value in the dominant hand was used in our analysis. Dynapenia was defined as grip strength < 16 kg for women and < 26 kg for men (Alley et al., 2014).

2.4. Classification of the groups

The participants were divided into four groups based on their anemia and dynapenia status as follow: "non-anemic/non-dynapenic (NA/ND)"; "dynapenic", "anemic", and "anemic/dynapenic (A/D)".

2.5. Mortality ascertainment

Mortality data were obtained from the Office for National Statistics for participants consenting to data linkage. For the present analyses, all-cause mortality over a 10-year follow-up were obtained.

2.6. Covariates

The covariates presented were collected at baseline. Sociodemographic variables were age (50–59; 60–69; 70–79; 80 or older), marital

status (with or without conjugal life), level of education (>13 years; 12–13 years; ≤ 11 years), and total household wealth (classified in quintiles) (de Oliveira Máximo et al., 2021).

The health behaviors included smoking status (non-smokers, former smokers and current smokers), frequency of alcohol consumption (rarely/never, frequently, daily and did not respond) (Alexandre et al., 2017), and physical activity categorized into four groups as previously described: inactive (no activity on a weekly basis); only mild activity at least once a week; at least moderate but no vigorous activity at least once a week; and any vigorous activity at least once a week (Hamer et al., 2014).

The clinic conditions were self-reported medical diagnosed of hypertension, diabetes, cancer, stroke, lung disease, heart failure, abnormal heart rhythm and ischemic heart disease. Hypercholesterolemia (≥ 5.3 mmol/L), hypertriglyceridemia (≥ 1.7 mmol/L) and low HDL (≤ 0.9 mmol/L for men and ≤ 1.3 mmol/L for women) were based in blood samples.

The presence of depressive symptoms was recorded when a score on the shortened version of the Center for Epidemiologic Studies Depression Scale (CES-D) was ≥ 4 (Radloff, 1977). Cognitive function was measured by a memory test that consisted of 10 randomly selected words that the respondents were asked to recall immediately and five minutes later. We used the total number of recalled words (possible range: 0 to 20 words) as a marker of memory performance (Ofstedal & Fisher, 2005).

The body mass index was calculated dividing weight by height squared (kg/m2) and classified as "underweight" (< 18.5 kg/m^2), "normal weight range" (≥ 18.5 and < 25 kg/m^2), "overweight" (≥ 25 and < 30 kg/m^2) and "obesity" (≥ 30 kg/m^2) (World Health Organization, 2000).

Basic activities of daily living (BADL) were assessed by self-reported of difficulty in dressing, walking across a room, bathing or showering, eating, getting in or out of bed, using the toilet, according to the modified Katz Index (Katz, 1963). Instrumental activities of daily living (IADL) were assessed by self-reported of difficulty in preparing meals, managing money, using transportation, shopping, using the telephone, house cleaning, washing clothes, and taking medications according to the adapted Lawton scale (Lawton, 1971). BADL and IADL impairment were analyzed as continuous variables.

2.7. Statistical analyses

The sample characteristics at baseline were expressed as means ±, standard deviations (SD) and proportions. Differences in baseline characteristics between the four analytical groups according to sex were assessed using chi square test and analysis of variance (ANOVA one way) ($p < 0.05$).

We examined all deaths occurred during a 10-year follow-up using Cox proportional hazard models controlled for socioeconomic characteristics, lifestyle, clinical conditions, and disability, previously selected in univariate analyzes ($p < 0.20$) (Maldonado & Greenland, 1993). The hazard ratios (HR) and their 95% confidence intervals (CI) for mortality risk according to anemia and dynapenia status were calculated. Based on the final Cox proportional hazards model, we analyzed the survival curves, and differences between curves were evaluated using Log-rank test. The assumption of proportional hazards was verified graphically by means of a log-log plot of the response variable ($p < 0.001$).

All the analyses were stratified by sex and performed using Stata 16 SE (Stata Corp, College Station, TX, USA).

3. Results

Among the 5,310 individuals at baseline, 84% were NA/ND, 10.7% had dynapenia, 3.8% had anemia and 1.5% were A/D. A total of 984 deaths (18.5%) were computed over the 10-year of follow-up, of which 63.7% were related to NA/ND individuals, 22.8% to dynapenic, 7.5% to anemic, and 6.0% to A/D individuals. The sample characteristics at baseline according to the status of anemia and dynapenia, as well the gender differences in each status and between the status are shown in **Table 1**.

Compared to NA/ND, participants from the other three groups were older, had a lower wealth quintile and lower educational level, had a lower proportion of conjugal life, were more sedentary, with a higher prevalence of depression, greater IADL impairment and worse memory performance.

A/D individuals drank less, had lower cholesterol levels and were more obese compared to NA/ND. In addition, A/D men smoked less and had a higher prevalence of underweight, while A/D women had a higher prevalence of high HDL levels, heart failure, and greater BADL impairment. Dynapenic individuals drank more and had a greater impairment in BADL compared to NA/ND. Furthermore, dynapenic men had a higher prevalence of diabetes, lung disease and obesity, and a lower prevalence of hypercholesterolemia and abnormal heart rhythm, while dynapenic women had a higher prevalence of underweight compared to their respective NA/ND counterparts. Anemic individuals smoked less and had higher prevalence of hypercholesterolemia compared to NA/ND. Anemic men had a higher prevalence of high HDL levels, cancer, while anemic women drank less and had a higher prevalence of heart failure compared to their respective NA/ND pairs.

Compared to dynapenic, A/D individuals were older. Men smoked less, had a higher prevalence of abnormal heart rhythm, and poorer memory performance, while women had a higher prevalence of high HDL levels and greater functional impairment. Compared to anemic, A/D individuals were older. A/D men had greater BADL impairment and poorer memory performance, while A/D women had lower education level, were more sedentary, had greater functional impairment, and poorer memory performance. In the comparison between anemic and dynapenic, anemic men had greater functional impairment, while anemic women were older, with lower educational level, smoked and drank less, had greater IADL impairment and worse memory performance.

Fully adjusted Cox proportional hazards models for men showed that anemia increased in 68% (HR: 1.68; 95% CI: 1.22 – 2.32) the mortality risk, and when combined with dynapenia, the risk was 64% (HR: 1.64; 95% CI: 1.08 – 2.50), compared to NA/ND. For women, dynapenia increased in 37% (HR: 1.37; 95% CI: 1.09 – 1.72) the mortality risk, and when combined with anemia, the risk increased to 117% (HR: 2.17; 95% CI: 1.44 – 3.26), compared to NA/ND (**Table 2**). The complete final models can be viewed in supplementary **Table S1**. The survival curves according to anemia and dynapenia status in men and women on 10-year are shown in **Fig. 2**.

4. Discussion

Our main findings showed that anemia combined with dynapenia was significantly associated with a higher all-cause mortality risk in a 10-year follow-up. This association was independent of socioeconomic factors, health behaviors, and comorbidities.

Cross-sectional studies have already indicated an association between low hemoglobin levels and low muscle strength. Alexandre et al., (2018) found that anemia is associated with dynapenia (HGS < 20 kg for women and < 30 kg for men) (RRR: 1.99; 95% CI: 1.03 – 3.87) in 1,168 older Brazilian adults. Cesari et al., (2004) when evaluating 909 older Italian adults, identified that anemic individuals presented a weaker ankle extension strength (β: -3.266; p = 0.005) compared with non-anemic. There also seems to be a sex difference in these associations, as demonstrated by Gi et al., (2020) where low HGS (< 16 kg for women and < 26 kg for men) was more strongly associated with anemia in men (OR: 2.13, 95% CI: 1.35–3.34) than in women (OR: 1.71; 95 % CI: 1.35 – 2.16) in 16,638 Korean adults. Jang et al., (2022) support similar results, with the association between anemia and dynapenia (HGS < 18 for women and < 26 kg for men) being higher in men (OR, 2.06, 95% CI,

Table 1
Characteristics of 5,310 participants at baseline according to anemia and dynapenia status and stratified by sex, ELSA (2004)

Variables	Non-anemic/Non-dynapenic		Dynapenic		Anemic		Anemic/Dynapenic	
	Men (n = 2,116)	Women (n = 2,344)	Men (n = 204)	Women (n = 363)	Men (n = 91)	Women (n = 112)	Men (n = 35)	Women (n = 45)
Age (mean ± SD)	64.2 ± 8.2	64.3 ± 8.5	73.5 ± 10.1 †	74.2 ± 10.7 †	72.3 ± 10.3* †	68.2 ± 10.3* † ‡	81.9 ± 8.5 † ‡ §	80.3 ± 10.1† ‡ §
Age %								
50 - 59 years	35.6	35.8	11.3 †	12.4 †	17.6 †	27.7 ‡	-	4.4 † §
60 - 69 years	37.7	37.8	25.5 †	18.2 †	19.8 †	25.0 †	2.8 † ‡ §	8.9 † ‡ §
70 - 79 years	22.0	21.0	29.9	35.5 †	41.7 †	28.6	34.3	31.1
≥80 years	4.7	5.4	33.3 †	33.9 †	20.9 †	18.7 † ‡	62.9 † ‡ §	55.6 † ‡ §
Wealth %								
Highest quintile	26.1	25.0	15.2 †	12.7 †	15.4 †	16.1 †	22.9	8.9 †
4th quintile	24.8	21.8	22.1	14.9 †	19.8	23.2	11.4 †	6.7 † §
3rd quintile	21.1	21.4	19.6	19.6	26.3	16.1	14.3	20.0
2nd quintile	17.0	18.2	20.1	25.3 †	17.6	20.5	22.8	28.9
Lowest quintile	11.0	13.6	23.0 †	27.5 †	20.9†	24.1 †	28.6 †	35.6 †
Education level %								
> 13 years	34.5*	21.8*	20.1 †	12.4 †	25.3	23.2	17.1 †	11.1
12 – 13 years	26.2	27.0	17.7 †	17.6 †	9.9 †	21.4	20.0	8.9 †
0 – 11 years	39.3	51.2*	62.2 †	70.0 †	64.8 †	55.4 ‡	62.9 †	80.0 † §
Conjugal Life %								
Without	21.0*	35.4*	31.9* †	55.4* †	34.1 †	38.4 ‡	37.1	64.4 † §
Smoking %								
Non-smoker	29.5*	44.5*	24.5*	46.0*	26.4*	50.0*	17.1*	51.1*
Former smoker	56.4*	41.2*	59.8*	41.0*	67.0*	45.5* ‡	80.0* †	42.2*
Current smoker	14.1*	14.3*	15.7*	13.0	6.6†	4.5 †	2.9 † ‡	6.7
Alcohol intake %								
Rarely/Never	22.2*	39.9*	29.4*	51.2* †	28.6*	53.6* †	40.0	55.6
Frequently	48.2*	39.5*	36.8* †	23.4* †	46.1	33.9	28.5 †	24.4 †
Daily	22.1*	14.1*	14.2* †	10.2	14.3	3.6 † ‡	8.6 †	4.4 †
Did not answer	7.5*	6.6	19.6†	15.2 †	11.0	8.9	22.9	15.6
Physical activity %								
High	37.2*	29.7*	18.1 †	12.7 †	20.9 †	22.3	17.2 †	6.7 †
Moderate	50.6	53.5*	50.5	49.0	54.9	50.0	60.0*	26.7* † ‡ §
Low	10.0*	14.7*	24.0 †	28.4 †	15.4	24.1	17.1	42.2 †
Sedentary	2.2	2.1	7.4 †	9.9 †	8.8 †	3.6	5.7	24.4 † §
Hypertension %	48.1	46.1	56.4	50.7	44.0	47.3	54.3	51.1
Diabetes %	9.3*	5.8*	22.1* †	9.6*	17.6	12.5	22.9	13.3
Cholesterol %								
Elevated	64.8*	80.2*	48.5* †	74.1*	37.4* †	62.5* †	28.6 †	55.6 †
Triglycerides %								
Elevated	47.8*	39.4*	47.1	41.6	44.0	39.3	34.3	35.6
HDL %								
Low	6.0*	20.2*	7.4*	22.3*	16.5 †	25.0	8.6*	44.4* † ‡
IHD %	4.1	2.6	6.4	5.0	8.8	4.5	8.6	13.3
AHR %	2.6	2.8	0.5* †	3.6*	4.4	5.4	5.7 ‡	6.6
Heart failure %	0.1	0.1	-	1.1	-	0.9 †	-	2.2 †
Cancer %	2.5	2.2	3.4	3.0	12.1 †	6.3	8.6	8.9
Lung disease %	4.5	4.4	11.8†	6.3	14.3	2.7	5.7	4.4
Stroke %	0.7	0.9	2.5	2.2	3.3	-	-	6.7
Depression %	8.1*	14.5*	17.2* †	28.1* †	19.8 †	18.8	11.4	33.3 †
BMI %								
< 18.5 kg/m^2	0.4	0.7	2.5	2.7 †	-	1.8	2.9 †	-
18.8 – 24.9 kg/m^2	50.9*	39.2*	44.1	38.0	48.4	42.0	37.1	33.3
25.0 – 29.9 kg/m^2	26.1*	30.0*	20.6	27.6	22.0	26.8	14.3	17.8
> 30 kg/m^2	22.6*	30.1*	32.8†	31.7	29.7	29.4	45.7 †	48.9 †
ADL, (mean ± SD)	0.2 ± 0.7	0.2 ± 0.7	0.7 ± 1.2 †	0.7 ± 1.2 †	0.4 ± 0.6 ‡	0.4 ± 0.9	0.6 ± 1.4*	1.3 ± 1.5* † ‡ §
IADL, (mean ± SD)	0.2 ± 0.6*	0.2 ± 0.7*	0.7 ± 1.3 †	0.9 ± 1.3 †	0.2 ± 0.4* ‡	0.5 ± 0.9* † ‡	0.9 ± 1.3* † §	1.6 ± 1.6* † ‡ §
Memory, (mean ± SD)	10.2 ± 3.2*	10.9 ± 3.3*	8.1 ± 3.4 †	8.7 ± 3.8 †	8.4 ± 3.2* †	9.7 ± 3.6* † ‡	6.2 ± 3.8 † ‡ §	7.8 ± 3.9 † §

Note: SD: standard deviation; IHD: ischemic heart disease; AHR: abnormal heart rhythm; BMI: body index mass; ADL: activities of daily living; IADL: instrumental activities of daily living

* Significant gender difference for each anemia and dynapenia status

† Significant difference from non anemic/non dynapenic

‡ Significant difference from dynapenic

§ Significant difference from anemic ($p < 0,05$)

1.38–3.09) than in women (OR, 1.41, 95% CI, 1.04–1.91) in 4,812 older Korean adults.

Isolated anemia and dynapenia are well recognized risk factors associated with all-cause mortality in older adults. According to Penninx et al., (2006) anemia increased the mortality risk by 51% (HR: 1.51; 95% CI: 1.19 – 1.92) in comparison to non-anemic over a 4-year follow-up in a study with 1,571 older American adults. Likewise, Zakai et al., (2005) reported that anemia increased the risk of all-cause mortality by 57% (HR: 1.57; 95% CI: 1.38 – 1.78) compared to non-anemic over a 11-year follow-up in a study with 5,888 older American adults. As for dynapenia, Alexandre et al., (2014) in a study with 1,149 older Brazilian adults, found that those with dynapenia (HGS

Table 2
Final Cox proportional hazards models predicting mortality in men and women during a 10-years follow-up, ELSA (2004-2014)

Variables	Men* (n = 2,446)		Women* (n = 2,864)	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Anemia and dynapenia status				
Non-anemic/Non-dynapenic	1.00		1.00	
Dynapenic	1.15 (0.89-1.48)	0.298	1.37 (1.09-1.72)	0.007
Anemic	1.68 (1.22-2.32)	0.002	1.34 (0.90-2.01)	0.153
Anemic/Dynapenic	1.64 (1.08-2.50)	0.020	2.17 (1.44-3.26)	< 0.001

Note: 95% CI: 95% confidence interval; HR: hazard risk
* Adjusted by age, smoking, marital status, physical activity, heart failure, cancer, lung disease, BMI, IADL and memory performance.

< 20 kg for women and < 30 kg for men) presented a higher mortality risk over a 10-year follow-up, compared to those without dynapenia (HR: 2.19; 95% CI 1.32 - 3.62). Al Snih et al., (2002) in a sample of 2,488 older Mexican American adults followed up for 5 years, identified that men in the lowest quartile of HGS (< 22 kg) had a higher mortality risk (HR: 2.10; 95% CI: 1.31 – 3.38) compared to woman in the lowest quartile of HGS (< 14 kg) (HR: 1.17; 95% CI: 1.95 – 2.93).

Considering the existing evidence, our study goes a step further by identifying that anemia combined with dynapenia increases considerably the mortality risk. Our findings can be explained by the reduction in oxygen supply due to low hemoglobin levels, that create a chronic hypoxia which leads to several pathophysiological complications. Among them, peripheral arterial vasodilation, decreased capillary angiogenesis, myocardial dysfunction, inadequate activation, and function of renin-angiotensin-aldosterone, which favor the development of cardiovascular diseases and systemic repercussions increasing the mortality risk (Silverberg et al., 2001). Simultaneously, chronic hypoxia also damages the musculoskeletal system, compromising muscle strength, which may progress to dynapenia. In addition, fatigue resulting from anemia can also triggers dynapenia, as it makes the individual less active, and more subject to muscle disuse (Dodd et al., 1993). In view of these mechanisms and their systemic repercussions, when anemia and dynapenia are present simultaneously, such mechanisms are potentiated with an overload on the body systems, which significantly increases the mortality risk.

Our analyzes also demonstrated that anemia is associated with mortality in men. Andropause may be a mechanism involved in this process. Reduced testosterone levels may inadequately suppress hepcidin levels, decreasing iron absorption and its directing towards erythrocyte maturation, which potentiates anemia as well as the all-cause mortality risk (Latour et al., 2014). In addition, we identified that anemic men had a higher prevalence of cancer and lung disease compared to NA/ND men, which are highly disabling diseases associated with an inflammatory condition, which can raise hepcidin levels causing greater iron trapping within macrophages, intensifying the process.

Our main findings have also showed an association between dynapenia and the mortality risk in women. Low muscle strength is a risk factor for functional outcomes, such as mobility limitation and, disability (Hairi et al., 2010; Hicks et al., 2012). Such outcomes promote a decrease in physiological reserves with a rupture in body homeostasis, making individuals more vulnerable to intrinsic and extrinsic stressors, and consequent mortality risk (Cullati et al., 2018). In view of this, we identified that dynapenic women had greater functional impairment compared to NA/ND women, which may have made them more susceptible to death. Furthermore, they had a higher prevalence of underweight than NA/ND women, which confer a greater mortality risk (Peterson et al., 2017; Rantanen et al., 2003).

The present study has strengths and limitations that should be considered. Among the strengths, are the long follow-up period and the large and representative sample of community-dwelling English individual, which enable us to perform analyzes stratified by sex. The wide range of covariates is also highlighted, which allows an adequate adjustment of the models. In addition, the collection of laboratory tests and anthropometric measures follows validated and standardized protocols, ensuring excellent quality of the information obtained. Regarding the limitations, the ELSA Study only includes community-dwelling individuals, which does not allow estimations for those institutionalized, who tend to have more anemia and dynapenia. Losses during the follow-up are an unavoidable source of bias in longitudinal studies, however, they were small and did not compromise the analyzes. The number of individuals in the high-risk category i.e. A/D status is small. However, this did not prevent us from finding significant results for this group. Finally, the individuals excluded from our analyzes due to the lack of information could be a source of bias. However, even after

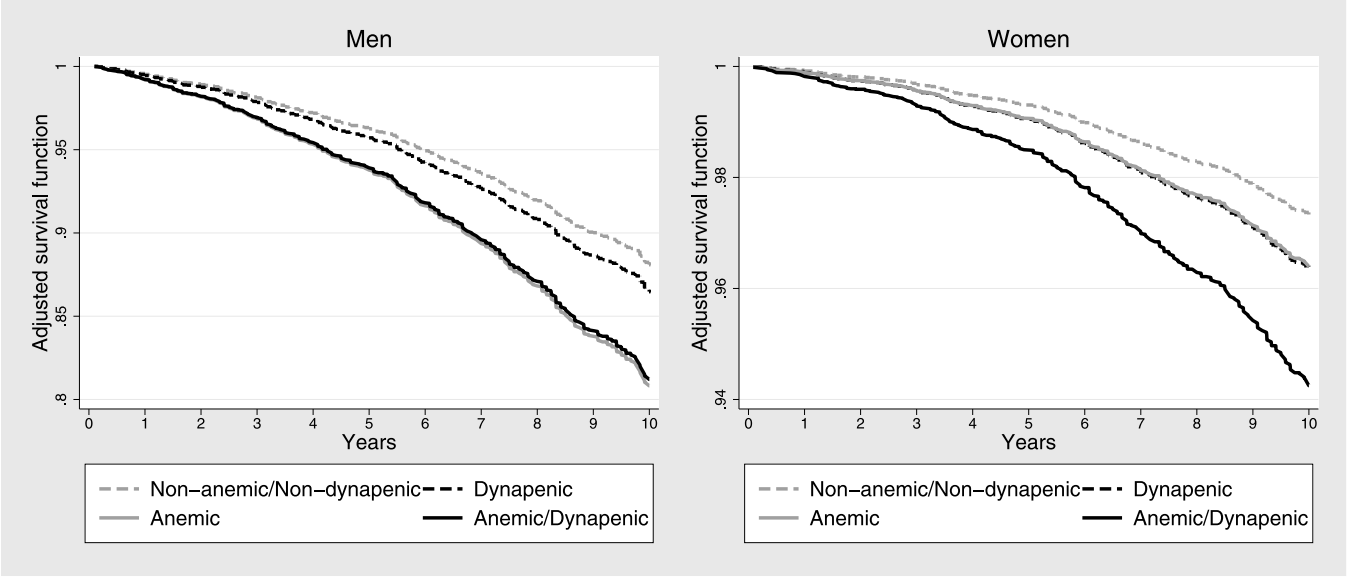

Figure 2. Survival analysis of anemia and dinapenia status based on the final Cox proportional hazards models.

their exclusion, we found a significant association between combined anemia and dynapenia and risk of death.

5. Conclusion

In conclusion, we found a higher mortality risk when anemia and dynapenia occur simultaneously in older adults. Such conditions are modifiable, which reinforces the need for an early detection and treatment of anemia and dynapenia to reduce the overload generated on the body systems and promote healthy ageing.

Data statement

The English Longitudinal Study of Ageing data are available to the scientific community from the UK Data Service for researchers who meet the criteria for access to confidential data, under conditions of the End User License http://ukdataservice.ac.uk/media/455131/cd137-enduserlicence.pdf. The data can be accessed from: https://beta.ukdataservice.ac.uk/datacatalogue/series/series?id=200011#!/access-data.

Contact with the UK Data Service regarding access to the English Longitudinal Study of Ageing can be made through the website https://www.ukdataservice.ac.uk/about-us/contact, by phone +44 (0)1206 872143 or by email at help@ukdataservice.ac.uk

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.archger.2022.104739.

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