Trajectories of Accumulation of Health Deficits in Older Adults: Are There Variations According to Health Domains?

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Abstract

Objectives: To analyze sex- and education-specific trajectories of health deficits accumulation (DA) throughout old age, and to examine whether these trajectories differ according to health domains.

Design: Population-based prospective cohort study

Setting and participants: In Spain, 3,228 community-dwelling individuals aged 60 years or older followed-up for 10 years.

Measures: At baseline and three follow-up visits, a DA index (0 to 100% deficit) was calculated based on the number and severity of 52 health deficits across the domains of physical and cognitive function, self-rated health and vitality, mental health, and morbidity. Trajectories of overall and domain-specific DA indexes were estimated using mixed models for repeated measurements, allowing for homogeneous linear, piecewise linear and smooth nonlinear DA trends over age.

Results: Women showed greater DA than men, but differences leveled out with age: annual increments in DA index (95% confidence interval) for participants aged <70, 70-80 and ≥80 years were, respectively, 0.40 (0.30-0.50), 0.68 (0.57-0.80), and 1.30 (1.07-1.54) in men; and 0.63 (0.53-0.73), 0.99 (0.89-1.10) and 1.31 (1.09-1.53) in women. These changes were mainly driven by a progressive accumulation of chronic diseases and by quadratic declines in physical and cognitive function. Both men and women showed improvements in mental health with age. In general, women and participants with lower education decreased physical and cognitive function and accumulated morbidities faster than their counterparts. Only individuals with very fast declines in function and fast accumulation of morbidities showed a significant worsening of self-rated health and vitality over time.

Conclusions: Public health interventions aimed to healthy ageing should focus on prevention and early-control of chronic diseases, as well on the preservation of function and early rehabilitation, with the latter being more relevant during the latter stages of life. Post-acute and long-term care services should incorporate adequate physical therapy and nursing facilities to promote attainable levels of functionality in older adults.

Key words: Deficit accumulation, function, healthy ageing, mental health, mixed models, morbidity, repeated measures

INTRODUCTION

Ageing is the result of cumulative molecular and cellular damage over time, which leads to a progressive decline in physical and cognitive function, and a growing risk of chronic diseases, disability and death [1]. Ageing does not evolve linearly throughout old age and greatly differs across subjects. Monitoring ageing pathways or trajectories in older adults is needed to understand how these changes unfold and helps identify which public health interventions may be effective at a given time to prevent, treat or support the decline in specific abilities with age [2].

Over the past years, an increasing number of longitudinal studies have evaluated trajectories of health deficits accumulation (DA) in older adults and their main determinants [3-9]. Most of these studies have relied on the frailty index, a multidimensional index defined as the proportion of health deficits present in an individual out of the total number of deficits considered, which has shown to be a good predictor of adverse outcomes (i.e., falls, hospitalization, disability, institutionalization and death) in older adults [10]. However, none of these studies has specifically evaluated DA trajectories across the different health domains that encompass this syndrome, such as physical function, mental health and morbidity. Within this context, the present manuscript aims to deepen understanding of the dynamics of ageing by examining the overall and domain-specific DA trajectories over age in the 10-year follow-up of a representative cohort of 3,289 community-dwelling older adults in Spain.

METHODS

Study population

The Seniors-ENRICA cohort was established in 2008-2010 with 3,289 individuals selected by multi-stage stratified random sampling from the non-institutionalized Spanish population aged 60 years or older [11;12]. Of the initial cohort, 61 participants were excluded from the present study because they lacked information on health deficits or potential confounders. The remaining 3,228 participants were followed-up until 2017, for a total of 8,562 baseline and follow-up visits (mean follow-up time between successive visits of 2.5 years). During the 10-year study period, 267 participants (8.3%) died, 1,840 (57.0%) were lost to follow-up due to non-response, and the remaining 1,121 (34.7%) completed the three follow-up visits (**supplementary figure 1**). Participants lost to follow-up were more likely to be women (59.1% vs 51.0%; p<0.001), older (69.1 vs 67.1 years; p<0.001) and had lower education level (62.3% with primary education or less vs 48.0%; p<0.001) than those who took part in all follow-up visits.

Baseline and follow-up information regarding sociodemographic, lifestyle, self-rated health and morbidity was collected using computer-assisted telephone interviews and dietary histories. Samples of urine and blood were collected and mental and physical exams were performed by trained staff in home visits. All participants gave informed consent, and the Clinical Research Ethics Committee approved the study [11;12].

Health deficits accumulation and lifestyle risk factors

Based on the Rockwood’s frailty index [10], a DA index was calculated at baseline and each follow-up visit using a total of 52 health deficits, including 22 impairments in physical and cognitive functioning, 7 self-reported health and vitality problems, 6 mental health deficiencies and 17 items on morbidities, polypharmacy and use of health services. The index summarizes age-related vulnerability, so the more health deficits (symptoms, signs, diseases or disabilities) an individual has, the higher their risk of death, institutionalization, health service use or further deficit accumulation. Most deficits in the index were assessed in a dichotomous way (1 point if present and 0 otherwise), with the exception of cognitive functioning, self-rated health, vitality, mental health, body mass index and use of outpatient health care, whose deficits were graded according to severity (0 points for no deficit, 0.25 to 0.75 points for mild to moderate deficits and 1 point for severe deficit). The complete list of health deficits and associated scores are outlined in **supplementary table 1** and a detailed description of the construction of frailty index domains is provided in **Methodological Appendix 1**. The overall DA score was calculated as the sum of points assigned to each health deficit divided by the 52 deficits considered and further multiplied by 100 to obtain a summary range from 0 to 100% deficit.

At baseline and follow-up visits, self-reported information was obtained on age, sex, educational level, smoking status and alcohol consumption. Physical activity was measured with the questionnaire used in the EPIC-Spain cohort [13], and sedentary behavior was estimated by time spent watching television as assessed by the Nurse´s Health Study questionnaire validated in Spain [14]. There is evidence that time spent watching TV is the main component of sedentary time among older adults [15-17], and, compared to other types of sedentary behaviors, shows a distinct demographic and health profile [18]. Food consumption in the previous year was collected using a validated computerized dietary history developed from that used in the EPIC-Spain cohort [19]. Adherence to the Mediterranean diet was summarized with the Mediterranean Diet Adherence Screener index [20]. Height and weight were measured on physical exams in home visits and body mass index was calculated as weight in kilograms divided by height in meters squared.

Statistical methods

The longitudinal change in the DA index with age was estimated by using linear mixed models for repeated measurements over time on the same participants [21;22]. The models are specified in detail in the **Methodological Appendix 2**. In brief, a linear mixed model with random intercept and random age slope was used to estimate the average longitudinal change in DA index per one-year increase in age, while allowing for individual variation in DA trajectories around the average linear trend. This mixed model was then extended with fixed coefficients for linear splines of age with knots at 70 and 80 years in order to estimate distinct longitudinal annual changes in DA index within age intervals 60–69, 70–79, and ≥ 80 years, as well as with fixed coefficients for restricted quadratic splines of age with identical knots in order to display the smooth longitudinal trend in DA index with age [23].

To control for potential sociodemographic confounders and to assess the longitudinal effect of age on DA index mediated by lifestyle changes, the above mixed models were fitted with (models II-VI) and without (model I) adjustment for sociodemographic and lifestyle risk factors, including fixed effects for sex (men or women), educational level (primary or less, secondary, or university), baseline Mediterranean diet score (0 to 14 points), and changes over time in smoking status (never, former, or current), alcohol drinking (never, former, moderate, or heavy), physical activity (MET-hours/week), sedentary behavior (TV hours/day), and body mass index (kg/m^2). To evaluate potential heterogeneity of DA trajectories by sex and education, interactions of sex or educational level with the linear age term, linear age splines, and restricted quadratic age splines were included as fixed effects in the corresponding mixed models.

In addition to the overall DA index, mixed models were also used to estimate longitudinal changes in domain-specific DA indexes (physical and cognitive function, self-rated health and vitality, mental health, and morbidity) adjusting for changes over time in the other health dimensions. Modifications in domain-specific DA trajectories by quartile of change in other dimensions were evaluated including fixed-effects interactions between these quartiles and the abovementioned age terms. Statistical analyses were performed in Stata, version 14 (StataCorp) and graphics were produced in R, version 3 (R Foundation for Statistical Computing).

RESULTS

Participants mean age at baseline was 69.0 years (range 6.6). There was a higher proportion of women (53.8%) than men (46.2%). More than half of the study participants only had primary education or less and had never smoked, an approximately one third had never drunk, all these proportions being higher among women. Men showed a higher adherence to the Mediterranean dietary pattern, were more physically active, watched less TV, and had lower mean DA index scores than women at baseline. Participants with higher education were more frequently men, younger, and more active, and showed a lower prevalence of smoking and obesity , a higher prevalence of alcohol consumption and a better adherence to the Mediterranean dietary pattern. (**Table 1**).

The baseline mean (range) number of health deficits was 2.7 (0-22) for physical and cognitive *function*, 4.2 (0-7), for *self-rated health and vitality*, 1.2 (0-6) for *mental health*, and 3.6 (0-17) for *morbidities*. Compared to participants in the lowest quartile of baseline DA index, as well as in the *functional impairments*, *self-rated health and vitality*, and *morbidities* domains, those in the highest quartile exhibited an increased death risk during the 10-year follow-up: hazard ratios (95% confidence intervals [CI]) were 2.87 (1.87, 4.42), 1.95 (1.29, 2.94), 1.77 (1.25, 2.52) and 1.67 (1.13, 2.46), respectively (data not presented in tables).

Table 2 shows the longitudinal changes in overall and domain-specific DA indexes per one-year increase in age and their 95% CI. In crude models (model I), on average, participants accumulated 0.40 deficits per year, with an accelerated increase with age. These 0.40 deficits correspond to the 0.77 percentage annual change in the DA index observed in model I. Because the DA index ranges from 0 to 52, a 0.77% change in the DA scale would correspond to an accumulation of 0.40 deficits [$0.40=0.77_{\text{unadjusted annual change in overall DA index]}}*52_{\text{[maximum number of health deficits]}}/100$)). These figures remained almost unchanged after adjustment for baseline educational level and changes over time in health behaviors. Results from interaction models showed that women aged 60-79 had greater DA than men, but differences leveled out with age; specifically, at ages 60-69, 70-79 and ≥ 80, average increments in the DA index were (model II), respectively, 0.40 (0.30, 0.50), 0.68 (0.57, 0.80) and 1.30 (1.07, 1.54) in men; and 0.63 (0.53, 0.73), 0.99 (0.89, 1.10) and 1.31 (1.09, 1.53) in women. Both men and women increased functional loss [mean annual increases in the deficits score over the entire follow-up (95%CI): 0.90 (0.76, 1.04) and 1.40 (1.26, 1.54), respectively; model III], experienced no changes in self-rated health and vitality [0.04 (-0.08,0.16) and -0.03 (-0.15, 0.09), respectively; model IV], had progressive improvements in mental health [-0.97 (-1.13, -0.81) and -1.17 (-1.33, -1.01) ; model V], and underwent an increase in their number of chronic conditions and health care visits [0.79 (0.72, 0.86) and 0.93 (0.86, 1.00) ; model VI] with age. In general, women lost function, improved mental health and accumulated morbidities faster than men (p-values for interaction were < 0.001, 0.06 and <0.001, respectively). **Figure 1** shows the smooth longitudinal trend in the overall DA index, and helps illustrating both the accelerated increase in the frailty index with age, as well as the observed sex differences. Additionally, this figure shows that DA index changes are driven both by increasing morbidities and function decline, with the latter being more relevant in older age. Moreover, it shows that women bear a larger burden of health deficits at any given time and in all dimensions.

Table 3 and **Supplementary figure 2** present changes in the overall DA index and its main dimensions according to baseline educational status. In general, participants in the highest educational level exhibited the lowest scores in the studied domains at all ages (p-values for homogeneity of annual changes among participants with different educational level were <0.001 for the overall DA index, <0.001 for the functional impairments dimension, 0.44 for the self-rated health and vitality dimension, <0.001 for mental health, and 0.02 for morbidities). However, differences were not statistically significant after the age of 70 (p-values for homogeneity of annual DA changes among participants with different educational level 0.49 and 0.48 for those aged 70-79 and ≥80, respectively).

Finally, **figure 2** exhibits changes in each DA index dimension according to quartiles of change in the other three. On average, participants who experienced the highest declines in self-rated health and vitality, the lowest improvements in mental health, and the fastest accumulation of chronic diseases, presented the fastest declines in function [mean changes for those in the fourth vs first quartile of self-rated, mental, and chronic health changes: 2.55 (2.34 to 2.75), 1.71 (1.51 to 1.91), and 1.63 (1.44 to 1.81), respectively]. Similarly, participants who suffered the fastest deterioration in function or the fastest accumulation of morbidities, showed the sharpest declines in self-perceived health and vitality [mean annual change for those in the fourth vs first quartile of functional deterioration and morbidities accumulation: 0.92 (0.75 to 1.10) and 0.38 (0.22 to 0.54) , respectively]; while those who suffered the fastest deterioration in functional, self-rated, and mental health, displayed the fastest increments in number of chronic diseases [mean annual increase in the number of chronic conditions for those in the fourth vs first quartile of functional deterioration, self-rated health decline, and mental health improvement: 1.23 (1.13 to 1.33), 1.34 (1.24 to 1.45), and 1.04 (0.94-1.14), respectively].

As sensitivity analyses, we repeated all models including only participants with at least three follow-up visits, with consistent findings (see **supplementary table 2**).

DISCUSSION

Our results provide important information on the dynamics of ageing. First, they suggest that unhealthy ageing is mainly driven by an accelerated accumulation of morbidities and by quadratic declines in function during old age. Second, they illustrate how, despite having an increasing number of morbidities and functional problems over time, mental health in older individuals seems to improve with age. Third, they show that only individuals with very fast declines in function and fast accumulation of morbidities present a significant worsening of self-rated health over time.

Consistent with extent findings, our analyses indicate that women [24] and participants with low education [3;9] lose function and accumulate morbidities faster than their counterparts. Moreover, our results extend knowledge about the timing of change in slope of DA, and, as proposed by some authors [24], suggest that the health gap between men and women may reach a plateau in the oldest age groups. Similarly, they suggest that the observed differences across educational groups may level off with age, which could be due to equalization of resources in later life and because of the selective survival of low-educated individuals who have acquired resistance against adversity [25;26]. Still, we are aware that the ability to find statistical significant differences in DA slopes for the oldest age groups is limited by the relatively low number of subjects aged >80 in the present analyses.

Previous investigations have also reported improvements in mental health- and in particular of hedonic wellbeing- with advancing age [27]. This phenomenon has been attributed to increases in wisdom with age, so that, despite declining health, older people may experience less stress, anger or worry thanks to adaptive shifts in emotional regulation [28].

Our results are of clinical significance, as they show average annual increments in the overall DA index of 0.74 (0.69 to 0.79) points, which are associated with a 1.02 (95%: 1.01-1.03) increase risk of mortality in our cohort. In particular, men in our cohort suffer the highest risk of mortality associated with high DA index values (HR (95%CI) for mortality among those in the second, third and fourth quartiles of the DA index compared to those in the lowest: 2.11 (1.33, 3.37), 2.63 (1.58, 4.37) and 2.79 (1.66 to 4.71) in men; 0.92 (0.41, 2.08), 1.21 (0.51, 2.84) and 2.54 (1.18, 5.47) in women). The pattern of sex differences in the frailty index and in mortality observed in our study is consistent with the so-called male-female health-survival paradox [29], which implies that women experience lower mortality than men despite their higher rates of DA. Future analyses should evaluate whether sex-differences in the type of deficits accumulated over time, could help explain this paradox [24].

Several limitations of the present study warrant consideration. First, even if analyses of the potential impact of attrition revealed no major differences in the main results, the fact that those who were lost to follow-up were more likely to be older, female and low educated might have led to underestimating the DA index slope. Another limitation is that, despite our study included a greater number of health deficits than most previous reports [3;4;6;8], it did not include sensory impairments, which are highly prevalent and have shown to predict mortality in older adults [30]. Also, although adjustment for functionality was performed, results for dimensions that relied on self-reported data (i.e. the “self-rated health and vitality” dimension) may have been affected by the presence of cognitive impairment. Finally, our results cannot be extrapolated to institutionalized populations.

Still, our study has notable strengths compared to published research. First, it systematically evaluates for the first time the trajectories of DA by health domains, and addresses potential interactions between domains. Second, unlike most previous studies evaluating trajectories of DA based on self-reported data [3;4], ours included a number of validated measures of physical function (i.e. gait speed, grip strength) and chronic conditions (obesity, hypertension, diabetes) , and adjusted for a range of potentially confounding health behaviors. Finally, our study expands the results of previous reports (mostly based on Anglo-Saxon cohorts) to a Mediterranean county, not only with one of the highest female life expectancies in the world [31], but also with very high rates of frailty [32].

CONCLUSIONS

Our results are of public health importance because they support that population-level interventions aimed to healthy ageing should focus on the prevention and control of chronic diseases, as well as on the preservation of function and early rehabilitation, with the latter being more relevant during the latter stages of life. The above implies that post-acute and long-term care services should incorporate adequate physical therapy and nursing facilities to promote attainable levels of functionality in older adults.

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