Depressive symptoms and muscle weakness: a two-way relation?

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ABSTRACT

The potential association between depressive symptoms and dynapenia – i.e. muscle weakness – is limited to few, mainly cross-sectional, studies. We use SHARE (Survey on Health, Ageing and Retirement in Europe) panel data to investigate whether the onset of dynapenia at 4-year follow-up can be explained by pre-existing (either at baseline, or at 2-year follow-up) depressive symptoms, or vice versa. Depressive symptoms were identified as a score of 4 or more on the 12-item EURO-D scale. Individuals were classified as affected by dynapenia if they had handgrip strength of less than 20kg for women and 30kg for men. We estimate whether being affected by symptoms of depression at baseline or becoming symptomatic between baseline and a 2-year follow-up increases the odds-ratio (OR) for dynapenia at a 4-year follow-up among individuals with no muscle strength impairment at baseline. We also carry out the reverse analysis, and study whether dynapenia at baseline or incidental dynapenia between baseline and first follow-up increase the probability that individuals develop depressive symptoms by the second follow-up. The analysis is carried out using multivariate logistic regression. After adjusting for a full set of potential confounders, being symptomatic for depression at baseline did not increase the risk of dynapenia at the 4-year follow-up. Instead, individuals developing depressive symptoms between baseline and the 2-year follow-up had a 34% increased risk of developing dynapenia at the 4-year follow-up (OR 1.34, 95% CI 1.02 1.66). No significant association was detected between dynapenia at baseline or the onset of dynapenia between baseline and the 2-year follow-up and the incidence of depressive symptoms at the 4-year follow-up. In conclusion, our results support the effect of the onset of depressive symptoms on the onset of dynapenia, even after considering the role of confounding factors.

Keywords: depressive symptoms; dynapenia; Europe; SHARE.

INTRODUCTION

Depression is a common condition among the elderly, particularly among young-older persons. [1, 2] It affects up to one over ten community-dwelling senior individuals, and is even more common in other settings (e.g. hospitals and nursing homes). [1, 2] Depression is a significant and independent risk factor for several diseases and negative health outcomes, including disability, reduced quality of life, increased mortality and higher cardiovascular disease risk. [1, 2] Numerous risk factors for depression in older age have been identified and, among them, low physical performance has recently attracted attention. For example, in about 1,000 senior participants in an Italian study, low physical performance predicted the onset of depression over 4 years of follow-up. [3]

Sarcopenia is another common condition of older individuals, and its prevalence rate varies between 10%-33%, according to the settings and the target population and usually increases with age. [4] The presence of low muscle strength – or dynapenia – is used in conjunction with low muscle mass to diagnose sarcopenia. [4] Similar to depression, sarcopenia and dynapenia are associated with physical inactivity, disability, metabolic and cardiovascular diseases, and ultimately mortality. [4-11]

Since depression and dynapenia have similar consequences and similar risk factors (such as inflammation [12, 13]), some authors report epidemiological evidence of an association between sarcopenia and depression. Also, some studies reported that decline in muscle mass is reduced in people with depression, and vice versa. [14-17] In a cross-sectional study involving Korean men and women aged 60 years or older, subjects with self-reported depression or those taking antidepressants had a significantly lower appendicular skeletal muscle mass than those not affected by depression or not using antidepressants. However, after adjusting for potential confounders, this association remained significant only in men. [18] In another study, involving only hospitalized patients, sarcopenic individuals were more likely to suffer from depressive symptoms. [19] These findings (i.e. people with sarcopenia suffered more frequently of depressive symptoms and vice versa) were substantially confirmed by other cross-sectional studies in Asiatic subjects [20, 21], with the exception of one large study of older Korean individuals that did not find any significant association

between sarcopenia and depression. [22] In a recent systematic review and meta-analysis of the cross-sectional studies, it was reported that dynapenia was significantly associated with a higher presence of depression and depressive symptoms, even after adjusting for potential confounders. [23]

Even if all these studies advance our knowledge regarding the possible association between dynapenia and depressive symptoms, they all suffer from some limitations. First, they consider mainly Asian subjects, and there may be significant differences in depressive symptoms and dynapenia prevalence between Asians and Europeans or Americans. Second, the cross-sectional nature of these studies did not let them explore a possible causal association.

In this paper, we have used harmonized panel data from the Survey of Health Ageing and Retirement in Europe – SHARE – on handgrip strength and depressive symptoms, where individuals are observed at a given time ("baseline"), at a first follow-up two years later and at a second follow-up two more years later. With these data, we explore whether depressive symptoms at baseline or its incidence between baseline and the first follow-up increase the likelihood of developing dynapenia (dynapenia) by the time of the second follow-up. We also investigate the reverse question, concerning whether dynapenia at baseline or the incidence of dynapenia between baseline and the first follow-up increase the probability that individuals develop depressive symptoms symptoms by the second follow-up.

METHODS

We used data covering twelve European countries participating in the SHARE (Survey of Health, Ageing and Retirement in Europe) study. SHARE is a multidisciplinary and cross-country survey providing longitudinal information about the health and socio-economic status of the European population aged 50+ that is collected in a harmonized way across countries and over time. [24] Ethical approval for SHARE has been provided by the institutional review board at University of Mannheim, Germany (until 2011) and by the Ethics Council of the Max-Planck-Society for the Advancement of Science (MPG) (from 2011 onward).

Depressive symptoms

Depressive symptoms were assessed in SHARE using the EURO-D scale, which was validated in a cross-European prevalence study. [25] The scale contains 12 items: sadness, pessimism, wishing death, guilt, sleep, interest, irritability, appetite, fatigue, concentration, enjoyment, and tearfulness. Each item is given a score of 1 for the negative case. Then, items are summed and the presence of depressive symptoms was defined as a EURO-D score equal to 4 or more.

Dynapenia

Dynapenia was assessed in SHARE through a handgrip dynamometer. [26] This test was carried out using a harmonized protocol across all countries and waves. After the dynamometer was set up to fit the respondent's hand, interviewees were instructed to possibly stand up, to keep their arms tight to the body with their elbows forming a 90° angle, and to push on the dynamometer as hard as they could. Four measurements were taken for each respondent, two for each hand. After each measurement, interviewers reported the value displayed by the dynamometer on their answer sheet first, and typed them on the interview software at the end of the GS test. The GS scale ranges between 0 and 100 kilograms. We considered individuals as affected by dynapenia if their highest recorded GS measurement was below 20 Kg for females and 30 Kg for males [4].

Covariates

In our analysis we used other variables concerning respondents' demographics, socio-economic status, health conditions and health behaviors. We considered their values at the baseline interview at wave 4 and – for the ones indicated with an asterisk in the list here below – also their evolution between wave 4 and the 2-year follow-up, at wave 5. The covariates we include are the following (for details, see Appendix Table A1):

- Demographics: age, gender and country of residence.

- Socio Economic Status (SES): education, homeownership, income, marital status, number of children and grandchildren.

- Health conditions*: having ever had a heart attack, stroke, cancer, hip fracture, diabetes, arthritis, and short-term recall ability.

- Mobility limitations*: reporting limitations in walking 100 meters; getting up from a chair after sitting for long periods; climbing several flights of stairs without resting; climbing one flight of stairs without resting; stooping, kneeling, or crouching.

- Healthy behaviors: having ever smoked, smoking currently, being physically inactive*, overweight*, obese*, carrying out at least a social activity once a week*.

- Nutrition*: indicators for frequency of consumption of fruits and vegetable, dairy products, legumes and eggs, fish and meat.

Statistical analysis

We first present a descriptive analysis of the characteristics of our sample in terms of the means and standard deviations of the key variables we use. Then, we run multivariate logistic regression with standard errors robust to the presence of heteroscedasticity to assess whether – among the participants without dynapenia (without depressive symptoms) at baseline – individuals affected by depressive symptoms (dynapenia) at baseline, or who become symptomatic between the baseline and the 2-year

follow-up, have an increased odds-ratio for dynapenia (depressive symptoms) at the 4-year follow-up.

We started by considering a model that includes as regressors only the presence of depressive symptoms (dynapenia) at baseline or their insurgence between the baseline and the 2-year follow-up. Then, we report how our estimated effects for baseline and incidental depressive symptoms (dynapenia) change as we sequentially include in the model the covariates, in the following order: baseline demographics (age-by-gender dummies and country dummies) and socio-economic status (SES); baseline health conditions; baseline health behaviors; baseline nutrition; baseline mobility limitations; changes in health conditions; changes in health behaviors; changes in nutrition; changes in mobility limitations.

All analyses were conducted using STATA version 14. Two-sided $p < 0.05$ was considered statistically significant.

RESULTS

Sample Selection

As our longitudinal research design requires three consecutive observations per individual, we first select countries that took part in three consecutive waves of SHARE, starting from wave 4 (carried out in 2011, which has the largest sample size per country and that we considered as our baseline), wave 5 (2013) and 6 (2015): Austria, Germany, Sweden, Spain, Italy, France, Denmark, Switzerland, Belgium, the Czech Republic, Slovenia and Estonia. We selected individuals who were 70 years of age or older at the baseline interview and who were present in all the three waves we considered.

In total we had information on 10,059 such individuals. We dropped 1,246 proxy interviews from the analysis and 1,432 interviews with missing data on grip strength. We also excluded interviews of individuals who were ever diagnosed with Parkinson disease (117 individuals). Finally, we dropped individuals with missing value on other covariates used in our analysis, or with likely reporting errors for grip strength (top percentile by wave and gender) (n=738). This leaves a sample of 6,526 individuals.

Descriptive characteristics

Baseline

Descriptive statistics for all variables in our final dataset are presented in Appendix Table A1. At baseline, 1,695 individuals present depressive symptoms (26.0%), while 1,160 (17.8%) are affected by dynapenia. Average baseline age in the sample is 76.0 years, with a standard deviation of 4.8 years. In total, 56.0% of the sample individuals are women, 24.3% have a college degree, 73.9% are homeowners, 26.1% are widowed and 63.3% live with a partner. The average number of children and grandchildren are 2.2 and 3.7. Additionally, 20.0% of respondents in our sample ever had heart-related problems, 3.2% had a hip fracture, 4.6% had a stroke and 6.9% had cancer. The prevalence of diabetes and arthritis are respectively equal to 13.6% and 29.0%. Close to 38% of respondents ever

smoked and 3.8% are current smokers. Only 9.2% do not carry out any physical activity at least once a week, but 44.3% is overweight and 19.8% is obese.

<u>Follow-up</u>

At the first follow-up interview, 1,465 (22.5%) individuals were affected by dynapenia and 1,747 (26.8%) by depressive symptoms, while 1,752 (26.9%) and 1,827 (28.0%) individuals were respectively affected by dynapenia and reported depressive symptoms at the second follow-up.

Regression outcomes

We summarized our main findings by graphically reporting the odds ratios corresponding to the variables of interest for all the logistic regression models we estimated, starting from the one with no controls and ending with the model with the richest set of controls.

Figure 1 shows the incidence of dynapenia in wave 6 by presence of depressive symptoms at baseline or during follow-up. After adjusting for all the potential confounders, the presence of depressive symptoms at baseline was not associated with incidental dynapenia (OR 1.084, 95% CI 0.88 1.29), whilst the onset of depressive symptoms during follow-up period was associated with incidental dynapenia (OR 1.34, 95% CI 1.02 1.66).

Figure 2 reports the incidence of depressive symptoms by the presence of dynapenia at baseline or during the follow-up. In the fully-adjusted model, neither baseline (OR 1.11, 95% CI 0.87 1.35) nor incidental (OR 0.89, 95% CI 0.65 1.13) dynapenia were associated with the onset of depressive symptoms.

DISCUSSION

In this paper, we used panel data covering a large number of individuals across Europe to assess whether the incidence of dynapenia (dynapenia) can be explained by pre-existing depressive symptoms, or vice versa. Our results support the hypothesis that depressive symptoms could be associated with the onset of dynapenia, even after adjusting for several confounding factors. Conversely, we found no evidence that dynapenia is independently associated to depressive symptoms.

Our knowledge regarding the possible association between sarcopenia (defined through both body composition and functional parameters) and depressive symptoms (or vice versa) is limited, as mentioned in the Introduction section, to some cross-sectional studies. [18-21] Very few longitudinal studies investigated the possible association between dynapenia (assessed through low hand grip strength) and incidental depressive symptoms. As reported in a systematic review published in 2016 discussing the uses and the outcomes of low handgrip strength in the elderly [27], only one study assessed the impact of low handgrip strength on depressive symptoms, reporting no significant findings. [28] On the contrary, in a cohort of Italian older people followed for 4 years, low baseline hand grip strength was associated with incident depressive symptoms. [3] In our study, we did not find any significant association between dynapenia at baseline and the onset of depressive symptoms during follow-up period. Even if dynapenia (both at baseline and incident) was associated with depressive symptoms before adjusting for potential confounders, after introducing the effect of these factors in our analysis, the association became not significant. It is important that in our study (see figure 2) the association is significant when the information on controls is limited to baseline only – while it turns out to be not significant when we control for health and behavior changes between baseline and the first follow-up.

Since the literature regarding this topic is conflicting, and low hand grip strength is common in older people and potentially reversible, other studies are needed to investigate the potential link between dynapenia at baseline and subsequent depressive symptoms.

To the best of our knowledge, our study is the first to report a possible association between incident depressive symptoms and low muscle strength. Several mechanisms could explain our findings. First, depressive symptoms is probably associated with social isolation and loneliness is associated with poor physical performance and disability, that are strictly related to dynapenia. [29] Second, malnutrition that is common in older depressed people [30], is a significant risk factor for low muscle strength in the elderly population.[31-33] Third, depression is defined by DSM according to some criteria [34] (such as diminished interest, weight loss or weight gain, fatigue) which all might be responsible for dynapenia. Thus, the presence of common factors can further explain the association found in our research. Finally, some common biological or physiological pathways between depressive symptoms and muscle strength could further explain our findings. For example, depressive symptoms seems to predict the onset of frailty (a consequence of dynapenia and sarcopenia), also independently of potential confounders. [35] In this sense, depression might exert detrimental effects on muscle mass and strength via specific molecular pathways (particularly reduced levels of androgens and increase in glucocorticoids or inflammatory parameters [14, 36]) leading to fat mass increase and eventually to dynapenia and sarcopenia. Hence, we believe that further research is needed on this topic, given its important clinical implications. Depressive symptoms is a common condition in the elderly population, and knowing whether it is predictive of the onset of dynapenia (that is associated with several negative outcomes) is of paramount importance.

The findings of our study should be considered within its limitations. The main one is that we do not assess sarcopenia, but only muscle strength (that is, dynapenia) through the hand grip strength. Similarly, depressive symptoms is assessed through a questionnaire, but a clinical diagnosis of depression is not available in the data. Thus, other longitudinal studies are needed to confirm if sarcopenia defined through body composition as well as functional parameters and depressive symptoms through clinical criteria are associated. Second, in SHARE the information regarding medical comorbidities is based on self-reported information. Finally, no information regarding medication is available, but drugs may affect both muscle strength and depressive symptoms. Among

the strengths of our work, we can include the large sample size, the long follow-up, and its novelty, given that we were the first to investigate a possible bi-univocal association between muscle strength and depressive symptoms in a dynamic setting.

In conclusion, our study showed that incident depressive symptoms could be associated with the successive onset of dynapenia, whilst we found no evidence that dynapenia is associated with incident depressive symptoms. Since both these conditions are common in the elderly population and reversible if appropriately treated, future longitudinal studies are needed to confirm or refute our findings.

ACKNOWLEDGEMENTS

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FIGURE LEGEND

Figure 1. From depressive symptoms to dynapenia **– estimated odds-ratios with 95% confidence intervals**

Abbreviations: SES: socio-economic status; C.I.: confidence intervals.

Figure 2: From dynapenia to depressive symptoms – estimated odds-ratios with 95% confidence intervals

Abbreviations: SES: socio-economic status; C.I.: confidence intervals.