Dose-Response Association Between Handgrip Strength and Hypertension: A Longitudinal Study of 76,503 European Older Adults

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Abstract: To examine the prospective dose-response association between handgrip strength and the incidence of hypertension in a representative sample of older European adults. We retrieved data from the Survey of Health, Ageing and Retirement in Europe (SHARE) waves 1, 2, 4, 5, 6, 7, and 8. Handgrip strength was measured and participants reported whether they had a medical diagnosis of hypertension. We assessed the longitudinal dose−response associations of handgrip strength with hypertension using restricted cubic splines. During the follow-up, 27,149 (35.5%) were diagnosed with incident hypertension. At the fully adjusted model, the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension was 28 Kg (HR: 0.92; 95%

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CI: 0.89-0.96) and 54 Kg (HR: 0.83; 95% CI: 0.78-0.89), respectively. There exists an association between increased handgrip strength and reduced risk of developing hypertension in older European adults. (Curr Probl Cardiol 2023;48:101813.)

Introduction

Hypertension, or elevated blood pressure, is one of the leading global risk factors for stroke, cardiovascular disease, and chronic kidney disease.[2,3] In fact, hypertension is the main risk factor for attributable deaths worldwide, causing more than 10 million of them annually.[3] Alarmingly, hypertension has doubled in adults aged 30-79 years over the last 3 decades, with its prevalence in certain European nations surpassing 50%.[4]

Hypertension has a multifactorial etiology,[5] with risk factors such as family history, advanced age, presence of target organ damage, or sleep apnea syndrome.[6] Nevertheless, most of the risk factors are modifiable, such as obesity, high blood glucose,[6,7] high total cholesterol, alcohol and tobacco consumption, excessive salt, and fat diet and lack of physical activity.[7,8] Despite this, hypertension may remain unnoticed over extended periods due to its asymptomatic nature.[7] Considering the major public health problem that this silent disease represents, it is imperative to establish effective and readily implementable preventive measures.

Muscle strength is a good measure of overall health[9,10] and may therefore also be important in relation to risk of hypertension. Because muscle strength is a modifiable factor that can be improved with targeted training, identifying the association between muscle strength and risk of hypertension is important to provide evidence-based preventive guidelines. In this sense, handgrip strength is a reliable biomarker for general muscle strength.[9,11] Based on its convenient and cost-effective application, it has the potential to serve as an early screening factor for people at risk of developing hypertension. A limited number of cohort studies reported an inverse association between handgrip strength and the risk of hypertension.[12–15] However, to date, only 2 studies have been conducted in Europe,[14,16] and only 1 of them[14] confirmed a significant association between handgrip strength and hypertension. Furthermore, the current literature has been restricted to the analysis of samples from a single country. Given the substantial variability in hypertension prevalence across countries,[4] further large-scale studies with representative samples from multiple nations are crucial to improve general public health recommendations at the European level. Likewise, to our knowledge, the minimum and optimal dose of handgrip strength associated with a reduced incidence of hypertension remains unknown, which could enable the implementation of more targeted and readily applicable preventive and interventional strategies (eg exercise prescription).

The aim of this study was to examine the prospective dose-response relationship between handgrip strength and the incidence of hypertension in a representative sample of older European older adults.

Methods

Study Design and Population

The present study included data from waves 1, 2, 4, 5, 6, 7, and 8 from the Survey of Health, Ageing, and Retirement in Europe (SHARE).[1] We did not consider wave 3 in the current study because handgrip strength was not examined. Representativeness of SHARE waves is assured by using a multistage stratified sampling design in which countries are assigned different strata according to their geographical area. Municipalities or zip codes within these strata represent primary sampling units.[1] Data collection was collected through home computer-assisted personal interviews from February 2004 to January 2021. SHARE data uses ex-ante harmonized interviews. Moreover, new respondents are added in each wave to compensate for the attrition bias due to losses.[1] In this study, only participants aged 50 years or older who had not been diagnosed with hypertension at any time prior to or at baseline were included. Individuals with missing values in any of the study variables or less than 2 follow-ups were removed from the analyses. More information on the study cohort profile is shown in Figure 1. This study received the approval of the Ethics Committee of

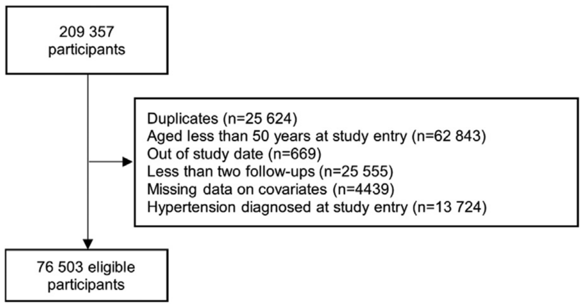

FIG 1. Study profile.

Research in Humans of the University of Valencia (registered code 1510464) and was reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[17]

Handgrip Strength (Exposure)

Trained interviewers measured handgrip strength twice for each hand using a handheld dynamometer (Smedley, S Dynamometer, TTM, Tokyo, 0-100 kg). In accordance with the SHARE protocol and assisted with trained interviewers, participants held their elbow in a 90° angle flexion while either standing or sitting, keeping a neutral wrist position, and their upper arm vertically positioned against the trunk. The interviewers encouraged participants with verbal-standardized instructions to squeeze the dynamometer with maximum effort for a few seconds. We considered handgrip strength as the maximum value of either hand.

Hypertension (Outcome)

Participants were followed throughout the study period to determine whether they had a first medical diagnosed of hypertension. This was determined through the following question that participants responded in each SHARE wave: *"Has a doctor ever told you that you had/currently have any of the conditions on this card? With this we mean that a doctor has told you that you have this condition, and that you are either currently being treated for or bothered by this condition."* The referred card included the *"High blood pressure or hypertension"* option among other 18 options related to other chronic conditions.

Possible answers comprised "*Yes*," "*No*," "*Refuse*" or "*Dont know*." Participants selecting these two last options were removed from the analyses.

Covariates

Based on a literature review on the topic,[14,18] age, sex, country of residence at the time of the interview, education, body mass index, smoking habit, alcohol consumption, physical inactivity, and fruits and vegetables consumption were identified as potential confounders. More details on the aforementioned covariates have been provided elsewhere.[19]

Statistical Analyses

We conducted all statistical analyses in Stata version 16.1 (StataCorp, Texas). We assessed the longitudinal dose−response associations of handgrip strength (modelled as a continuous exposure) with hypertension using restricted cubic splines to allow for potential nonlinearity; we trimmed observations less than 5% and greater than 95% of the distribution, and prespecified knots were placed at the fifth, 50th, and 95th percentiles of the exposure distribution. Departure from linearity was checked with a Wald test assessing the null hypothesis that the coefficient of the third spline was equal to zero. We assumed linearity for values below the fifth percentile and for values above the 95th percentile. Participants were censored at either final of follow-up, date of first onset of diagnosed hypertension or date of death. Time in months was used as the timescale. We did not detect any interaction between handgrip strength and age or sex using a Wald test, thus we conducted the main analyses without stratification. Due to the potential clinical interest of the dose-response analyses by sex, we conducted additional sex-stratified analyses. Two models were tested: a model with both sex and age at the time of the interview as time- invariant confounders (Model A), and a fully adjusted model (Model B) including Model A confounders along with other time-invariant confounders (age at the time of interview, sex, country, and education) and time-variant confounders (body mass index, physical inactivity, smoking, alcohol consumption, and fruits and vegetables consumption). The results were visualized as restricted cubic spline plots. We estimated the minimum dose (ie, the handgrip strength value at which the risk reduction was 50% of the observed maximum significant risk reduction) and the optimal dose (ie, the handgrip strength value at which the maximum significant risk reduction was observed). Results are reported as HRs with 95% CIs and levels of significance were set at $P < 0.05$.

Sensitivity Analyses

To minimize the potential influence of reverse causality, we excluded the first two years of follow-up from the analyses (eFigure 1).

Results

Overall, 76,503 participants were followed-up during a median of 4.8 years (Interquartile range 2.2-9.6) (219,881 persons/years), in which 27,149 (35.5%) were diagnosed with incident hypertension. Figure 1 shows information of the study cohort profile.

At study entry, average age was 65.0 (SD: 9.9) of whom 54.8 % were women and mean handgrip strength was 34.0 kg (SD: 12.0). Table 1 presents the characteristics of participants at study entry.

TABLE 1. Characteristics of participants at study entry (N = 76,503)

	n (%)	Mean (SD)
Age (y)		65.0 (9.9)
Sex		
Men	34,564 (45.2)	
Women	41,939 (54.8)	
Body Mass Index (kg/m^2)		
Underweight (<18.5 kg/m^2)	850 (1.1)	
Normal (18.5-<25 kg/m^2)	27,566 (36.0)	
Overweight (25-<30 kg/m^2)	31,888 (41.7)	
Obese (≥30 kg/m2)	16,199 (21.2)	
Education		
None	2945 (2.1)	
Primary	13,515 (17.7)	
Lower secondary	13,544 (17.7)	
Upper secondary	25,742 (33.7)	
Post-secondary non-tertiary	3583 (4.7)	
First stage of tertiary	16,220 (21.2)	
Second stage of tertiary	643 (0.8)	
Other	311 (0.4)	
Current smoking habit		
No	55,270 (72.3)	
Yes	21,233 (27.7)	
Country		
Austria	4638 (6.1)	
Belgium	6355 (8.3)	
Czech Republic	5849 (7.7)	
Denmark	4173 (5.5)	
Estonia	6653 (8.7)	
France	5481 (7.2)	
Germany	4735 (6.2)	
Greece	2930 (3.8)	
Hungary	1479 (1.9)	
Israel	2174 (2.8)	
Italy	5046 (6.6)	
Luxembourg	1524(2.0)	
Netherlands	3567 (4.7)	
Poland	2716 (3.6)	
Portugal	1267 (1.7)	
Slovenia	4129 (5.4)	
Spain	6038 (7.9)	
Switzerland	3465 (4.5)	
Sweden	4284 (5.6)	
Fruits and vegetables consumption		
Every day	58,284 (76.2)	
3-6 times a week	12,859 (16.8)	
Twice a week	3300 (4.3)	
Once a week	1221 (1.6)	
Less than once a wk	839 (1.1)	
Physical inactivity		

(continued)

TABLE 1. (*continued*)

	n (%)	Mean (SD)
No	68,538 (89.6)	
Yes	7965 (10.4)	
Alcohol consumption		
Almost every day	13,353 (17.5)	
5 or 6 d a wk	2157 (2.8)	
3 or 4 d a wk	5413 (7.1)	
Once or twice a week	13 781 (18.0)	
Once or twice a month	9389 (12.3)	
Less than once a month	8057 (10.5)	
Not at all in the last 6 months	24,353 (31.8)	
Handgrip strength (kg)		34.0 (12.0)

The dose-response analyses exhibited a close-to-linear inverse association between handgrip strength and hypertension. For model A, the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension was 25 kg (HR: 0.93; 95% CI: 0.90-0.96) and 45 kg (HR: 0.87; 95% CI: 0.83-0.92), respectively (Fig 2).

For model B, the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension was 28 kg (HR: 0.92; 95% CI: 0.89-0.96) and 54 kg (HR: 0.83; 95% CI: 0.78-0.89), respectively (Fig 3).

Additional sex-stratified analysis showed that the minimum and optimal dose of handgrip strength for a significant reduction in the risk of

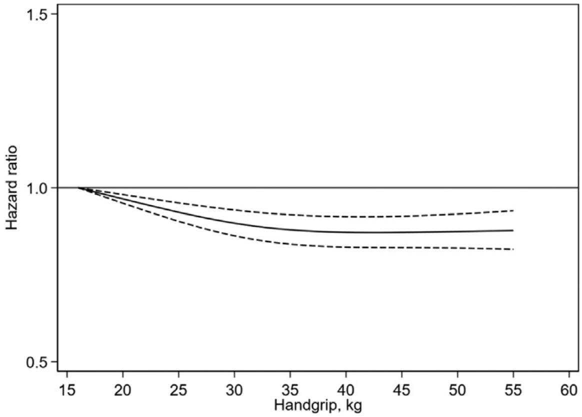

FIG 2. Dose−response association (Adjusted hazard ratios and associated 95% confidence interval band) between handgrip strength (kg) and hypertension in adults aged 50 years or older. Adjusted for Model A (age and sex). Reference 16 kg. Note: continuous line represents hazard ratio values whereas dotted lines represent 95% CI.

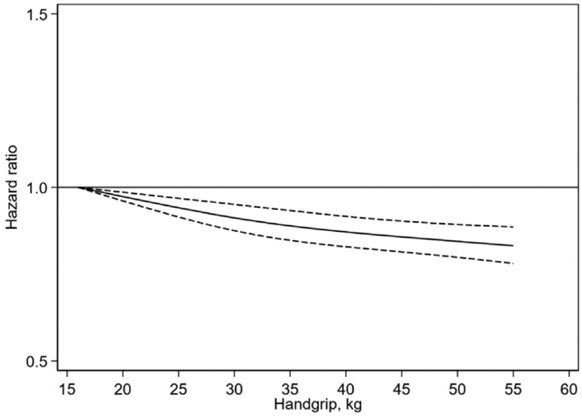

FIG 3. Dose−response association (Adjusted hazard ratios and associated 95% confidence interval band) between handgrip strength (kg) and hypertension in adults aged 50 years or older. Model B adjusted for time invariant age, sex, country, and education, and time-variant body mass index, physical inactivity, smoking, alcohol consumption, and fruits and vegetables consumption. Reference 16 kg. Note: continuous line represents hazard ratio values whereas dotted lines represent 95% CI.

hypertension for men (Fig 4) was 48 kg (HR: 0.92, 95% CI 0.85-0.99) and 58 kg (HR: 0.80, 95% CI 0.74-0.87), respectively, whereas for women (Fig 5) was 29 kg (HR:0.92, 95% CI 0.86-0.99) and 38 kg (HR: 0.84, 95% CI, 0.78-0.91), respectively.

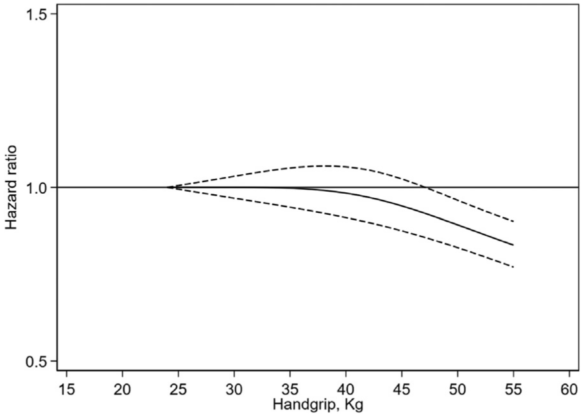

FIG 4. Dose−response association (Adjusted hazard ratios and associated 95% confidence interval band) between handgrip strength (kg) and hypertension in men aged 50 years or older. Model adjusted for time invariant age, sex, country, and education, and time-variant body mass index, physical inactivity, smoking, alcohol consumption, and fruits and vegetables consumption. Reference 24 Kg. Note: continuous line represents hazard ratio values whereas dotted lines represent 95% CI.

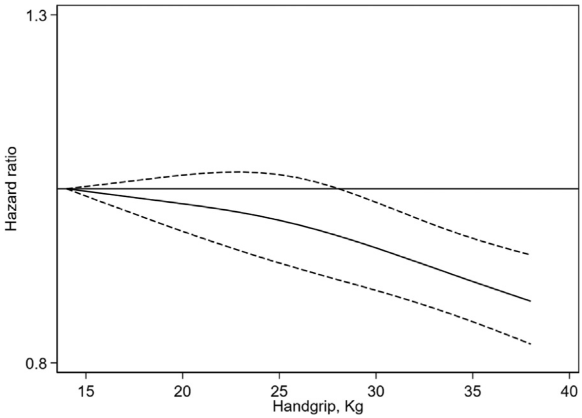

FIG 5. Dose−response association (Adjusted hazard ratios and associated 95% confidence interval band) between handgrip strength (kg) and hypertension in women aged 50 years or older. Model adjusted for time invariant age, sex, country, and education, and time-variant body mass index, physical inactivity, smoking, alcohol consumption, and fruits and vegetables consumption. Reference 14 Kg. Note: continuous line represents hazard ratio values whereas dotted lines represent 95% CI.

Sensitivity analyses showed slight variations concerning the main results, with a minimum and optimal dose of 28 kg (HR: 0.89; 95% CI: 0.85-0.94) and 54 kg (HR: 0.77; 95% CI: 0.71-0.84), respectively (see eFigure 1).

Discussion

We examined the prospective dose-response association between handgrip strength and the incidence of hypertension in a representative sample of older adults from several European countries. Our main finding was an almost linear inverse association between handgrip strength and incident hypertension. At the fully adjusted model, we found that the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension was 28 and 54 kg, respectively.

Our findings are consistent with some previous cohort studies from Asia. For instance, the study by Feng et al.[12] used data from a Chinese national survey of 712,442 adults aged 20 years and older, in which they reported a negative association between handgrip and hypertension. However, another study conducted in China with 8480 adults aged 40 years and older from Tianjin[13] found that a higher level of weight-normalized handgrip strength was associated with lower risk of hypertension, but this was not the case for absolute strength. Similarly, a study conducted in Iran with 3784 adults also demonstrated that medium and high levels of relative handgrip were associated with a lower risk of hypertension.[15] Regarding the studies conducted in Europe, previous evidence shows inconclusive results. For example, a recent study by He et al[14] including 214,214 UK Biobank participants reported that the greater the handgrip strength, the lower the risk of hypertension. However, in contrast to these and our results, a study[16] conducted with 463 Finnish men and women aged 61-73 years found no inverse association between weight-normalized handgrip strength and the risk of hypertension when the analysis was adjusted for age, sex, and several cardiovascular and lifestyle factors.

It is plausible that the absence of association reported in certain studies[13,16] is primarily attributed to statistical type 2 errors due to small sample sizes. It ought to be taken into consideration that the prevalence of hypertension in these countries is less than 30%.[4] This could mean that there is greater control of the risk factors for this disease, and a higher prevalence of other healthy behaviors related to hypertension as the practice of physical activity.[7] In fact, the latter along with other factors such as variations in BMI and the age across the studies, among others, may in part elucidate the discrepancies observed in the results when normalizing handgrip strength to body weight.

There may be several explanations that support the inverse association between handgrip strength and hypertension. For example, handgrip strength is a strong predictor of overall muscle strength and a marker of muscle mass[9] and even also nutritional status.[20] Hence, those with higher handgrip values could be involved in other healthy lifestyle behaviors affecting hypertension risk and general health. In this sense, a recent systematic review and meta-analysis[10] demonstrated a clear significant inverse association between handgrip and overall cardiovascular mortality and heart attack mortality. From a physiological perspective, increased muscular fitness has been associated with the release of cytokines and myokines into the circulation that enhance antiatherogenic properties.[21] In fact, handgrip strength has been inversely linked with vascular function markers such as reflected wave indicator and arterial stiffness in hypertensive patients.[22] Arterial stiffness has been identified as a pivotal component in the pathophysiology of hypertension, which in turn is associated with cardiovascular mortality,[23] sarcopenia[24] and inflammation,[25] with each of these being inversely associated with handgrip strength.[9,10,26]

Since handgrip strength is a modifiable factor, our results might help not only to prevent but also to manage hypertension. Recent studies have shown antihypertensive effects after isometric strength training, where handgrip exercise has been widely used as an effective way to reduce blood pressure.[27,28] Isometric handgrip exercise is thought to fully or partially occlude the brachial artery and upon cessation of occlusion, arterial blood flow causes vasodilation.[27] It has been suggested that isometric handgrip training may improve the vasodilatory response and over time, could even increase the diameter of blood vessels,[27] reducing total peripheral resistance, potentially mediated through enhanced autonomic vasomotor control.[29]

Our study provides the first dose-response analysis of the association between handgrip strength and the incidence of hypertension, providing information with relevant implications in older European adults. Our findings estimate that the minimum and optimal levels of handgrip strength associated with a lower risk of hypertension are 28 kg and 54 kg, respectively. As a result, these levels of handgrip strength should be used for the prevention of this condition, providing an efficient and cost-effective means of identifying those at greater risk. Our minimum and optimal handgrip values for hypertension prevention are similar to those reported for reduction of all-cause, cancer and cardiovascular mortality in older adults.[10] Importantly, we found in the sex-stratified analysis that the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension differed between men and women. This highlights the need for tailored screening, where reaching a minimum of 48 kg for men and 29 kg for women could be used as a reference for public health promotion, although ideally the goal should be to attain even greater improvements in handgrip strength (eg, 58 kg for men and 38 kg for women).

This study used a large representative cohort of European adults of 50 years and older, providing objectively measured handgrip strength. The analyses accounted for time-varying confounding of a wide set of covariates and attempted to address potential reversal causation. However, different limitations should be considered. First, although time-varying confounders were used to adjust our models, there is a possibility for both residual and time-varying confounding. Second, since the outcome was obtained through a proxy-relative, there is still a chance for a certain degree of misclassification bias. Third, the estimations obtained in this study are limited to the range of values obtained. Lastly, while our study sample comprised individuals within an age range associated with a greater prevalence of hypertension,[4] it is plausible that the protective benefits of handgrip strength extend to younger age groups as well, warranting further investigation.

In conclusion, there exists an association between increased handgrip strength and reduced risk of developing hypertension in older European adults. We found that the minimum and optimal dose of handgrip strength for a significant reduction in the risk of hypertension are 28 and 54 kg, respectively. These and our sex-stratified values could potentially be utilized as a screening tool to identify individuals at a heightened risk for hypertension, with the aim of mitigating and managing this important risk factor for mortality.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cpcardiol.2023.101813.

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