Longitudinal association between grip strength and the risk of heart diseases among European middle-aged and older adults

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\textbf{ABSTRACT}

\textit{Background:} Few multi-country European studies have investigated the association between grip strength and heart diseases incidence. Thus, the aim of this study is to analyse the longitudinal relationship between grip strength and the diagnosis of heart diseases in European middle-aged and older adults.

\textit{Method:} A prospective cohort study was conducted using data from the Survey of Health, Aging and Retirement in Europe (2004–2017). Participants were 20,829 middle-aged and older adults from 12 countries. GS was objectively measured by a dynamometer and heart diseases diagnosis was self-reported. Incidence rate of heart diseases was calculated and a Cox proportional hazard regression was performed.

\textit{Results:} The heart diseases incidence rate decreased from 930 per 100,000 person-years in the lowest quartile to 380 per 100,000 person-years in the highest grip strength quartile. During the 13 years of follow-up, compared to being in the lowest grip strength quartile, being in the highest quartile decreased the hazard of being diagnosed with a heart disease in 36\% (95\% confidence interval [CI]: 0.53, 0.78) for the whole sample, 35\% (95\% CI: 0.51, 0.84) for men and 46\% (95\% CI: 0.40, 0.73) for women.

\textit{Conclusions:} Grip strength seems to be inversely associated with the incidence of heart diseases among European middle-aged and older adults. Scientific evidence has highlighted the potential role of grip strength as a risk stratifying measure for heart diseases, suggesting its potential to be included in the cardiovascular risk scores used in primary care. However, further research is still needed to clarify it.

1. Introduction

Cardiovascular diseases (CVD) are the leading causes of mortality and morbidity worldwide, and a major public health concern (GBD 2017 DALYs, 2018). Heart diseases are a key component of CVD. They can be defined as a range of conditions that affect the heart, such as coronary heart disease, arrhythmias, congenital heart disease, heart attack and heart failure (WHO Cvd Risk Chart Working Group, 2019). Heart diseases led by coronary heart disease, are responsible for more than half of CVD prevalence and incidence (Thomas et al., 2018; Timmis et al., 2020). The highest prevalence and incidence of heart diseases are among middle-aged and older adults (WHO, 2020). As in most European countries average life expectancy is increasing, in addition to trends in population aging, the burden of heart diseases is very high (European Comission, 2014). Therefore, prevention at a population level is critical to improve outcomes.

Age, blood pressure, cholesterol, diabetes and smoking are known CVD risk factors present in most risk assessment tools for CVD (Lind et al., 2018). More recently, research has demonstrated low grip strength, a maximum hand static force measure commonly used to capture the overall muscular strength, to be associated with CVD mortality and incidence (Wu et al., 2017; Prasitsiriphon and Pothisiri, 2018; Leong et al., 2015). Thus, some authors have proposed grip strength as a potentially indicator of cardiovascular health to be included in CVD risk
assessment tools (Leong et al., 2015; Bohannon, 2019; Leong and Teo, 2015; Celis-Morales et al., 2018). A recent meta-analysis, estimated a hazard ratio (HR) (95% confidence interval [CI]) of 1.21 (1.14, 1.29) for the combined CVD incidence and mortality per 5 kg decrease in grip strength (Wu et al., 2017). From the 12 studies considered in this meta-analysis, only four included CVD incidence as the outcome, and from those four none included a population-based sample of several European countries (Leong et al., 2015; Andersen et al., 2015; Silventoinen et al., 2009; Celis-Morales et al., 2017).

To the best of our knowledge the association between grip strength and heart disease incidence in middle-aged and older adults, remains unexplored in multi-country European studies considering population-based samples. Such knowledge is of great importance, as this population is at a higher risk of developing such diseases. The identification of potential simple tools, such as the measurement of grip strength, in middle-aged and older adults can help to identify people at higher risk of developing heart diseases, who can benefit the most from preventive interventions (Karmali et al., 2017). Therefore, this study aimed to analyse the longitudinal relationship between grip strength and the diagnosis of heart diseases in European middle-aged and older adults.

2. Methods

2.1. Study design and data sources

A multi-country prospective cohort study, using longitudinal data from the Survey of Health, Aging and Retirement in Europe (SHARE) project was employed. Information about SHARE can be found elsewhere (Börsch-Supan et al., 2013; Mehrbrodt et al., 2019; de Luca and Lipps, 2005). For this study, longitudinal data from 2004 (wave 1) to 2017 (wave 7) was used. In the SHARE project, data is collected through a face-to-face computer-assisted personal interview, supplemented by a self-administered paper and pencil questionnaire (de Luca and Lipps, 2005). The first three waves of the SHARE (2004, 2007, 2009) received ethical approval from the Ethics Committee of the University of Mannheim. From the fourth wave onward (2011, 2013, 2015, 2017), the SHARE was granted ethical approval from the Ethics Council of the Max-Planck Society (Wolfrum, 2016).

2.2. Study populations and participants

For this study, the target populations were community-dwelling middle-aged and older adults aged 50 years old or older, including adults who turned 50 years old or more in 2004, from 11 European countries and Israel. The 11 European countries included in the study are Austria, Germany, Sweden, the Netherlands, Spain, Italy, France, Denmark, Greece, Switzerland and Belgium. Taking into account the aim of the study, 26,716 individuals with valid information on grip strength in wave 1 (2004) were considered in the first step. Afterwards, the study sample was limited to participants with valid data on the age at diagnosis of the heart disease, the age of death, and all covariates, and participants without a history of heart disease prior to the beginning of the SHARE wave 1 survey. From the 26,716 participants, 5887 were excluded for the following reasons: 2666 did not report the age at diagnosis of the heart disease; 2794 had a history of heart disease prior to the beginning of the study; 45 had no information on the age of death; and 382 had no information on at least one of the covariates. Thus, the final sample comprised of 20,829 participants.

2.3. Measures

Heart diseases diagnosis (outcome variable) was self-reported, along with the age at the time of the diagnosis. For reporting a diagnosis of heart diseases participants were asked ‘Has a doctor ever told you that you had/Do you currently have a heart attack including myocardial infarction or coronary thrombosis or any other heart problem including congestive heart failure?’. For reporting the age at the time of the diagnosis the following question was asked ‘About how old were you when you were first told by a doctor that you had a heart attack or any other heart problem?’ In the cases where a participant deceased, a proxy-respondent was asked about the cause and age at the time of death. Mortality by heart, if no previous heart diseases diagnosis was observed, diseases was considered as a heart disease incident event that resulted in death (Sillars et al., 2019).

Grip strength (exposure variable) was measured using a handheld dynamometer (Smedley, S Dynamometer, TTM, Tokyo, 100 kg) with respondents standing or sitting, their elbow fixed at a 90° angle, and a neutral wrist position. Respondents were asked to squeeze the dynamometer with each of their hands as hard as possible and maintain it for 5 s. The force of grip was recorded in kg and was only generated for individuals with two valid measures for each hand and if the two measures did not differ >20 kg. Because grip strength significantly differs between men and women, and declines with age (McGrath et al., 2020; Leong et al., 2016), sex and age specific quartiles were calculated, in which higher quartiles indicate stronger grip strength for a particular sex and age group. The grip strength quartiles were obtained by stratifying the sample simultaneously by sex and five years age groups (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and ≥85 years).

Covariates considered in the analysis represent baseline (SHARE wave 1, 2004) characteristics of the participants, including age, sex, country, educational level, height, weight status, physical activity behaviour, smoking cigarettes, drinking alcohol, hypertension, high blood cholesterol, stroke and diabetes. All covariates were self-reported.

Education level was self-reported and categorized according to the International Standard Classification of Education Degrees (ISCED) (UNESCO, 2006). Weight status categories were formed according to World Health Organization guidelines (WHO, 2000). Physical activity behaviour, including vigorous physical activity and moderate physical activity, was assessed with the two questions. Participants indicated if he/she never smoked cigarettes, was an ex-smoker, or a current smoker, and the frequency in which he/she drank alcohol in the last six months. Information on stroke, hypertension, diabetes and high blood cholesterol was obtained from the participants’ responses to questions asking whether their doctor had informed them of having the condition.

2.4. Statistical analysis

Descriptive statistics were calculated for all variables. Survival analysis was used to assess the risk of being diagnosed with heart diseases in middle-aged and older adults during the 13 years of follow-up (2004 to 2017), dependent on grip strength quartile. The lowest grip strength quartile was used as the reference group in the analyses. Cox proportional hazards regression was conducted to estimate the hazard ratio (HR) and the 95% confidence interval (CI) for the association between grip strength (sex and age specific quartiles) and the diagnosis of heart diseases, for the whole sample and stratified by sex. Time to heart disease diagnosis was calculated as the difference in months between the reported date of the heart disease diagnosis and the date of the interview in SHARE wave 1 (2004). Data was right-censored, thus participants that were not diagnosed with heart disease were censored at their follow-up length, including end of study (wave 7, 2017), dropout wave year and date of death from other causes. Two models of the Cox proportional hazards regression were performed. First, a crude model (model 1) using only the exposure variable (sex and age specific grip strength quartile) the outcome variable (diagnosis of heart diseases), and follow-up time (until event, until death, until drop-out or until end of study) was computed. Then, using the method enter, model 1 was further adjusted to sex, age, education level, country, moderate and vigorous physical activity frequency, body mass index, smoking tobacco and drinking alcohol, hypertension, diabetes, obesity, stroke, and high blood cholesterol (model 2). Analysis was performed using the SPSS 25 software (IBM Corp., Armonk, N.Y., USA). For all analysis, the significance level was set at 0.05.
3. Results

Table 1 shows the cut-off-values for the sex and age specific grip strength quartiles by sex and age group. Overall, men presented greater grip strength cut-off values than women and cut-off values decreased from the youngest to the oldest age groups.

The baseline characteristics of participants for the whole sample and stratified by sex and by grip strength quartile are presented in Table 2. Overall, 11,489 (55.2%) women, mean age 63.1 years, and 9340 (44.8%) men, mean age 63.0 years, participated in the study. The distribution of the participants by grip strength quartiles was the following at baseline: 4943 (23.7 %) were in the lowest (first) quartile; 4830 (23.2%) were in the lower-middle (second) quartile; 5445 (26.2 %) were in the higher-middle (third) quartile; and 5611 (26.9 %) were in the highest (fourth) quartile.

The HR for the diagnosis of heart diseases according to grip strength quartiles in European adults aged 50 years or more are presented in Table 3. A total of 1062 heart disease diagnoses were reported during the follow-up time of 13 years. The incidence rate per 100,000 person-years decreased from 930 in the lowest quartile to less than half, 380 in the highest grip strength quartile. In the final adjusted model (model 2), the risk of being diagnosed with heart disease was 16 % (95%CI: 0.71, 0.99) and 36 % (95%CI: 0.53, 0.78) lower for adults in the higher-middle and highest quartiles, respectively, when compared to the lowest grip strength quartile.

Results of the HR for the diagnosis of heart diseases according to grip strength quartiles and stratified by sex are presented in Fig. 1. Considering the final adjusted model (model 2), women in the highest grip strength quartile (HR = 0.54, 95 % CI: 0.40, 0.73) appeared to have a greater risk reduction for the diagnosis of heart diseases than men in the same quartile (HR = 0.65, 95 % CI: 0.51, 0.84), when comparing to women and men in the lowest quartile, respectively. Additionally, while men in the higher-middle quartile (HR = 0.77, 95%CI: 0.62, 0.96) had a lower hazard of heart diseases diagnosis than men in the lowest quartile, women in the same quartile did not.

The probability of not being diagnosed with a heart disease plotted against time (survival curve) according to grip strength quartiles for all disease is always higher in participants from higher grip strength and 3, respectively. The probability of not being diagnosed with a heart disease increased 12 % by each 5 kg increase and that people in the highest, middle-higher and lower-middle grip strength quartiles had less hazard of having heart failure than those in the lowest quartile. It was inversely associated with CVD overall and coronary heart disease, heart failure and arrhythmia in particular (Andersen et al., 2015; Silventoinen et al., 2009). A more recent population-based cohort study of more than half a million British people indicated that grip strength was associated with a 19 % heart failure's hazard reduction per 5 kg increment and that people in the highest, middle-higher and lower-middle grip strength quartiles had less hazard of having heart failure than those in the lowest quartile (Sillars et al., 2019). In accordance with previous findings, in this study grip strength was associated with a lower risk for heart diseases. Among older adults, grip strength has been suggested to be a biomarker related to healthy aging and cardiovascular health (Blohmann, 2019; Sayer and Kirkwood, 2015).

4. Discussion

During the 13 years of follow-up (2004 to 2017) of this prospective cohort study grip strength was associated with the incidence of heart diseases and may therefore have a role in identifying individuals who are at a higher risk at a population level. Heart disease incidence rate per 100,000 person-years decreased from the lowest to the highest grip strength quartile, it was 930 in the lowest, 670 in the middle-lower, 530 in the higher-middle, and 380 in the highest.

To the best of our knowledge, this is the first prospective cohort study that presented the incidence rate of heart diseases according to the grip strength quartiles. Notwithstanding, previous studies have reported that the prevalence of CVD decreases from the highest to the lowest grip strength quartile or tertile (Leong et al., 2015; Celis-Morales et al., 2018). This study’s findings are in accordance with previous research and are indicative of possible differences in the incidence of heart diseases according to grip strength among middle-aged and older adults. However, to bring further insight into this possibility more research is needed, especially prospective cohort studies with large and representative samples using objective measures of disease rather than self-report, reducing information bias.

Grip strength has previously been suggested to be associated with the incidence of CVD and specific heart diseases. In a multicounty research, the PURE study observed a 21 % increase in CVD hazard for each standard deviation decrease in grip strength (Leong et al., 2015). Similarly, a study conducted in a cohort of adults aged 40 to 69 years old from the United Kingdom found that the hazard for CVD incidence increased 12 % by each 5 kg decrease in grip strength (Celis-Morales et al., 2018). The research focused on the incidence of specific heart diseases has also observed an association with grip strength. Two studies performed in a cohort of Swedish men found that greater grip strength was inversely associated with CVD overall and coronary heart disease, heart failure and arrhythmia in particular (Andersen et al., 2015; Silventoinen et al., 2009). A more recent population-based cohort study of more than half a million British people indicated that grip strength was associated with a 19 % heart failure's hazard reduction per 5 kg increment and that people in the highest, middle-higher and lower-middle grip strength quartiles had less hazard of having heart failure than those in the lowest quartile. In accordance with previous findings, in this study grip strength was associated with a lower risk for heart diseases. Among older adults, grip strength has been suggested to be a biomarker related to healthy aging and cardiovascular health (Blohmann, 2019; Sayer and Kirkwood, 2015). Grip strength reflects overall muscle strength and is low-cost, easily measured, quick and reproducible, capable of being used in a variety of clinical settings and epidemiological studies (Roberts et al., 2011). Therefore, several authors have encouraged the use of grip strength as a health marker and risk stratifying tool to be considered in the risk scores, namely, in primary healthcare (Leong et al., 2015; Leong and Yeo, 2015; Celis-Morales et al., 2018). From a public health perspective, it is still relevant the identification of a potential simple tool for middle-aged and older adults which may help to identify people at higher risk of developing heart diseases, who should benefit the most from preventive interventions (Karmali et al., 2017). For this purpose, it is fundamental to further examine this relationship and better understand the potential role of grip strength as an indicator of heart disease risk, which could be used, namely, in primary healthcare.

Even if the analysis was stratified by sex, for both men and women grip strength was associated with heart disease incidence. Women in the highest grip strength quartile presented a 46 % lower hazard of being diagnosed with heart disease, compared to women in the lowest quartile; while, men in both the higher-middle grip strength quartile and highest strength quartile presented 23 % and 35 % less hazard of being diagnosed with heart disease, compared to men in the lowest quartile. It seems that for men, being in the higher-middle grip strength quartile was protective against heart diseases, but women had to be on the
In a prospective cohort study, Celis-Moralez et al. (Celis-Morales et al., 2018) observed that per 5 kg lower grip strength women in the highest grip strength quartile may benefit from it. Although some studies found no differences in the highest grip strength quartile to have a reduced hazard of being diagnosed with heart diseases. Additionally, women seem to have a stronger association than men. Previous research has presented dissimilar findings in this regard. Although some studies found no differences in the strength of the association, others did (Celas-Morales et al., 2018; Lee et al., 2018). In a prospective cohort study, Celas-Moralez et al. (Celas-Morales et al., 2018) observed that per 5 kg lower grip strength women had a higher hazard of CVD than men (HR = 1.15, 95% CI: 1.13, 1.17).
This study presents a set of limitations that should be taken into account when interpreting its findings and conclusions. The diagnosis of heart diseases was self-reported, along with the age at the time of the diagnosis. Using a self-reported measure of diagnosis is subject to misclassification bias, namely memory bias. Furthermore, participants were partly older adults, thus the risk of memory bias may be greater. When using self-reported measures, the memory bias effect on the outcome should be taken into consideration. Memory bias may lead to participants reporting less often and less accurately the diagnosis of heart diseases. Having less diagnosis of heart diseases reported, especially in older participants, can produce an underestimation of the HR for lower grip strength quartiles. Therefore, the heart disease diagnosis being self-reported can lead to misclassification of the outcome variable. This misclassification may reduce internal validity of the results and thus, findings regarding the magnitude of the associations should be interpreted with caution. Because of its observational nature, this study does not allow to establish strong interpretations of the causal role of grip strength in the diagnosis of heart diseases. Even though statistical analysis was adjusted for several covariates, it is not possible to exclude residual confounding. The censoring of participants lost to follow-up is

### Table 3
Hazard ratio for the diagnosis of heart diseases during the 13 years of follow-up according to grip strength quartiles in European middle-aged and older adults.

<table>
<thead>
<tr>
<th>Grip strength</th>
<th>Total n/ events</th>
<th>Events per 100,000 person-years</th>
<th>Hazard ratio (95%CI) Model 1</th>
<th>Hazard ratio (95%CI) Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest</td>
<td>4943/367</td>
<td>930</td>
<td>1.00 (ref.)</td>
<td>1.00 (ref.)</td>
</tr>
<tr>
<td>Lower-middle</td>
<td>4830/272</td>
<td>670</td>
<td>0.72 (0.62, 0.85)</td>
<td>0.81 (0.77, 1.07)</td>
</tr>
<tr>
<td>Highest-middle</td>
<td>5445/245</td>
<td>530</td>
<td>0.58 (0.50, 0.68)</td>
<td>0.81 (0.71, 0.99)</td>
</tr>
<tr>
<td>Highest</td>
<td>5611/178</td>
<td>380</td>
<td>0.41 (0.34, 0.53, 0.68)</td>
<td>0.64 (0.53, 0.78)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval.

Model 1: Unadjusted analyses.
Model 2: Analyses were adjusted for sex, age, education level, country, moderate and vigorous intensity physical activity, body mass index, drinking alcohol and smoking tobacco, hypertension, cholesterol, stroke and diabetes.

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**Fig. 1.** Hazard ratio for the diagnosis of heart diseases during the 13 years of follow-up according to grip strength quartiles in European middle-aged and older adults stratified by sex.
another important limitation of the study. These were participants that were not followed for the entirety of the study and thus, it was impossible to assess whether they were diagnosed with heart disease during the study period. This may lead to an underestimation of the heart disease incidence. Finally, the sub-sample of the SHARE project used in this study is not representative of the countries enlisted in the analysis, mainly because only participants with grip strength data in baseline were able to be accounted for. Therefore, caution is advised when generalizing the descriptive findings of the study, such as the incidence rate or the population characteristics.

5. Conclusion

Higher grip strength was associated with a decreased hazard of heart diseases, highlighting its possible role as an indicator of heart disease to be used in risk assessing scores, namely, in primary care. Future studies should explore the inclusion of grip strength in CVD risk assessment scores to assess whether its potential role can be achieved. In particular, studies that account for the addition of grip strength in commonly used risk assessing scores for CVD.

Data availability

Data is publicly available upon request in the SHARE project website.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2022.112014.

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