Mediator Effect of Balance Problems on Association Between Grip Strength and Falls in Older Adults: Results From the KORA-Age Study

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Abstract
Objective: To examine the association between grip strength and history of falls among older individuals, and to assess the possible mediating effect of balance problems on this relationship. Method: Data originate from KORA (Cooperative Health Research in the Region of Augsburg)-Age Study of 808 individuals (65 years and above). Follow-up assessment occurred 3 years later. Results: The risk of falls within the last 12 months was reduced on average by 3% (odds ratio [OR] 95% confidence interval [95% CI] = 0.97 [0.94, 0.99]; p value = .026) per 1-kg increase in maximum grip strength after adjusting for age and gender. There was a trend toward an indirect effect of grip strength through the mediator variable balance problems (p value = .043). Discussion: Increased muscular strength is associated with a reduced risk of falls in older age after adjustment for age and gender. The association is partially mediated by balance problems. Thus, in older adults, muscle-strengthening exercises may decrease the risk of falling.

Keywords
aged, balance, grip strength, falls

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Introduction
Normal physiological function begins to decline at a rate of 3% to 8% each decade after the age of 30 years, and the loss of muscle mass has negative consequences for maintaining muscle strength, walking speed, reaction time, and balance—all important variables for maintaining an independent lifestyle in older age (Cruz-Jentoft et al., 2010; Harms, Cooper, & Tanaka, 2011). In older individuals, decreased muscle strength is highly predictive of functional limitations and disability (Rantanen et al., 1999), and a minimum level of strength is needed to perform tasks of daily living. Most functional tasks used in normal day-to-day activities are of relatively short duration and, therefore, more strongly related to muscular strength than to muscular endurance. In the last decade, evidence from epidemiological studies has shown that muscle weakness, especially low muscular strength, is inversely associated with risk of falling in older adults (Chan et al., 2007; de Rekeneire et al., 2003; Pijpers et al., 2012; Xue, Walston, Fried, & Beamer, 2011) even after adjusting for several confounders including disease burden, lifestyle, inflammation, and mental well-being. Sarcopenia, a condition characterized...
provided written informed consent. This study was approved by the local authorities, and all subjects at follow-up remained for the main analyses. The study adults over the age of 60 years (Rubenstein, 2006). Furthermore, the increase in body sway, generally observed with aging, has been identified as a major factor responsible for an increased risk of falling among older adults (Maki, Holliday, & Topper, 1994). It was hypothesized that the decrease in maximal muscle strength could be a main cause of postural instability (Cattagni et al., 2014). Thus, muscle strength may be a marker of other factors, such as balance, which itself affect falls. The objective of this study was to examine the association between grip strength and history of falls among older men and women in a prospective population-based cohort study. We hypothesized that grip strength is inversely associated with falls and that this association is mediated by balance problems.

Materials and Methods

Participants

Data used in this study stemmed from the KORA (Cooperative Health Research in the Region of Augsburg)-Age Study conducted in the years 2008 and 2009. This study is a follow-up of all participants who took part in at least one of the four cross-sectional MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Diseases)/KORA surveys that were performed between 1984 and 2001 in the city of Augsburg and the two adjacent counties. Altogether, 1,079 people aged 65 years and older took part in the KORA-Age baseline examination, and 822 people participated in the follow-up about 3 years later. Participants with incomplete data on falling (dependent variable) and maximum grip strength (main exposure) at baseline and follow-up were excluded. After these exclusions, 808 individuals (409 men/399 women) aged 75 years ($M \pm 6$ (SD) years at baseline and 78 ± 6 years at follow-up) remained for the main analyses. The study was approved by the local authorities, and all subjects provided written informed consent.

Grip Strength

Handgrip strength was assessed using the Jamar dynamometer (Saehan Corp.). The Jamar dynamometer was placed in the dominant hand of the participant. Three trials, with brief pauses, were allowed at baseline and at follow-up. Participants were encouraged to exert their maximal grip strength. The maximum value of three handgrip measurements in kilograms at baseline and at follow-up were used in different analyses as the main independent variable.

Falls

During a standardized face-to-face interview, participants were asked whether they had fallen in the previous 12 months before the date of interview at baseline and at follow-up. In case of a positive answer, they were asked whether they had one or more falls. In this study, a dichotomous variable with the values 0 for participants with no falls and 1 for those with one or more falls at baseline and at follow-up was defined as the outcome.

Confounders and Mediators

Age and gender were considered as the two main confounders. In a face-to-face interview, using standardized questions from the balance section of the National Health and Nutrition Examination Survey Questionnaire (http://www.cdc.gov/nchs/data/nhanes/ba.pdf), participants were asked whether they had vertigo or dizziness, difficulty with balance, or did fall in the past 12 months before baseline and before follow-up. If the answer was “yes,” the exact type of problems (i.e., vertigo/dizziness; balance problem, falls) were assessed.

Statistical Analysis

Descriptive results are presented as mean values with standard deviation for continuous variables and as frequencies (%) for categorical variables at both baseline and follow-up. Appropriate statistical tests ($\chi^2$ test for categorical variables and the Wilcoxon–Mann–Whitney test for continuous variables) were performed to detect statistically significant differences between men and women at baseline and at follow-up. Logistic regression analysis was performed to examine the association between grip strength per 1-kg increase and falls (yes/no) at enrollment and at follow-up. As sensitivity analysis, ordinal logistic regression models with the outcomes (falls at baseline and at follow-up) coded as an ordinal variable (falls: no, one, more than one) were performed.

Generalized estimating equations (GEE) with empirical covariance matrix and unstructured (and exchangeable) working correlation matrix were applied to determine the association between grip strength at baseline and follow-up and falls during the previous 12 months at baseline and at follow-up as repeated measurements. Crude and adjusted (for age and gender) odds ratios (OR) with 95% confidence intervals (95% CI) were determined. The interaction term between gender and maximum grip strength in the main and sensitivity analyses at baseline and at follow-up was also added to the models and controlled for significance.
Table 1. Characteristics of Eligible Participants in the KORA-Age Study (2008-2011) Stratified by Gender at Baseline and at Follow-Up (n = 808).

|                     | Baseline          | Follow-Up         |
|---------------------|-------------------|-------------------|
|                     | Men (n = 409)     | Women (n = 399)   | p value<sup>a</sup> | Men (n = 409) | Women (n = 399) | p value<sup>a</sup> |
| Age, years—M (SD)   |                   |                   | .6124               |                   |                   | .6124               |
| Falls, n (%)        |                   |                   | .0086               |                   |                   | .0160               |
| No falls            | 362 (88)          | 323 (81)          | .008               | 351 (86)         | 312 (78)         | .156               |
| 1 fall              | 27 (7)            | 49 (12)           | .156               | 34 (8)           | 55 (14)           | .156               |
| More than 1 fall    | 20 (5)            | 27 (7)            | .156               | 24 (6)           | 32 (8)            | .156               |
| Balance problems (yes), n (%) | 62 (15) | 82 (21) | .0765 | 90 (22) | 104 (27) | .1565 |
| Maximum grip strength, M (SD) | 36 (8) | 22 (5) | .0001 | 35 (9) | 21 (6) | <.0001 |
| Prevalence of at least one fall by tertiles of maximum grip strength (kg)<sup>b</sup>, n (%) |                   |                   |                   |                   |                   |                   |
| Low<sup>c</sup>     | 16 (34)           | 39 (51)           | .047               | 31 (53)          | 30 (35)          | .199               |
| Moderate            | 21 (45)           | 21 (28)           | .520               | 14 (24)          | 34 (39)          | .031               |
| High                | 10 (21)           | 16 (21)           | .038               | 13 (22)          | 23 (26)          | .035               |

Note. KORA = Cooperative Health Research in the Region of Augsburg.
<sup>a</sup>The p value of the differences between men and women.
<sup>b</sup>Tertiles at follow-up are based on the distribution of maximum grip strength at follow-up.
<sup>c</sup>Low: baseline: men, ≤31 (kg); women, <=20 (kg); follow-up: men, ≤31 (kg); women, ≤19 (kg). Moderate: baseline: men, >31 (kg) and ≤37 (kg); women, >20 (kg) and ≤24 (kg); follow-up: men, >31 (kg) and ≤37 (kg); women, >19 (kg) and ≤23 (kg). High: baseline: men, >39 (kg); women, >24 (kg); follow-up: men, >37 (kg); women, >23 (kg).

Furthermore, Baron and Kenny and bootstrap methods were performed and compared to assess the indirect effect of the potential mediator “balance problems” on the association between grip strength and falls after adjusting for age and gender at follow-up. Significant differences in the mediator by outcome were assessed by χ² test. We tested mediation to divide the association between the outcome and independent variable into direct and indirect effects (through a mediator variable). For each model, as falling is a binary variable, the residuals were normalized and regression coefficients were standardized in the logistic regression analysis prior to estimating mediation effects. The pathways from the independent variable to the mediator (alpha) and then to the outcome (beta), and to the outcome (crude and adjusted for the mediator; tau, tau prime) were estimated, and the association between the outcome and independent variable was divided into direct and indirect parts. Sobel, Goodman, and Aroain tests were performed to determine whether the effect of the potential mediator was significant. Data analysis was performed using the statistical software package SAS 9.4 (SAS Inc., Cary, NC, USA).

Results

Descriptive Characteristics

Baseline and follow-up characteristics of the 808 individuals used in the main analyses (409 men/399 women) are presented in Table 1. Mean age values were the same in men and women at follow-up and at baseline. Men displayed higher maximum grip strength compared with women (M: 36 kg and 35 kg vs. 22 kg and 21 kg at baseline and at follow-up, respectively; p value < .0001). In contrast, women were more frequently affected by falls (p value = .009 and .016 at baseline and at follow-up, respectively) in the previous 12 months and by balance problems (p value = .077 and .157 at baseline and at follow-up, respectively). Both men and women had more falls and balance problems at follow-up in comparison with baseline (p value = .0001 and <.0001, respectively).

Association Between Grip Strength and Falls

To picture the relationship between grip strength and falls, maximum grip strength was classified into three groups using gender-specific tertiles as cutoff points. Table 1 also presents the frequencies of falls by tertiles of maximum grip strength for both men and women at baseline and at follow-up. Women had slightly more falls than men in the first tertile of maximum grip strength at baseline (51% vs. 34% at baseline and 35% vs. 53% at follow-up). Looking into the groups of women and men separately, both women and men exhibited more falls in the first tertile (i.e., participant with low maximum grip strength) in comparison with the third tertile (i.e., participants with high maximum grip strength; p value = .204 and .120 at baseline and p value = .0003 and .014 at follow-up for men and women, respectively; results not shown).

Initially, crude ORs with 95% CI and the p values were calculated for the confounders’ age and gender. The odds for falls were lower in men than in women (baseline: OR [95% CI] = 0.55 [0.37, 0.82], p value = .003; follow-up: 0.59 [0.41, 0.85], p value = .005). Age was significantly associated with falls (age [continuous]: .
1.06 [1.03, 1.09], p value = .0002; 1.10 [1.07, 1.14], p value < .0001, at baseline and at follow-up, respectively; results not shown). Table 2 summarizes the results of the logistic regression models examining the association between maximum grip strength and falls, with and without adjustment for age and gender at baseline and at follow-up. Grip strength was inversely associated with at least one fall in the previous 12 months prior to baseline and prior to follow-up (crude OR [95% CI] = 0.96 [0.94, 0.98], p value < .0001, and 0.95 [0.93, 0.97], p value < .0001, per 1-kg increase). The association became borderline nonsignificant after adjustment for age and gender at baseline (0.98 [0.94, 1.01], p value = .153) and borderline significant after adjustment for age and gender at follow-up (0.97 [0.94, 0.99], p value = .026). As a sensitivity analysis, falls were taken as an ordinal variable into an ordinal logistic regression model. An OR (95% CI) of 0.98 [0.95, 1.00], p value = .154, was observed in the sensitivity analysis in the adjusted model at baseline and 0.96 [0.93, 0.99], p value = .006, at follow-up. The interaction term between gender and maximum grip strength in the main and in the sensitivity analysis at baseline and at follow-up was not significant. Results from GEE analysis are shown in Table 2. The results show that, before and after adjustment for age and gender, grip strength was significantly associated with falls. Thus, individuals with low grip strength at baseline had a higher risk of falls during the 12 months prior to baseline and during the 12 months prior to follow-up. Figures 1 and 2 visualize the relationship between grip strength at baseline and at follow-up and falls and gender. Figure 1 shows that most individuals with low grip strength at baseline have low grip strength at follow-up and more falls. In addition, most individuals with high grip strength at baseline have high grip strength at follow-up and fewer falls. Figure 2 shows that most individuals with low grip strength at baseline have low grip strength at follow-up and most individuals with high grip strength at baseline have high grip strength at follow-up (the same as in Figure 1). In addition, it shows that women have less grip strength than men at both baseline and follow-up.

Figure 3 illustrates the results of the analysis performed using the methods of Baron and Kenny and bootstrap, which were used to detect the indirect effect of grip strength through the mediator variable balance problems in the presence of the two confounders, age and gender. The total relationship between grip strength and falls was partitioned into the direct part of tau prime (−0.11) and the mediated part of alpha multiplied by beta (α·β = −.048). Repeating the analysis using the bootstrap method with 100,000 repeated sampling of data, almost the same results were achieved (τ′ = −0.11 and α·β = −.055). The values of the standardized coefficients with 95% CI gained through the bootstrapping method are shown in Figure 3. The results of different tests for significance of the indirect effect (Sobel, Aroain, and Goodman) showed that the indirect relationship between grip strength and falls through the mediator variable balance problems was significant (p value = .043 for Sobel and Goodman, and .041 for Aroain tests).

**Discussion**

The primary findings from the present study are as follows. First, grip strength is inversely associated with a history of falls among older men and women from the general population. More advanced age and female gender were significantly associated with falls and, after adjustment for them, the association between grip strength and falls became borderline nonsignificant at baseline and borderline significant at follow-up. The GEE approach, which considered data as repeated measurements of falls and grip strength over time, confirmed the results. Individuals with at least one fall during the 12 months prior to baseline and lower grip strength had
a higher risk of falls during the 12 months prior to follow-up.

Falls are a common event among older adults and are associated with serious consequences including decreases in social and physical activities, disability, hospitalization, and loss of independence (Peeters et al., 2015). In the Longitudinal Aging Study Amsterdam (Pijpers et al., 2012), low grip strength and physical performance were significantly related to an increased risk of recurrent falls in older community-dwelling participants with and without diabetes. The Women’s Health and Aging Study tested the hypothesis, using longitudinal data from older women, whether those with a faster rate of decline in grip strength would be at higher risk of falls compared with those who had a weaker single grip measurement (Xue et al., 2011). The latter study suggests that at least some of the risk attributable to weakness can be restated as risk attributable to the rate of losing strength.

The Prospective Urban–Rural Epidemiology study, a large, longitudinal population study carried out in 17 countries of varying incomes and sociocultural settings, found no strong association between grip strength and the risk of injury from a fall (Leong et al., 2015). It has been assumed that muscle strength may be a marker of other factors, such as balance, as the most important component in mediating the risk of falls (Sherrington, Whitney, & Close, 2008). Therefore, we assessed the mediating role of balance problems on the relation between grip strength and falls using two different methods. Although this is a common method in sociological and psychosocial studies, this method has rarely been used in the evaluation of health care studies (Mackinnon & Dwyer, 1993). The results from our study confirm the potential impact of balance on reduction in falls, as the indirect effect of grip strength through the mediator variable balance problems was statistically significant after adjusting for age and gender. However, the significant association between grip strength and falls continued to exist when the indirect effect of balance problems was statistically removed. Of note, a most recent meta-analysis revealed merely small correlations between measures of balance and lower extremity muscle strength in
older adults (Muehlbauer, Gollhofer, & Granacher, 2015). Possible explanations behind this observation may include different neural mechanisms involved during the execution of a strength- or balance-related task with different activation patterns (Schubert et al., 2008). In addition, balance itself may affect muscle strength through transfer effects (Gruber et al., 2007). In the Lifestyle integrated Functional Exercise (LiFE) approach, which embeds strategies to improve balance, ankle strength, a prime factor for postural stability, significantly improved compared with the structured control program (Clemson et al., 2012). Accordingly, the integration of both balance and muscle-strengthening exercises into daily life activities may reduce the rate of falls in older people.

Our study has several strengths and limitations. A major strength of this study is the inclusion of a number of participants aged ≥80 years and the use of an objective and standardized test for the assessment of maximal muscular strength. Handgrip strength is considered a strong predictor of muscle mass and leg strength in frail older people (Tieland, Verdijk, de Groot, & van Loon, 2015). Furthermore, we have investigated the indirect effect of balance problems on the relation between grip strength and falls. We adjusted the model for two main confounders, age and gender; however, as shown by Hernan and colleagues via causal graph illustration (Cole & Hernan, 2002), there are situations in which such analyses can be biased because of unmeasured confounders. Therefore, the results of the mediator analysis should be interpreted with caution. More complicated mediator analyses and models including multiple mediators in one model were not considered in our study. Also, due to the definition of mediator, we should take the balance problems variable prior to the outcome but, as we had only two measurements of balance problems at baseline and at follow-up and as the time difference between the two measurements was about 3 years, we took the values of balance problems at follow-up as a proxy in our analysis. Furthermore, although the GEE method is able to take all available data into account in a balance problems design (fewer numbers of observations at follow-up in our study), which leads to a more efficient effect estimate, we preferred to have one dataset with fewer individuals but full information for the variables required, namely, grip strength, falls, age, and gender, to be able to compare the results of logistic regression with GEE analysis. Finally, as this is an observational study, we could only assess statistical associations and not causal relationships. Ultimately, randomized intervention studies aiming to increase muscular strength in older adults will be needed to show whether the observed associations are causal and whether falls can be prevented by increasing muscular strength.

In conclusion, our findings suggest that low muscle strength is inversely associated with falls in old age. The observed association may be partly mediated by balance problems. Thus, the integration of both balance and muscle-strengthening exercises into daily life activities seems to be a promising means of reducing the adverse effects of low muscle strength on falls.

Authors’ Note
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