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REVIEW ARTICLE (META-ANALYSIS)

Muscular Strength as a Predictor of All-Cause Mortality in an Apparently Healthy Population: A Systematic Review and Meta-Analysis of Data From Approximately 2 Million Men and Women

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Abstract

Objectives: The aims of the present systematic review and meta-analysis were to determine the relationship between muscular strength and all-cause mortality risk and to examine the sex-specific impact of muscular strength on all-cause mortality in an apparently healthy population.

Data Sources: Two authors systematically searched MEDLINE, EMBASE and SPORTDiscus databases and conducted manual searching of reference lists of selected articles.

Study Selection: Eligible cohort studies were those that examined the association of muscular strength with all-cause mortality in an apparently healthy population. The hazard ratio (HR) estimates with 95% confidence interval (CI) were pooled by using random effects meta-analysis models after assessing heterogeneity across studies.

Data Extraction: Two authors independently extracted data.

Data Synthesis: Thirty-eight studies with 1,907,580 participants were included in the meta-analysis. The included studies had a total of 63,087 deaths. Higher levels of handgrip strength were associated with a reduced risk of all-cause mortality (HR = 0.69; 95% CI, 0.64-0.74) compared with lower muscular strength, with a slightly stronger association in women (HR = 0.60; 95% CI, 0.51-0.69) than men (HR = 0.69; 95% CI, 0.62-0.77) (all $P<.001$). Also, adults with higher levels of muscular strength, as assessed by knee extension strength test, had a 14% lower risk of death (HR = 0.86: 95% CI, 0.80-0.93; $P<.001$) compared with adults with lower muscular strength.

Conclusions: Higher levels of upper- and lower-body muscular strength are associated with a lower risk of mortality in adult population, regardless of age and follow-up period. Muscular strength tests can be easily performed to identify people with lower muscular strength and, consequently, with an increased risk of mortality.

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Muscular strength is recognized as a marker of cardiometabolic risk that has been associated with morbidity in adults and elderly people[1] and is independently associated with adult metabolic syndrome over the long term.[2] Similarly, studies have shown that low handgrip strength is associated with sarcopenia,[3] functional limitations and disabilities,[4] and is considered a useful marker for frailty in the

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elderly.[5] Several studies have also suggested that lower extremity muscle mass is an important determinant of physical performance in older persons.[6,7] Moreover, reduced muscular strength has been associated with an increased risk of mortality in many longitudinal studies.[8-12] Therefore, muscular strength might be used as a potential predictor of morbidity and mortality in the population.[10,11] This emphasizes the importance of accumulating knowledge from studies in different contexts to determine the cutoffs for different diseases, because they are not currently available in the literature. In 2015, Volaklis and colleagues[12] conducted a narrative review of epidemiologic studies to investigate the role of muscular strength as a predictor of mortality and described a strong and inverse association of muscular strength with all-cause mortality. This association has also been confirmed among people with specific disorders, such as cardiovascular disease, peripheral artery disease, cancer, renal failure, chronic obstructive pulmonary disease, rheumatoid arthritis, and patients with critical illness.

A meta-analysis published in 2010[13] suggested that the pooled hazard ratio (HR) for mortality comparing the weakest with the strongest group of handgrip strength (14 studies with a total of 53,476 adults) was 1.67 (95% confidence interval [CI] 1.45-1.93). Apart from this meta-analysis, many studies have added new insights,[14-27] but most studies used handgrip strength test. No previous meta-analysis has analyzed the sex-specific impact of muscular strength on all-cause mortality, and there is no information about the role of other muscular strength measures such as knee extension strength. Although consistent evidence has proven that lower limb muscular strength is a predictor of the ability to perform activities of daily living and this ability is associated with frailty and mortality,[28] the direct relationship between lower limb strength and the risk of mortality is still unclear because previous cohort studies have shown inconsistent findings. Because handgrip and lower limb muscular strength tests are easy to perform, noninvasive, and inexpensive, it is important to include these tests in clinical settings to better understand the clinical importance of muscular strength for the development of public health guidelines. Therefore, the aims of this systematic review and meta-analysis were (1) to determine the relationship between muscular strength and all-cause mortality risk, and (2) to examine the sex-specific impact of muscular strength on all-cause mortality in an apparently healthy population.

Methods

A systematic review and meta-analysis was conducted following the guidelines of the Cochrane Collaboration. Findings were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[29] The review was registered in PROSPERO (registration number: CRD42016032733).

Search strategy

Two authors (A.G-H. and R.R-V.) systematically searched MEDLINE, EMBASE, and SPORTDiscus databases until July 1, 2017 (supplementary data 1, available online only at http://www.archives-pmr.org/). The following terms were used: "muscles" OR "muscle strength" OR "muscular" OR "strength" AND "mortality" OR "survival rate" OR "cause of death." Only articles published in English were included in the study. In addition, the literature search was supplemented through the manual review of reference lists in the selected articles.

List of abbreviations:

HR	**hazard ratio**
PRISMA	**Preferred Reporting Items for Systematic Reviews and Meta-Analyses**

Selection criteria

The a priori inclusion criteria for this meta-analysis were (1) exposure: muscular strength measured using a validated strength test; (2) main outcome: all-cause mortality risk assessed with hazard ratios (HR-Cox proportional hazards model); (3) participants: relatively healthy youth and adults excluding studies in which all patients had chronic diseases such as diabetes, heart failure, hypertension, peripheral artery disease, chronic obstructive pulmonary disease, cancer, and patients with critical illness (i.e. we excluded studies of patient groups); and (4) study design: prospective cohort studies. Two authors (A.G-H. and R.R-V.) independently assessed the electronic search results. When an article title seemed relevant, the abstract was reviewed for eligibility. When more information was required, the full text of the article was retrieved and appraised. Any differences in the assessments between the 2 authors were discussed and, if necessary, a third author (I.C-R.) was involved in decision making. Reasons for exclusion of identified articles were recorded in all cases. Finally, when 2 studies used the same sample, we included the study with longer follow-up.

Data collection process and data items

Two authors (A.G-H. and R.R-V.) independently extracted data including the first author's name, year of publication, enrollment year, duration of follow-up, study location, sample size, a participant's age at baseline examination, HRs (and their associated 95% CIs or standard errors, adjusted variables, method of muscular strength assessment, and outcome of interest and number of cases.

Risk of bias in individual studies

An assessment of risk of bias in selected studies was made using an adjusted format of the Newcastle-Ottawa Scale for quality assessment by 2 authors (A.G-H. and R.R-V.) independently.[30] This scale contains 8 items categorized into 3 domains (selection, comparability, and exposure). A star system is used to enable semiquantitative assessment of study quality; such that the highest-quality studies are awarded a maximum of 1 star per item with the exception of the comparability domain, which allows allocating 2 stars. Thus, the score ranges from 0 to 9 stars.

Summary measures

All analyses were carried out using STATA.[a] HRs with associated 95% CIs from studies for each outcome of interest were extracted (used to estimate the risk for mortality), and a pooled HR using random effect (DerSimonian and Laird) models was then calculated. The likelihood approach with random effects was used to better account for the inaccuracy in the estimate of between-study variance.[31] When the HR was unavailable, we requested corresponding authors to send us their HR data.