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REVIEW

Grip Strength: An Indispensable Biomarker For Older Adults

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Abstract: Grip strength has been proposed as a biomarker. Supporting this proposition, evidence is provided herein that shows grip strength is largely consistent as an explanator of concurrent overall strength, upper limb function, bone mineral density, fractures, falls, malnutrition, cognitive impairment, depression, sleep problems, diabetes, multimorbidity, and quality of life. Evidence is also provided for a predictive link between grip strength and all-cause and disease-specific mortality, future function, bone mineral density, fractures, cognition and depression, and problems associated with hospitalization. Consequently, the routine use of grip strength can be recommended as a stand-alone measurement or as a component of a small battery of measurements for identifying older adults at risk of poor health status.

Keywords: biomarker, muscle strength, health outcomes, epidemiology, mortality, rehabilitation, aging

Introduction

Biomarkers are medical signs at the level of pathology, body function or structure, or activity/participation that provide an objective indication of medical status.[1,2] Grip strength, a measure of body function, has been suggested as a biomarker of aging.[3] As such, its value as an explanator of current status and predictor of future outcomes has been widely researched and reviewed.[4,5] The purpose of this narrative review is to provide an up-to-date, thorough, and balanced synopsis of research addressing grip strength as a biomarker of current and future medical status.

Grip Strength As A Biomarker Of Current Status

Use of grip strength as a biomarker of current health status is most directly supported by research showing a cross-sectional association between grip strength and the strength of other muscle actions of both healthy individuals and adults with pathology.[6–9] Based on this research and the practicality of hand-grip dynamometry, the measurement of grip strength has been widely adopted as a singular indicator of overall strength. This adoption notwithstanding, clinicians and scientists should be cautious in using grip strength as an indicator of overall strength as there is evidence that grip strength may not always be reflective of overall strength[10] and may provide a better indication of overall strength if used in conjunction with a measure of lower limb strength.[11]

In any case, grip strength is related concurrently to measures other than the strength of different muscle actions. Chief among such measures are those of activities[2]

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involving the upper limbs, of which the hands are a part. Research by Wang and Chen supports this declaration.[12] They identified cutoffs for grip strength needed by older adults (18.5 kg for women, 28.5kg for men) to manage heavy tasks (eg, lifting or carrying 11kg objects). Giray and Akyüz found that the grip strength of women with postmastectomy edema, had low to moderate but significant correlations (r= −0.32 and −0.51) with self-reported upper limb function as characterized by the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire.[13] A low but significant correlation (r= −0.32) between grip strength and DASH scores has also been reported for patients examined one month after cardiac surgery.[14] Sunderland et al demonstrated high correlations between grip strength and performance on the Frenchay Arm Test (r= 0.91), Motor Club Assessment (r= 0.86), and Peg Test (r= 0.79) by patients with stroke.[15]

Although grip strength is not directly required for the performance of functional activities such as gait, it does distinguish between older adults on the basis of their mobility. Forrest et al noted significantly lower grip strengths among older Americans who reported physical limitations-including standing from a chair, walking, climbing steps, and "going out".[16] Zhang et al demonstrated a significant, albeit low (r= 0.36), relationship between grip strength and the distance walked during the 6 min walk test.[17] Specific grip strength thresholds have been determined that identify older adults who are weak and likely to have walking limitations. In 6 studies identifying walking as slow (< 0.80m/s), grip strength thresholds for men ranged from 23.2kg to 39.0kg. For women they ranged from 15.9kg to 22.0kg.[18–23] Sallinen found that thresholds of 37.0kg for men and 21.0kg for women identified older adults with difficulty walking 0.5km or climbing stairs.[24]

As the pull of muscles on bones has a trophic effect on the latter, it should not be surprising that muscle strength is related to bone mineral density. What is noteworthy is the consistent demonstration across cultures of a relationship between grip strength and bone mineral density/osteoporosis at different sites- not all involving bones attached to muscles involved in hand-grip (eg, calcaneus, spine and hip.[25–33] Of note, strength is a better explanator of bone mineral density/osteoporosis than muscle mass.[26,33]

Potentially related to the concurrent association of grip strength with bone mineral density/osteoporosis is the relationship between grip strength and fractures. In a systematic review Denk et al found that all of 11 included studies confirmed a relationship between decreased hand grip strength and the incidence of hip fractures.[34] Similarly, Kim et al found that hand grip strength along with bone mineral density was associated with an increased risk of fragility fractures.[27] Of course a key cause of fractures is falls. Therefore, the demonstration of an association between grip strength and falls might also be expected. Yang et al reported such an association, specifically they noted a mean grip strength of 17.6 kg in a group that had recently fallen compared to 20.7 kg in a group that had not fallen.[35] Van Ancum et al determined that lower grip strength was present among males (but not females) with pre-hospitalization falls.[36]

Grip strength has been studied as a potential biomarker of malnutrition among diverse patient groups - with varying results. Examining a sample of older Chinese inpatients tested at hospital admission, Zhang et al noted that those with lower grip strength had an increased risk of malnutrition measured using the Nutritional Risk Screening and Subjective Global Assessment.[37] For the Nutritional Risk Screening the best cut-points were 27.5kg for men 65–74 years, 21.0kg for men 75–90 years, 17.0kg for women 65–74 years, and 14.6kg for women 75–90 years. For the Subjective Global Assessment, the optimal cut-points were 24.9kg for men 65–74 years, 20.8kg for men 75–90 years, 15.2kg for women 65–74 years, and 13.5kg for women 75–90 years. Among patients on maintenance hemodialysis, Silva et al found low but significant inverse correlations (r_s= −0.38 [men] and −0.36 [women]) between grip strength and the Malnutrition–Inflammation Score.[38] The correlation was present regardless of race, diabetic status, age, and gender. They calculated grip strength cut points of 28.3kg for men and 23.4kg for women. Ozorio et al classified patients with gastrointestinal cancer into 4 levels of cachexia.[39] Patients with the greatest degree of cachexia (refractory) had the lowest grip strength. They reported the most discriminating grip strength cutoff for refractory cachexia was 19.3 kg for men and 14.7 kg for women. Byrnes et al, who studied older adults admitted to general surgical wards, concluded that grip strength was not "suitable for screening older inpatients for malnutrition".[40] Although finding a significant association between grip strength and nutritional status, McNicholl described grip strength as having "poor validity as a single nutrition indicator".[41] As more of the patients they tested completed a grip strength assessment (92%) than a 5 meter walking assessment (43%), they concluded that grip strength "is a more useful functional measure" than the 5 meter walk test.

Weakness is a commonly observed impairment in the lower limbs of Individuals with diabetes, with weakness

being greater in the presence of neuropathy.[42] Some research, however, also evinces limited grip strength in individuals with diabetes[43–45] or prediabetes.[46] That strength has also been shown in a few studies to be inversely related to measures of glucose control such as fasting glucose, HBA1c, and hyperglycemia[43–45] and to systemic inflammation.[43] Grip strength is also related to multimorbidity whether or not diabetes is a component of the morbidity load;[47–50] as the number of comorbidities rises the grip strength diminishes.

Up to this point, relationships between grip strength and variables of a physical nature have been addressed. Considerable research, however, notes a covariance of grip strength with cognition, depression, and sleep as well. In a recent systematic review examining the relationship between grip strength and cognitive function in older adults, Kobayashi-Cuya et al reported that 6 of 7 studies documented significant relationships.[51] Vancampfort et al recently reported that among middle-aged and older adults, weak grip strength was associated with increased odds of having mild cognitive impairment.[52] Others have shown a correlation between grip strength and the Mini-Mental State Examination scores of geriatric inpatients,[53] information processing speed and executive functioning of patients attending a memory clinic,[54] Stroop Task and 6-item Cognitive Impairment Test scores of physically active adults,[55] visual memory,and reaction time of patients with schizophrenia,[56] and Animal Fluency Test and Digital Symbol Substitution Test scores of cancer survivors.[57] A link between grip strength and depression has been demonstrated among residents of 6 low and middle income countries[58] as well as Brazil[59] and Korea.[60] Using a cut-point of less than 30kg for men and 20kg for women for weak grip, Ashdown-Franks et al found a prevalence of depression of 8.8% among adults classified as weak versus 3.8% among adults not classified as weak.[58] Kyu-Man et al determined in a sample of older adults that the correlation between grip strength and depression was lower in older adults with a higher household income.[61] Perhaps the high income of Australians explains why Gopinath et al did not find their grip strength to be associated with depression.[62] Greater sleep impairment,[63] lower sleep quality,[64,65] and longer sleep duration[66] have been shown to be related to lower handgrip strength.

Finally, grip strength has been shown to relate concurrently to quality of life, a variable not limited specifically to physical or mental domains. These relationships have been documented using generic measures of quality of life in patients with liver disease,[67] and disease specific measures of quality of life in patients with cancer,[68] chronic obstructive lung disease,[69,70] or surgery for spinal stenosis.[71]

Grip Strength As A Biomarker Of Future Outcomes

Grip strength is a predictor of numerous future outcomes. Mortality is probably the most widely studied outcome, with studies published as far back as the 1980s[72] and at least 3 meta-analyses supporting the association of weak grip strength with all-cause mortality in the general population. In one of these meta-analyses Rijk et al summarized 22 articles addressing mortality. Their pooled hazard ratio for mortality for categorical variables was 1.79.[73] In a more recent meta-analysis Wu et al consolidated the results of 40 studies addressing all-cause mortality.[74] They calculated a pooled hazard ratio 1.16) per 5kg reduction in grip strength. In an even more recent meta-analysis García-Hermosa et al combined the results of 33 studies addressing all-cause mortality.[75] They determined a pooled hazard ratio for a reduced risk of mortality for higher versus lower levels of grip strength to be 0.69. In addition to these meta-analyses, several recent large-scale studies have further reinforced the value of grip strength as a predictor of mortality in community-dwelling populations. These studies all involved over 1000 participants from each of several specific countries or regions: Japan;[76] Russia;[77] Denmark,[77] the United Kingdom,[77–79] Korea,[80] Norway,[81] the United States,[82,83] the Netherlands,[84] Switzerland,[85] Western Europe,[86] and Taiwan.[87] In the last of these studies, "malnutrition synergistically increased the mortality risk" in keeping with low grip strength.[87]

Grip strength is also supported as a predictor of disease and disease-specific mortality- with much of the literature focused on cardiovascular disease and cancer. Wu et al, in a summary of 12 studies, determined that a 5kg decrease in grip strength was associated with an increased risk of cardiovascular disease (overall hazard ratio 5.98).[74] Other studies not included in their review provide additional qualified support for measuring grip strength. Prasitsiriphon and Pothisiri found that grip strength was a significant predictor of cardiovascular mortality for men and women but that change in grip strength was not.[86] Yates et al determined that grip strength was associated with cardiovascular mortality but only in men (hazard ratio: 1.38).[88] Gubelman et al noted a significant association of low grip strength and cardiovascular events, but the difference was annulled after accounting for baseline cardiovascular risk.[85] Whitney and Peterson, who measured absolute grip strength as well as grip

strength normalized against body mass and body mass index, found only the latter 2 measures to covary with cerebrovascular events.[82] Perhaps most telling in regard to the relationship of grip strength and cardiovascular mortality, however, are the findings reported by Leong et al[89]. They determined that grip strength was a more powerful predictor of cardiovascular mortality (hazard ratio 1.17) than systolic blood pressure. They also found grip strength to be associated with all-cause mortality (hazard ratio 1.16), myocardial infarction (hazard ratio 1.07), and stroke (hazard ratio 1.09).

In regard to cancer mortality, the value of grip strength as a predictive biomarker is uncertain. Based on a meta-analysis of 7 studies, Garcia-Hermoso et al calculated a hazard ratio of 0.97 and suggested that a "higher level of muscular strength is not statistically associate with a lower risk of cancer mortality".[90] Wu et al came to a similar conclusion following a meta-analysis of 10 studies (hazard ratio 1.10).[74] In a more recently published study of more than 500,000 adults not included in these meta analyses, Celis-Morales et al found an association between lower grip strength and cancer mortality (all cause, colorectal, lung, and breast).[91] Their findings did not extend to prostate cancer. For individuals who already have cancer, there is inconsistent evidence that low grip strength is a predictor of mortality. For older patients with cancer Pamoukdjian et al and Versteeg et al both showed that higher grip strength was associated with prolonged survival.[92,93] Chen et al demonstrated a significant difference (p=0.016) in the 6 month mortality of patients with grip strength < 25kg versus normal grip strength who underwent esophagectomy for esophageal cancer.[94] Puts et al, on the other hand, did not find a significant relationship between grip strength and mortality in patients with cancer.[95] Unlike Versteeg et al, however, Puts et al did find an association between grip strength and treatment toxicity.

In addition to examining grip strength as a potential predictor of cardiovascular and cancer mortality, investigators have also shown the value of grip strength as a predictor of mortality in other pathologies. These pathologies include, but are not limited to, rheumatoid arthritis in women (relative risk 3.0),[96] type 2 diabetes in men (hazard ratio 0.90),[97] pneumonia (odds ratio 0.97),[98] renal disease (1.76 and 1.81),[99] and chronic obstructive pulmonary disease (hazard ratio 1.80).[100] For patients with chronic obstructive pulmonary disease Mohamed-Hussein et al noted a significant difference in mean grip strength between patients admitted to the intensive care who died (5.7kg) compared to those who survived (14.5kg).[101]

As grip strength explains function cross-sectionally, it also predicts future function and changes in function over time. Over 10 years ago Bohannon published a systematic review in which he included the results of 9 studies investigating the value of grip strength as a predictor of future function.[4] The studies included samples of healthy nondisabled, disabled, and diseased middle-aged and older adults whose function was measured a median 10 days to 25 years after their baseline grip strength. For the cohort followed a median 10 days, the grip strength of both sides was significantly less for patients who declined functionally during hospitalization.[102] For the cohort followed 25 years, individuals with the lowest baseline grip strength were significantly more likely to walk at ≤0.4m/s (odds ratio 2.77), be unable to rise from a chair (odds ratio 2.73), lifting 4.5kg (odds ratio 1.94), doing heavy housework (odds ratio 1.69), dressing (odds ratio 2.43), and bathing (odds ratio 2.06), but not walking 0.8km (odds ratio 1.25), walking up 10 steps (odds ratio 1.28), eating (odds ratio 2.33), or toileting (odds ratio 1.96).[103] More recent studies have confirmed the value of grip strength as a predictor of function. Dodds et al found the grip strength of a British cohort measured in "mid-life" to predict their mobility and/or personal care disability in early old age (odds ratio 1.84).[104] The value of grip strength as a predictor was roughly equivalent to that of sit-to-stand speed and unipedal stance time (eyes closed) and added to the predictive power provided by chronic conditions and behavioral risk factors. McGrath et al determined that high baseline grip strength decreased the odds of developing disability in activities of daily living (odds ratio 0.95) and instrumental activities of daily living (odds ratio 0.92) among older Mexican Americans.[105] For patients with specific problems grip strength was shown to be predictive of function as well. For example, Di Monaco et al documented that for women with hip-fractures, handgrip strength measured before rehabilitation was correlated weakly but significantly (p=0.001) with Barthel Index scores at the end of inpatient rehabilitation ($r_{partial}$ =0.25) and at 6-month follow-up ($r_{partial}$ =0.28).[106] Hashimoto et al demonstrated that preoperative grip strength was significantly greater (p=0.001) among patients who used a step-over-step pattern rather than a step-to-step pattern to negotiate stairs one year post total knee arthroplasty.[107] Incidentally, they also found preoperative grip strength to be better than preoperative knee extension strength for predicting the pattern used to negotiate stairs. Two studies have described the relationship between grip strength at hospital admission and functional decline. Garcia-Peña focused on functional decline between

admission and discharge.[108] In multivariable analysis they found that grip strength was related significantly to a 30-point decline in Barthel scores in men (odds ratio 0.87) but not in women (odds ratio 0.93). Olguín et al were concerned with functional decline over the 30 days after admission.[109] They found grip strength to be significantly related (odds ratio 0.97, p =0.007) to functional decline as measured using the Karnofsky index. Grip strength was more predictive than age, nutritional status, or a cancer diagnosis of such a decline.

Although the cross-sectional relationship between grip strength and bone mineral density has been firmly supported by literature cited heretofore, there is little research showing a predictive relationship between grip strength and future bone mineral density or changes in bone mineral density over time. The one relevant article I found via a PubMed search reported a low but significant correlation (r_s =0.25) between grip strength the annual percentage changes in bone mineral density of the femoral neck among a population-based cohort of women followed over 10 years.[110] As have numerous cross-sectional studies, many longitudinal studies have addressed the value of grip strength as a predictor of incident fractures.[111–115] Among healthy Saudi postmenopausal women, Rouzi et al found grip strength to be significantly lower for women who developed osteoporosis related fractures.[111] The odds ratios associated with their experiencing a fragility fracture (2.56 or 2.24) were greater than the odds ratios associated with various bone mineral density measures (1.24 to 1.96). They suggested, consequently, that grip strength and other risk factors may be useful alternatives for identifying fracture risk where the measurement of bone mineral density is impracticable. Dixon et al expressed similar conclusions, noting that low grip strength is associated with an increased risk of incident vertebral fractures that cannot be explained by differences in lifestyle or body size.[112] Rikkonen et al found grip strength to predict incident fractures (not corrected for bone mineral density) with hazard ratios of 2.0 and 1.3. Notably, both unipedal balance and squatting to the floor performance were more predictive of fractures and all 3 performance measures together were most predictive of fracture.[113] Sirola et al followed women with normal bone mineral density at baseline for 15 years.[114] While they found bone mineral density t-scores to be the best predictors of incident fractures, they determined that grip strength could be used as a "cost effective" supplemental predictor of fractures. As pointed out before the concurrence of fractures with falls renders the relationship between grip strength and falls important. Miller et al found that the risk of falling over a period of 1 year was low but significantly (p=0.034) greater among both men and women whose grip strength was below the 25th percentile of the older Australian population studied.[115] Studying Swedish men, Cöster et al et al also found grip strength to predict incident falls (odds ratio 1.52 right, 1.64 left) but recurrent incident falls as well (odds ratio 1.57 right, 1.64 left).[116] Notably, they reported that tests of sit-to-stand performance and walking time were also predictive of falls and recurrent falls (odds ratios 1.54 to 2.00). Van Ancum et al showed that grip strength was related to having at least 1 fall during the 3 months post hospital discharge. However, their finding was only validated with men (odds ratio 9.93).[36] Luukinen et al noted that reduced grip strength was related significantly (p=0.05) to fall-related fractures in home-dwelling older adults but that knee extension strength was related as well.[117]

As the relationships between grip strength and cognitive and depressive status have been examined cross-sectionally, they have also been investigated over time. Two recent systematic reviews draw different conclusions from the predictive literature. In the first review, Kobayashi-Cuya et al concluded that while grip strength and cognition are associated longitudinally, it is not clear "which variable at baseline affects the other in the long-term."[51] In the second review, Zammit et al opined that while both grip strength and cognitive performance decline with age, evidence for an association between longitudinal rates of change in the variables is limited.[118] Several original studies not included in the aforementioned reviews provide evidence supporting a predictive relationship between grip strength and cognitive decline. The studies include Japanese, Korean, and Italian populations, follow-up periods of 1 to 10 years, and cognitive tests as diverse as the Mini-Mental State Evaluation, Digit Symbol Substitution Test, Clock Drawing Test, and the Clinical Dementia Rating Scale.[119–123]

The final predictive value of grip strength addressed herein is that relative to hospitalization. Simmonds et al examined the association between grip strength and the combined rate of hospital admission/death over the following 10 years.[124] For a large sample of both men and women, lower grip strength was associated with a significantly greater risk of any emergency admission/death (hazard ratios 1.08 and 1.21) and any > 7 days admission/death (hazard ratios 1.14 and 1.20). For women low grip strength was also associated with a significantly greater risk of any admission/death (hazard ratio 1.10) and any elective admission/death (hazard ratio 1.09). Cowthon et al, who followed a cohort of Americans over a mean 4.7 years, found that participants with the weakest grip

strength had the highest risk of hospitalization.[125] Notably, participants with the poorest knee extension strength, sit-to-stand times, and waking speed were also at a significant risk for hospitalization. In a large sample of Japanese individuals with type 2 diabetes, Hamasaki et al found hospitalization over a mean 2.4 years was associated significantly with grip strength (hazards ratio 0.96). The only variable they found to have a stronger relationship with hospitalization was HbA1c (hazards ratio 1.33).[97]

Not only are patients with weak grip strength more likely to be admitted to the hospital, they are more likely to experience complications while there. In a review referred to heretofore,[4] weak grip strength was described as related to complications in patients undergoing surgery and in patients with cancer, hip fractures, and cirrhosis. In the study of patients with cirrhosis, grip strength was the only variable predicting a "significant increase in major complications."[126] More recent studies, not addressed in the review, have evinced a relationship between grip strength and complications/post-operative risk in patients undergoing surgery for abdominal cancer[127] or elective cardiac surgery.[128] A contemporary study of patients hospitalized for hip fractures showed their grip strength to be associated with a risk of pressure ulcers.[129]

The literature is inconsistent, but hospital and rehabilitation length of stay and readmission have been shown in several studies to correlate with grip strength. Specifically, significant relationships with length of stay have been reported with the stronger hand of older hospitalized patients,[130] both hands of patients with stroke,[131] the stronger hand of patients with pneumonia,[132] the average of both hands of patients undergoing hip or knee arthroplasty,[133] and handgrip strength normalized against body weight for patients undergoing implantation of a left ventricular assistive device.[134] Hospital readmission is also related to grip strength. Regarding hospital readmissions, a study referred to earlier demonstrated a significant relationship between low preadmission grip strength and death or readmission within 30 days (odds ratio 1.13 to 1.30).[124] Andeasen et al noted a significant relationship between low postadmission grip strength and death or readmission within 6 months.[135] Allard et al, who measured grip strength at discharge from an acute care hospital, showed higher grip strength to be accompanied by a lower 30-day rate of readmission.[136] Isaia et al found neither admission nor discharge grip strength to be predictors of readmission, but they were associated with mortality.[137] Vecchiarino et al did not verify grip strength as a predictor of readmission in patients admitted to the hospital with pneumonia.[132]

Discussion And Conclusions

Several authors have recommended grip strength as a "useful indicator for overall health,"[16] a vital sign[4,5] and as a biomarker of health status.[3,138,139] The purpose of this literature review was to provide an up-to-date, thorough and balanced synopsis of evidence for using grip strength as a biomarker of current and future health status. Based on the review it appears that there is adequate evidence to support the use of grip strength as an explanatory or predictive biomarker of specific outcomes such as generalized strength and function, bone mineral density, fractures, and falls, nutritional status, disease status and comorbidity load, cognition, depression, and sleep, hospital-related variables, and mortality. Based on this evidence and the promotion by others,[140] the routine implementation of the measurement of grip strength can be recommended for older adults in the community and health-care settings.

This review has several limitations. Most notable, it was a narrative rather than a systematic review. As such, it is not as comprehensive as it might be, and the performance of a meta-analysis was not possible. This limitation noted, a PubMed search using the terms "hand AND grip AND strength" was used to help identify relevant literature and every effort was made to not limit the findings reported to those supportive of using grip strength as a biomarker. Another limitation is the lack of standardized testing across studies. Numerous different procedures, cut points for grip weakness and statistics were used in the reviewed investigations. The possible effects of these differences have led Roberts et al to argue for the use of a standardized approach to measurement in both clinical and epidemiological studies.[141]

The incredible amount of research on grip strength and outcomes notwithstanding, further research on the topic is warranted. Of interest may be topics such as the relative value of different grip strength measures (eg, absolute versus relative),[142] alternative strength measures (eg, grip versus respiratory),[143] and various combinations of measures (eg, grip strength and self-reported activity).[53]

Disclosure

The author reports no conflicts of interest in this work.

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