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Association between handgrip strength and cognitive function in older adults living with cancer

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ABSTRACT

Introduction and aim. Handgrip strength (HGS) serves as a key indicator of muscle performance and may reflect cognitive status in older cancer patients. We examined whether handgrip strength was associated with cognitive function in this group of patients.

Material and methods. For this study, a cross-sectional design was used, analyzing data from patients aged 60 years and older diagnosed with cancer, collected through Comprehensive Geriatric Assessments (CGAs). The information included demographics, HGS levels, and Mini-Mental State Examination (MMSE) scores.

Results. Among 352 participants (average age 75.7 years), HGS showed a moderate positive correlation with cognitive function, stronger in females ($r=0.36$, $p<0.001$) than in men ($r=0.22$, $p=0.005$). Each 1 kg increase in HGS was associated with a 0.29-point increase in MMSE scores in women and 0.13 points in males.

Conclusion. Higher HGS appears to better cognitive outcomes in older adults with cancer. As muscle strength is potentially modifiable, future research should explore whether HGS-targeted interventions could preserve or enhance cognitive health. Implementing regular handgrip strength assessments in geriatric oncology could help to detect patients who are vulnerable to cognitive decline.

Keywords. cancer, cognition, aging, handgrip strength, sarcopenia

Introduction

Currently, it is estimated that over 57 million people worldwide are living with cognitive impairment, and this number is projected to increase to 153 million by 2050.[1] Such cognitive decline in older adults can result in a significant global economic burden, with estimates suggesting losses of up to $14.5 trillion USD between 2020 and 2050.[2] Among older adults, cognitive impairment is most frequently attributed to conditions such as Alzheimer's disease, vascular dementia, frontotemporal dementia, and Lewy bodies. However, cognitive dysfunction may also arise in the context of cancer and its treatments – a condition known as cancer-related cognitive impairment (CRCI).

CRCI refers to a variety of cognitive symptoms that are believed to be the result of the effects of systemic malignancies and/or their therapies, even when the central nervous system is not directly involved.[3] These symptoms can be self-reported or objectively identified through validated neuropsychological assessments and often include reduced attention, slower processing speed, and language retrieval difficulties.[4] CRCI can appear at different points in the cancer journey, including prior to diagnosis, during treatment, or in survivorship. Reported prevalence rates range from 23% to 31%, depending on the timing and type of assessment.[5]

Several risk factors have been associated with CRCI, including specific types of cancer (e.g. hormone-related tumors), chemotherapeutic agents ("chemo brain"), cranial irradiation, anti-hormonal treatments, genetic predisposition (e.g. *APOE, COMT, BDNF* polymorphisms), and various psychosocial influences such as depression, anxiety, fatigue and lack of social support.[7]

Among evidence-based strategies to reduce the risk of dementia, promoting regular physical activity is strongly recommended. Physical activity is associated not only with improved overall health, but also with better cognitive outcomes in aging populations.[8]

Comprehensive Geriatric Assessment (CGA) is a multidisciplinary approach used to assess the complex needs of older adults, particularly those with chronic illnesses such as cancer. It includes functional and cognitive assessments, among others, and is valuable for guiding treatment decisions and optimizing care plans in older cancer patients.[9] Since muscle strength, often measured through handgrip strength (HGS), is positively linked to physical activity, and physical activity is inversely associated with cognitive decline, an emerging area of research focuses on the association between muscle strength, particularly handgrip, and cognitive outcomes in aging cancer populations.[10] To date, only one published study has specifically investigated this association in older cancer patients. Our study aimed to address this gap in the literature by examining the correlation between handgrip strength and cognitive performance in a Latin American population of older people diagnosed with cancer.[11]

Aim

This study aimed to evaluate the relationship between handgrip strength and cognitive function among older adults with cancer treated in a Peruvian healthcare setting.

Material and methods

Design

We carried out a cross-sectional observational study within the Geriatrics Department at Almenara Hospital in Lima, Peru. We retrospectively reviewed data from electronic medical records corresponding to comprehensive geriatric evaluations (CGA) performed between January 2023 and February 2025. A nonprobability, convenience sampling method was applied to select eligible participants.

Inclusion criteria were: (a) adults aged 60 years or older, hospitalized or seen in outpatient settings; (b) confirmed cancer diagnosis; and (c) CGA request issued by the oncology team.

Exclusion criteria included: (a) people who were illiterate or unable to complete the Mini-Mental State Examination (MMSE) due to conditions such as visual or hearing impairment, or any other factor affecting test reliability; (b) patients with hand-related musculoskeletal disorders, such as rheumatoid arthritis, that could affect grip strength; and (c) those diagnosed with tumors or brain metastases of the primary central nervous system.

Peru's national education system is mandatory for children aged six and includes six years of primary school and five years of secondary education. University-level programs typically last between three and seven years. Pre-school education was not considered in this study.

Cognitive Function Assessment

Cognitive function was assessed with the Spanish version of the Mini-Mental State Examination (MMSE).[12] A score below 24 points was considered indicative of cognitive impairment. This tool has been recommended by the International Cognition and Cancer Task Force (ICCTF) for evaluating domains most commonly affected by cancer treatments.[13,14]. The MMSE is widely validated and has been used in previous studies involving cancer patients.[15]

Handgrip Strength Assessment

Handgrip strength (HGS) was evaluated using a Jamar hydraulic hand dynamometer, adhering to the standardized Southampton protocol.[16] Participants were seated with their forearm resting on the armrest, the wrist neutrally at the edge of the armrest, and the feet flat on the floor. During the test, patients were instructed to 'squeeze *as hard as possible until told to stop',* with timing guided by when the dynamometer needle stopped rising. Two to three measurements were taken per hand, on alternating sides. For analysis, the highest value recorded from either hand. Probable sarcopenia was defined using the criteria of the

European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria: <27 kg for men and <16 kg for women.[17]

Comprehensive Geriatric Assessment (CGA)

The CGA was conducted by trained geriatricians and encompassed multiple domains, including physical function, mobility, nutritional status, cognition, mood, comorbid conditions, and social support. Functional status was measured using the Katz Index of Basic Activities of Daily Living (BADL).[18] Nutritional screening was performed using the Short Form (MNA-SF).[19] Depressive symptoms were identified via a documented diagnosis, current use of antidepressants or semi-structured interviews based on DSM-IV criteria.[20] The burden was quantified with the Cumulative Illness Rating Scale for Geriatrics (CIRS-G).[21] Additional variables collected included demographic and clinical information such as age, sex, body mass index (BMI), and cancer diagnosis.

Statistical analysis

We used descriptive statistics to characterize the study population. Categorical variables were reported as counts and percentages, while continuous data were summarized using means and standard deviations or medians and ranges, depending on their distribution. Pearson correlation coefficients were calculated to assess the relationship between handgrip strength and MMSE scores. The interaction between sex and handgrip strength was statistically significant; therefore, all analyses were stratified by sex. Multivariate linear regression models were built to adjust for potential confounders, including age, educational attainment, BMI, depression, nutritional status, and comorbidity burden (CIRS-G). All statistical analyses were conducted using Epi Info version 7.2.

Ethical considerations

Ethical approval for the study was granted by the Research Ethics Committee of the Almenara Hospital in Lima, Peru (approval code: 80-CIEI-OIyD-GRPA-ESSALUD-2023, dated 27 March 2023). All patient information was treated confidentially and in accordance with ethical standards.

Results

In total, 352 patients who met the eligibility criteria were included in the analysis. The mean age was 75.7 years (SD: 7.2), with 169 (48.0%) males and 183 (52.0%) females. Males had significantly more years of formal education ($p<0.05$), while depression symptoms were more commonly observed among females ($p<0.05$) (Table 1).

The distribution of cancer types was as follows: colorectal (23.0%), stomach (9.1%), prostate (8.5%), lung and pancreatic (both 7.4%), breast (6.8%), biliary tract (5.7%), liver (5.1%), non-Hodgkin lymphoma (4.8%), skin (4.8%), head and neck (4.0%), endometrial, ovarian and kidney cancers (each 2.6%), multiple myeloma (1.4%), leukemia (1.2%), bladder (0.6%) and other types (2.5%).

Cognitive impairment, defined as an MMSE score below 24, was present in 24.8% of the total sample. The prevalence was almost identical between sexes: 24.9% in men and 24.7% in women ($p=0.545$). Probable sarcopenia, based on the strength cutoffs, was significantly more common among men (67.5%) than females (51.4%) ($p=0.0022$) (Table 1).

Linear regression analysis demonstrated that for each 1 kg increase in HGS, MMSE scores increased by an average of 0.29 points in women (95% CI: 0.18–0.40; $p<0.001$) and 0.13 points in men (95% CI: 0.04–0.23; $p=0.005$). Pearson's correlation coefficients indicated a moderate positive association between HGS and cognitive scores in females ($r=0.36$, $p<0.001$) and a weaker but significant correlation in men ($r = 0.22$, $p = 0.005$).

Multivariate linear regression further confirmed these associations. Among female participants, both handgrip strength ($p<0.001$) and education ($p<0.001$) were independently associated with MMSE scores (Table 2). In male patients, handgrip strength ($p<0.05$), educational level ($p<0.001$), and presence of depression ($p<0.05$) were significant predictors of cognitive performance (Table 3).

Table 1. Patient characteristics[a]

	Total (n=352)	**Male (n=169; 48%)**	**Female (n=183; 52%)**	**p**
Age (years), mean (SE)	75.7 (7.2)	76.3 (7.3)	75.1 (7.2)	NS
Handgrip strength (kg), mean (SE)	19.1 (7.2)	23.7 (6.6)	14.9 (4.6)	<0.001
Probably sarcopenia n (%)*		114 (67.5%)	94 (51.4%)	<0.001
MMSE, mean (SE)	24.8 (3.9)	24.9 (4.1)	24.7 (3.7)	NS
Cognitive disorder (MMSE <24), n (%)	105 (29.8%)	47 (27.8%)	58 (31.7%)	NS
Body mass index (BMI) (kg/m²), mean (SE)	24.7 (4.6)	24.6 (4.2)	24.9 (5.0)	NS
Years of education (years), mean (SE)	9.7 (4.4)	10.4 (4.2)	9.2 (4.5)	<0.05
Malnutrition MNA SF score (<8); n(%)	112 (31.8)	58 (34.3)	54 (29.5%)	NS
Depression (criteria DSM IV), n (%)	52 (14.8%)	18 (10.7%)	34 (18.6)	NS
CIRS-G Total score >10, n (%)	28 (8.0)	12 (7.1%)	16 (8.7%)	NS
CIRS-G Total score mean (SD)	5.6 (3.1)	5.7 (2.9)	5.5 (3.2)	NS
Katz Index of ADL (score < 6/6), n (%)	101 (28.7%)	47 (27.8%)	54 (29.5%)	NS

[a] * – handgrip strength: <27 kg in men and <16 kg in women, SE – standard deviation, MMSE – Mini-Mental State Examination, CIRS-G – Cumulative Illness Rating Scale-Geriatric, ADL –Activities of Daily Living

Table 2. Correlation between hand grip strength and cognitive function in older adult patients living with cancer: adjusted multivariate regression analysis in female patients[a]

Variable	**Coefficient**	**95% Confidence**	**Limits**	**Std Error**	**F-test**	**p**
Handgrip strength (kg)	0.193	0.082	0.305	0.057	11.654	<0.001
Years of education	0.259	0.153	0.365	0.054	23.2714	<0.001
CIRS-G Total score	-0.285	-0.448	-0.122	0.082	11.9605	NS

Depression (criteria DSM IV) (True/False)	-1.598	-2.836	-0.36	0.627	6.4876	NS
Body mass index (BMI)	-0.065	-0.171	0.041	0.054	1.4605	NS
Malnutrition (MNA SF score <8)	0.027	-0.172	0.226	0.101	0.0726	NS

[a] CIRS-G Cumulative Illness Rating Scale-Geriatric

Table 3. Correlation between hand grip strength and cognitive function in older adult patients living with cancer: adjusted multivariate regression analysis in male patients[a]

Variable	Coefficient	95% Confidence	Limits	Std Error	F-test	p
Handgrip strength (kg)	0.114	0.03	0.198	0.042	7.2164	<0.05
Years of education	0.324	0.199	0.449	0.063	26.2789	<0.001
CIRS-G Total score	-0.145	-0.34	0.049	0.098	2.1793	NS
Depression (criteria DSM IV) (True/False)	-3.027	-4.816	-1.238	0.906	11.1642	<0.05
Body mass index (BMI)	0.046	-0.098	0.191	0.073	0.3985	NS
Malnutrition (MNA SF score <8)	0.164	-0.067	0.395	0.117	1.9682	NS

[a] CIRS-G Cumulative Illness Rating Scale-Geriatric

Discussion

In a cohort of older Peruvian adults with cancer, this study found a positive correlation between handgrip strength (HGS) and cognitive function. To our knowledge, this is the first investigation to examine this relationship in a Latin American population of geriatric oncology.

Although only one prior study has directly addressed this topic, carried out in the United States with the National Health and Nutrition Examination Survey (NHANES)[11] —our findings are largely consistent. That earlier study by Yang et al. demonstrated a significant link between muscle strength and cognitive outcomes, but only in female participants. In contrast, our analysis revealed a statistically significant correlation in both men and females, although the strength of the association was greater in females. Several methodological differences may explain the observed discrepancies. For example, Yang et al. used the Animal Fluency Test (AFT)[22] and the Digit Symbol Substitution Test (DSST)[23], which assess executive function and processing speed. Our study utilized the Mini-Mental State Examination (MMSE), which evaluates a broader set of cognitive domains. Moreover, the US study included only certain types of cancer (eg breast, prostate, colon, and cervical), while our cohort encompassed a wider variety of malignancies. The cut-off values for sarcopenia also varied; our study used the EWGSOP2 criteria (<27 kg for men, <16 kg for women), while Yang et al. applied higher thresholds. The stronger correlation observed in women may be partly explained by two key factors: a higher prevalence of probable sarcopenia and a lower average level of formal education compared to men. Both factors are known to influence cognitive vulnerability and reserve.

Previous research in non-cancer populations has also reported a consistent association between reduced grip strength and lower cognitive scores, particularly on the MMSE.[24] Some authors have suggested that HGS can serve as a clinical indicator of cognitive decline in older adults.[25] Physiologically, the link between muscle function and cognition may be mediated by mechanisms such as myokine release, inflammatory signaling, or neurovascular changes.[26,27,28,29] For example, individuals with lower HGS have been shown to exhibit higher volumes of cerebral white matter hyperintensities, commonly associated with cognitive impairment.[30] Additionally, studies have demonstrated that unilateral handgrip exercises can influence brain connectivity and reduce reaction times in the contralateral limb, possibly through increased cortical excitability and altered GABAergic inhibition. These findings support the hypothesis of a bidirectional "muscle-brain" interaction.[31]

Cognitive reserve, the brain's resilience against damage, is shaped by factors such as education, socioeconomic status and engagement in cognitive and physical activities.[32] In our sample, women had lower education levels and higher rates of sarcopenia, which can reflect a lower cognitive reserve compared to men. These characteristics, combined with an older average age and diverse cancer diagnoses, make this population particularly vulnerable to cognitive decline.[33]

Recognizing the association between HGS and cognition can have practical implications. Interventions that target muscle strength, such as resistance training, may not only enhance physical function but also support cognitive health in older cancer patients.

Study limitations

This study has several limitations that must be considered. First, its retrospective and observational design prevents the establishment of causality between handgrip strength and cognitive performance. Furthermore, we lacked baseline data on cognitive function or muscle strength before cancer diagnosis or treatment, which limits the ability to assess longitudinal changes. Inclusion of patients with various cancer types of cancers may have introduced heterogeneity, as different malignancies and treatment regimens could have differential impacts on cognitive and physical function. Lastly, information regarding specific cancer therapies received by participants (eg chemotherapy, radiotherapy, hormonal therapy) was not available, which could represent a confounding factor.

Conclusion

In general, the findings revealed a meaningful positive correlation between handgrip strength and cognitive performance in older people with cancer, indicating that lower muscle strength may be associated with diminished cognitive abilities in this group. Given that the strength of the handgrip is a modifiable factor, future prospective studies should explore whether targeted interventions to improve muscular function could also benefit cognitive outcomes. Incorporating routine grip strength into geriatric oncology practice may help identify patients at risk of cognitive decline and guide comprehensive care strategies.

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Declarations

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Author contributions

Conceptualization, T.J.O.; Methodology, R.R.O.; Validation, E.C.M.; Formal Analysis, T.J.O.; Investigation, E.C.M.; Resources, T.J.O.; Data Curation, E.C.M.; Writing – Original Draft Preparation, T.J.O.; Writing – Review & Editing, T.J.O. and R.R.O.; Visualization, T.J.O.; Supervision, R.R.O.; Project Administration, T.J.O.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Data availability

Due to institutional privacy regulations, the datasets used and analyzed in this study are not publicly accessible. Nevertheless, the corresponding author may provide them on a justified request and with the necessary ethical clearance.

Ethics approval

Ethical approval for this study was obtained from the Institutional Research Ethics Committee of Almenara Hospital in Lima, Peru (approval No. 80-CIEI-OIyD-GRPA-ESSALUD-2023; March 27, 2023). All data was managed in accordance with national ethical regulations.

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