International Journal of Research in Medical Sciences
Alyssa NI et al. Int J Res Med Sci. 2022 Dec;10(12):xxx-xxx
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms2022????

Review Article

Handgrip strength as an indicator of decreased cognitive function in the elderly

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Received: 03 November 2022
Accepted: 18 November 2022

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ABSTRACT

In the elderly, the aging process occurs which is associated with a decrease in several functions in the body, including cognitive function and musculoskeletal function. According to the Centers for Disease Control (CDC), 1 in 9 elderly's has decreased cognitive function. This decline in cognitive function is a form of cognitive dysfunction and is a precursor to the symptoms of Alzheimer's disease and other dementias. According to one study, the prevalence of people who were not detected for dementia because they had never undergone a cognitive examination was 61.7%. One of the possible causes is the absence of cognitive examinations in primary health facilities due to the unavailability of fast and easy instruments. Low hand grip strength has been associated with decreased cognitive function, and can be an effective indicator for early detection of cognitive impairment. In addition, hand grip strength can also be a predictor of decreased cognitive function in the elderly. The exact mechanism between decreased motor power and cognitive function is still unclear. Probably caused by the same cause like the presence of neuropathology in brain such as Lewy bodies, amyloid plaques, neurofibrillary tangles, infarction and atrophy.

Keywords: Hand grip strength, Cognitive function, Congitive impairment, Alzheimer's disease, Dementia, Geriatrics

INTRODUCTION

Elderly is someone who has reached the age of ≥60 years.[1] In Indonesia, the percentage of elderly reached 9.60 percent or around 25.64 million people in 2019. In 2021, the proportion of elderly reached 10.82 percent or around 29.3 million people.[2] In the elderly, the aging process is associated with a decrease in several functions in the body, including cognitive function and musculoskeletal function.[3, 4]

Cognitive function is divided into five, namely: attention, memory, language, visuospatial and executive functions.[6] The Mini Mental State Examination (MMSE), and the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina) are instruments that can be used to assess cognitive function.[7] According to the CDC, the prevalence of cognitive decline in the elderly is 11.7%. That is, 1 in 9 elderly experience a decline in cognitive function. This decline in cognitive function is a form of impaired cognitive function and is the beginning of symptoms of Alzheimer's disease and other dementias.[8] Decreased cognitive function has experienced neuropsychiatric symptoms and decreased quality of life in the elderly.[9]

Therefore, it is important to investigate severe cognitive decline problems such as dementia from an early stage. It aims to identify any curable conditions and use appropriate medical treatment.[10]

A previous studies demonstrated that in the population, the prevalence of undetected dementia was quite high at

61.7%. One of the possible reasons is that there is no cognitive examination at primary health facilities.[11] This is because MMSE and MoCA assessments require special skills, and training is required to conduct assessments.[7,12] Therefore we need an easier way to measure cognitive function of individuals. If the results of the measurement of cognitive function have been obtained, then treatment can be carried out on individuals with dementia and mild cognitive decline.[13]

There is a relationship between the decline in cognitive function in the elderly with dementia and the occurrence of motor weakness.[14] In more detail, it was demonstrated that motor decline increased rapidly up to 12 years before the onset of cognitive decline or mild cognitive impairment (MCI). In more detail it was demonstrated that motor decline increased rapidly up to 12 years before the onset of cognitive decline or MCI. Thus, the rate of change in motor impairment such as decreased muscle strength can be used to identify individuals who are at risk of developing dementia.[15]

Measurement of muscle strength can be done by measuring hand grip strength using a handheld dynamometer.[16] The advantages of hand-held dynamometers include: inexpensive, easy to carry, non-invasive, fast, reliable, and does not require extensive training to use. Regarding the measurement of handgrip strength in dementia patients with MCI, several studies have shown that the use of a hand-held dynamometer has low variability and high reliability.[17,18]

Based on the foregoing, the decline in cognitive function many go undetected. This is because primary health facilities, including Pos Pelayanan Terpadu (Posyandu), are not involved enough to detect it. There are interesting questions, among others, that it can be a handgrip as an indicator or predictor of cognitive function decline in the elderly. In addition, it is also questionable how the relationship between handgrip strength and cognitive function decline in the elderly.

Furthermore, it is questionable how the mechanisms of decline in cognitive function and handgripth strength in the elderly. Therefore, this review specifically aims to discuss the relationship between handgripth strength and decreased cognitive function in the elderly.

COGNITIVE FUNCTION AND THE ELDERLY IN INDONESIA

There are three levels in human processing information, namely sensation, perception and cognition. Sensation is a direct result of stimulation received from sensory neurons, whereas perception involves the organization and awareness of the sensation. Cognition is a set of interrelated processes, such as memory, language, and problem solving, which will produce structures and strategies that will be applied to perception.[19] Cognitive function is a higher function of the brain to obtain information and is usually related to individual perceptual abilities, memory, language, thinking, reasoning, and awareness.[5]

The elderly in Indonesia increasing year by year. It has been reported that in 2019, the number of elderly people in Indonesia was around 25.64 million, while in 2021 it increased to 29.3 million people. This figure indicates that Indonesia has entered a phase of aging population structure, which is characterized by the proportion of the population aged 60 years and over in Indonesia that has exceeded 10% of the total population. The characteristics of the elderly in Indonesia are dominated by the young elderly with a percentage of 63.82%, followed by the middle-aged elderly at 27.68%, and the elderly at 8.50%.[2]

AGING, MOTOR CONTROL, AND COGNITIVE FUNCTION

As we get older, there are decreases in control and sensorimotor function. Decreased fine motor control, gait (attitude/way of walking) and balance affect their daily activities and independence. The cause of motor deficits in elderly is multifactorial. Among them are the involvement of a decrease in the central nervous system and changes in sensory receptors, muscles, and peripheral nerves.[20] Some changes in cognition appear in the normal aging process. The most important change is the decline in cognitive tasks that require speed in processing and information to make decisions. These include speed of processing, working memory and executive cognitive function.[3]

The cause of declining cognitive function and motor function in the elderly is still unclear. It is possible that neuropathology is the cause of decreased cognitive function as well as motor function in the elderly. The report is in line with the results of research that shows that in the elderly with dementia, several neuropathologies are found that can cause a decline in cognitive and motor function. Moreover, it is also reported that 80-90% of cases of Alzheimer's disease are found pathological lesions on post mortem examination. Pathological lesions found are neurofibrillary tangles (NFTs) and amyloid plaques.[14] NFTs consist of hyperphosphorylated tau proteins (PHF-tau).[21]

Amyloid plaques are caused due to the aggregation of amyloid beta peptide (Aβ) produced by the cleavage of the amyloid precursor protein (APP) due to the proteolytic action of β and γ secretions. In normal processing, what the APP involves is α and γ secretage. On the Aβ-amyloid hypothesis, it is explained that these amyloid plaques can cause synaptotoxicity and neurotoxicity that can proceed into neurodegeneration.

Neurodegeneration in Alzheimer's patients is characterized by deposits of Aβ-proteins of neuron death in large numbers and atrophy of neurons that can lead to the appearance of deficits.[22] The neuropathology also accumulates in the parts of the brain that regulate the

motor, such as the motor cortex, the striatum and also the substantia nigra. This can lead to decreased motor function characterized by muscle weakness.[14]

In vascular dementia, neuropathologies caused by blood vessels are found, one of which is infarction.[23] This infarction causes reduced blood flow to the brain so that symptoms such as forgetfulness, slowing down of thought processes and also motor skills. In vascular dementia, the incidence of chronic hypoperfusion and thromboembolism, causes a decrease in blood flow to the brain, hypoxia, oxidative stress and triggers an inflammatory response. The periventricular alba substantia, basal ganglia, and hippocampus are particularly susceptible to hypoperfusion-induced lesions. This disruption of the prefrontal-basal ganglia circuit causes cognitive deficits in vascular dementia.[24] It is well known that this disorder can also cause deficits in motor function.[25]

Dementia with lewy bodies is pathologically characterized by abnormal aggregation of α-synuclein synapse proteins called 'lewy bodies' in neurons and is associated with brain atrophy.[23] Lewy bodies can cause decreased cognitive and motor functions.[25] Another dementia, namely frontotemporal dementia, is found to have atrophy in the frontal and temporal lobes. This atrophy of certain lobes contrasts with diffusely occurring Alzheimer's disease.

In addition to atrophy, neuronal loss and gliosis were also found, vacuolization of the superficial cortex (spongiosis) and ballooned neurons.[23] Frontotemporal dementia is characterized by the appearance of a decrease in various aspects, including behavior, language and motor function.[26]

DISCUSSION

The strength of the hand grip is thought to be an indicator of cognitive function decline in the elderly.[27-29] Several studies have shown a positive relationship between the strength of the hand grip and cognitive function.[7,25,60] These studies were conducted by calculating the strength of the hand grip using a hand grip dynamometer and measuring cognitive function with instruments such as MMSE and MoCA.[31,34]

Research by McGrath et al showed that every 5 kg decrease in hand grip strength is associated with a 1.10 times the likelihood of a decrease in cognitive function (Table 1).[27] The results of another study demonstrated that weak hand grip strength was associated with a 1.41 times higher probability of MCI occurring. The prevalence of MCI was also found to be high among subjects with low hand grip strength (Table 2).[29] The results of the study are in line with the results of research that shows that physical fraility such as weak hand grip strength is associated with a decrease in cognitive function.[32]

Several studies have shown that a decrease in the strength of the hand grip precedes a decrease in cognitive function.[28,31,34] Likewise, it has been demonstrated that low hand grip strength initiates a decline in cognitive function.[29] It was also demonstrated that the low strength of the hand grip was related to the low MMSE score 4 years later (Table 3).[32] This is supported by a report stating that the discovery of severe dementia neuropathology in post mortem examinations in patients with signs of initial motor weakness without a decline in cognitive function.[25] The results of this study show that a decrease in the strength of the hand grip can predict the decline of cognitive function in the future.

Table 1: The relationship of low strength of hand grips with cognitive function.[27]

Handgrip strength (5 kg lower)	Odds ratio	95% CI	
	1.10	1.04	1.15

Table 2. The relationship between weak grip strength and cognitive function.[29]

Characteristics	OR total	OR (age 50-64 years)	OR (age>65 years)
Weak handgrip strength	1.14***	1.35***	1.54
Age (years)	1.01**	1.02	1.04***
No. of chronic diseases	1.20***	1.24***	1.17***
Low physical activity	1.24**	0.85	1.70**

Note: OR= Odds ratio;*-p<0.05; **-p<0.01; ***-p<0.001.

Table 3: Relationship between measurements and MMSE scores in 4-year follow-ups.[32]

Handgrip strength (kg)	Men	Women
	Unadjusted difference of MMSE score (95% CI) per unit change	
	0.448 **	0.358 **

Note: MMSE score= Mini mental state examination; *-p<0.01; **-p<0.001.

The occurrence of a decline in cognitive function is still unclear, but it is possible that neuropathology in the brain is one of the causes. It has been explained that skilled hand skills and control of handgrip strength involves not only cortical motor areas of the brain, but also higher cognitive performance. This can be seen from the activity in the frontal and parietal cortical areas of brain imaging. The results showed that the complexity of movement and coordination tasks is related to improving cognitive control. It has been proven that the frontal lobe area in healthy elderly has more activity than the unhealthy elderly.[35] The results of the study are in accordance with the theory of the occurrence of atrophy in the frontal lobe in fronto-temporal dementia which can cause a decrease in motor and cognitive functions.[26]

The results of previous studies demonstrated that the results of post-mortem examination of patients with gait impairment were found to be the presence of NFTs in the substantia nigra.[36] The results of this study are in accordance with the theory that the neuropathology of Alzheimer's disease, namely NFTs, can cause neurodegeneration, and if present in susbtansia nigra, it can cause weakness in motor function.[14] In addition, NFTs were also found in patients experiencing gait impairment with subcortical vascular dementia.[37] This result is similar to the theory that ischemia can cause problems with motor function.[25]

The results of previous studies have shown that young and healthy individuals have higher muscle strength compared to the elderly, this is because young individuals have higher testosterone levels than the elderly. This fact is supported by data that shows that during the aging process testosterone deficiency occurs. Decreased muscle strength in elderly is associated with a decrease in testosterone levels.[38]

The results of the study are in line with the results of a study that showed that total testosterone levels were negatively correlated with age.[39] With respect to testosterone levels within the circulation, only free testosterone is available for use by target cells with intermediary sex hormone binding globulin (SHBG).[40,41] It has been demonstrated that SHBG levels in cerebrospinal fluid correlate with decreased cognitive function.[42] Although in the population there is a polymorphism of SHBG, but the results of previous studies have shown that the polymorphism of the SHBG molecule does not affect testosterone levels in circulation.[43] Therefore, we argue that SHBG levels in cerebrospinal fluid are more important than the polymorphism of SHBG molecules in circulation. It is important to note that high levels of SHBG in the circulatory system decrease the bioavailability of testosterone. Therefore, it is necessary to strive so that SHBG levels in the circulation system are in a normal constellation, so that bioavailable testosterone remains high. This opinion is based onour research showing that isoflavone supplementation for the elderly for 6 months reduced SHBG levels by 31.1%.[44]

Other research results show that there is a correlation between testosterone concentration and handgrip strength. It was also shown that the strength of handgrip in the group of non-obese individuals was higher than that of obese individuals.[45] To keep handgrip strength strong, and cognitive function good, it is necessary to strive for a better quality of life for the elderly, for example by paying attention to nutritional intake. A good intake of nutrients will maintain the ideal body mass index. In addition, good nutrient intake also keeps muscle mass, handgrip strength, and cognitive function good. This is in accordance with research that shows that subjects with a BMI of <18.5 kg/m^2 actually have a low intake of macronutrients (proteins, fats, and carbohydrates), resulting in chronic energy deficiency with a low status.[46]

CONCLUSION

Low handgrip strength has been associated with decreased cognitive function in the elderly. Handgrip strength can be an indicator for early detection of cognitive impairment in the elderly. The exact mechanism between the decline in motor strength underlying the decline in handgrip strength and the decline in cognitive function in the elderly remains unclear. The occurrence of neuropathologies such as lewy bodies, amyloid plaques, neurofibrillary tangles, infarction and atrophy of the brain may be the cause of decreased cognitive function in the elderly.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Alyssa NI, Parwanto E. Handgrip strength as an indicator of decreased cognitive function in the elderly. Int J Res Med Sci 2022;10:xxx-xx.

Provide department of highlighted affiliation, if any. Provide highlighted reference (reference no. 60 mentioned).

International Journal of Research in Medical Sciences
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www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

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Accepted: 18 November 2022

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The elderly in Indonesia increasing year by year. It has been reported that in 2019, the number of elderly people in Indonesia was around 25.64 million, while in 2021 it increased to 29.3 million people. This figure indicates that Indonesia has entered a phase of aging population structure, which is characterized by the proportion of the population aged 60 years and over in Indonesia that has exceeded 10% of the total population. The characteristics of the elderly in Indonesia are dominated by the young elderly with a percentage of 63.82%, followed by the middle-aged elderly at 27.68%, and the elderly at 8.50%.[2]

AGING, MOTOR CONTROL, AND COGNITIVE FUNCTION

As we get older, there are decreases in control and sensorimotor function. Decreased fine motor control, gait (attitude/way of walking) and balance affect their daily activities and independence. The cause of motor deficits in elderly is multifactorial. Among them are the involvement of a decrease in the central nervous system and changes in sensory receptors, muscles, and peripheral nerves.[20] Some changes in cognition appear in the normal aging process. The most important change is the decline in cognitive tasks that require speed in processing and information to make decisions. These include speed of processing, working memory and executive cognitive function.[3]

The cause of declining cognitive function and motor function in the elderly is still unclear. It is possible that neuropathology is the cause of decreased cognitive function as well as motor function in the elderly. The report is in line with the results of research that shows that in the elderly with dementia, several neuropathologies are found that can cause a decline in cognitive and motor function. Moreover, it is also reported that 80-90% of cases of Alzheimer's disease are found pathological lesions on post mortem examination. Pathological lesions found are neurofibrillary tangles (NFTs) and amyloid plaques.[14] NFTs consist of hyperphosphorylated tau proteins (PHF-tau).[21]

Amyloid plaques are caused due to the aggregation of amyloid beta peptide (Aβ) produced by the cleavage of the amyloid precursor protein (APP) due to the proteolytic action of β and γ secretions. In normal processing, what the APP involves is α and γ secretage. On the Aβ-amyloid hypothesis, it is explained that these amyloid plaques can cause synaptotoxicity and neurotoxicity that can proceed into neurodegeneration.

Neurodegeneration in Alzheimer's patients is characterized by deposits of Aβ-proteins of neuron death in large numbers and atrophy of neurons that can lead to the appearance of deficits.[22] The neuropathology also accumulates in the parts of the brain that regulate the

motor, such as the motor cortex, the striatum and also the substantia nigra. This can lead to decreased motor function characterized by muscle weakness.[14]

In vascular dementia, neuropathologies caused by blood vessels are found, one of which is infarction.[23] This infarction causes reduced blood flow to the brain so that symptoms such as forgetfulness, slowing down of thought processes and also motor skills. In vascular dementia, the incidence of chronic hypoperfusion and thromboembolism, causes a decrease in blood flow to the brain, hypoxia, oxidative stress and triggers an inflammatory response. The periventricular alba substantia, basal ganglia, and hippocampus are particularly susceptible to hypoperfusion-induced lesions. This disruption of the prefrontal-basal ganglia circuit causes cognitive deficits in vascular dementia.[24] It is well known that this disorder can also cause deficits in motor function.[25]

Dementia with lewy bodies is pathologically characterized by abnormal aggregation of α-synuclein synapse proteins called 'lewy bodies' in neurons and is associated with brain atrophy.[23] Lewy bodies can cause decreased cognitive and motor functions.[25] Another dementia, namely frontotemporal dementia, is found to have atrophy in the frontal and temporal lobes. This atrophy of certain lobes contrasts with diffusely occurring Alzheimer's disease.

In addition to atrophy, neuronal loss and gliosis were also found, vacuolization of the superficial cortex (spongiosis) and ballooned neurons.[23] Frontotemporal dementia is characterized by the appearance of a decrease in various aspects, including behavior, language and motor function.[26]

DISCUSSION

The strength of the hand grip is thought to be an indicator of cognitive function decline in the elderly.[27-29] Several studies have shown a positive relationship between the strength of the hand grip and cognitive function.[7,25,60] These studies were conducted by calculating the strength of the hand grip using a hand grip dynamometer and measuring cognitive function with instruments such as MMSE and MoCA.[31,34]

Research by McGrath et al showed that every 5 kg decrease in hand grip strength is associated with a 1.10 times the likelihood of a decrease in cognitive function (Table 1).[27] The results of another study demonstrated that weak hand grip strength was associated with a 1.41 times higher probability of MCI occurring. The prevalence of MCI was also found to be high among subjects with low hand grip strength (Table 2).[29] The results of the study are in line with the results of research that shows that physical fraility such as weak hand grip strength is associated with a decrease in cognitive function.[32]

Several studies have shown that a decrease in the strength of the hand grip precedes a decrease in cognitive function.[28,31,34] Likewise, it has been demonstrated that low hand grip strength initiates a decline in cognitive function.[29] It was also demonstrated that the low strength of the hand grip was related to the low MMSE score 4 years later (Table 3).[32] This is supported by a report stating that the discovery of severe dementia neuropathology in post mortem examinations in patients with signs of initial motor weakness without a decline in cognitive function.[25] The results of this study show that a decrease in the strength of the hand grip can predict the decline of cognitive function in the future.

Table 1: The relationship of low strength of hand grips with cognitive function.[27]

Handgrip strength (5 kg lower)	Odds ratio	95% CI	
	1.10	1.04	1.15

Table 2. The relationship between weak grip strength and cognitive function.[29]

Characteristics	OR total	OR (age 50-64 years)	OR (age>65 years)
Weak handgrip strength	1.14***	1.35***	1.54
Age (years)	1.01**	1.02	1.04***
No. of chronic diseases	1.20***	1.24***	1.17***
Low physical activity	1.24**	0.85	1.70**

Note: OR= Odds ratio;*-p<0.05; **-p<0.01; ***-p<0.001.

Table 3: Relationship between measurements and MMSE scores in 4-year follow-ups.[32]

Handgrip strength (kg)	Men	Women
	Unadjusted difference of MMSE score (95% CI) per unit change	
	0.448 **	0.358 **

Note: MMSE score= Mini mental state examination; *-p<0.01; **-p<0.001.

The occurrence of a decline in cognitive function is still unclear, but it is possible that neuropathology in the brain is one of the causes. It has been explained that skilled hand skills and control of handgrip strength involves not only cortical motor areas of the brain, but also higher cognitive performance. This can be seen from the activity in the frontal and parietal cortical areas of brain imaging. The results showed that the complexity of movement and coordination tasks is related to improving cognitive control. It has been proven that the frontal lobe area in healthy elderly has more activity than the unhealthy elderly.[35] The results of the study are in accordance with the theory of the occurrence of atrophy in the frontal lobe in fronto-temporal dementia which can cause a decrease in motor and cognitive functions.[26]

The results of previous studies demonstrated that the results of post-mortem examination of patients with gait impairment were found to be the presence of NFTs in the substantia nigra.[36] The results of this study are in accordance with the theory that the neuropathology of Alzheimer's disease, namely NFTs, can cause neurodegeneration, and if present in susbtansia nigra, it can cause weakness in motor function.[14] In addition, NFTs were also found in patients experiencing gait impairment with subcortical vascular dementia.[37] This result is similar to the theory that ischemia can cause problems with motor function.[25]

The results of previous studies have shown that young and healthy individuals have higher muscle strength compared to the elderly, this is because young individuals have higher testosterone levels than the elderly. This fact is supported by data that shows that during the aging process testosterone deficiency occurs. Decreased muscle strength in elderly is associated with a decrease in testosterone levels.[38]

The results of the study are in line with the results of a study that showed that total testosterone levels were negatively correlated with age.[39] With respect to testosterone levels within the circulation, only free testosterone is available for use by target cells with intermediary sex hormone binding globulin (SHBG).[40,41] It has been demonstrated that SHBG levels in cerebrospinal fluid correlate with decreased cognitive function.[42] Although in the population there is a polymorphism of SHBG, but the results of previous studies have shown that the polymorphism of the SHBG molecule does not affect testosterone levels in circulation.[43] Therefore, we argue that SHBG levels in cerebrospinal fluid are more important than the polymorphism of SHBG molecules in circulation. It is important to note that high levels of SHBG in the circulatory system decrease the bioavailability of testosterone. Therefore, it is necessary to strive so that SHBG levels in the circulation system are in a normal constellation, so that bioavailable testosterone remains high. This opinion is based onour research showing that isoflavone supplementation for the elderly for 6 months reduced SHBG levels by 31.1%.[44]

Other research results show that there is a correlation between testosterone concentration and handgrip strength. It was also shown that the strength of handgrip in the group of non-obese individuals was higher than that of obese individuals.[45] To keep handgrip strength strong, and cognitive function good, it is necessary to strive for a better quality of life for the elderly, for example by paying attention to nutritional intake. A good intake of nutrients will maintain the ideal body mass index. In addition, good nutrient intake also keeps muscle mass, handgrip strength, and cognitive function good. This is in accordance with research that shows that subjects with a BMI of <18.5 kg/m^2 actually have a low intake of macronutrients (proteins, fats, and carbohydrates), resulting in chronic energy deficiency with a low status.[46]

CONCLUSION

Low handgrip strength has been associated with decreased cognitive function in the elderly. Handgrip strength can be an indicator for early detection of cognitive impairment in the elderly. The exact mechanism between the decline in motor strength underlying the decline in handgrip strength and the decline in cognitive function in the elderly remains unclear. The occurrence of neuropathologies such as lewy bodies, amyloid plaques, neurofibrillary tangles, infarction and atrophy of the brain may be the cause of decreased cognitive function in the elderly.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Alyssa NI, Parwanto E. Handgrip strength as an indicator of decreased cognitive function in the elderly. Int J Res Med Sci 2022;10:xxx-xx.

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Review Article

Handgrip strength as an indicator of decreased cognitive function in the elderly

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Received: 03 November 2022
Accepted: 18 November 2022

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ABSTRACT

In the elderly, the aging process occurs which is associated with a decrease in several functions in the body, including cognitive function and musculoskeletal function. According to the Centers for Disease Control (CDC), 1 in 9 elderly's has decreased cognitive function. This decline in cognitive function is a form of cognitive dysfunction and is a precursor to the symptoms of Alzheimer's disease and other dementias. According to one study, the prevalence of people who were not detected for dementia because they had never undergone a cognitive examination was 61.7%. One of the possible causes is the absence of cognitive examinations in primary health facilities due to the unavailability of fast and easy instruments. Low hand grip strength has been associated with decreased cognitive function, and can be an effective indicator for early detection of cognitive impairment. In addition, hand grip strength can also be a predictor of decreased cognitive function in the elderly. The exact mechanism between decreased motor power and cognitive function is still unclear. Probably caused by the same cause like the presence of neuropathology in brain such as Lewy bodies, amyloid plaques, neurofibrillary tangles, infarction and atrophy.

Keywords: Hand grip strength, Cognitive function, Congitive impairment, Alzheimer's disease, Dementia, Geriatrics

INTRODUCTION

Elderly is someone who has reached the age of ≥60 years.[1] In Indonesia, the percentage of elderly reached 9.60 percent or around 25.64 million people in 2019. In 2021, the proportion of elderly reached 10.82 percent or around 29.3 million people.[2] In the elderly, the aging process is associated with a decrease in several functions in the body, including cognitive function and musculoskeletal function.[3-5]

Cognitive function is divided into five, namely: attention, memory, language, visuospatial and executive functions.[6] The Mini Mental State Examination (MMSE), and the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina) are instruments that can be used to assess cognitive function.[7] According to the CDC, the prevalence of cognitive decline in the elderly is 11.7%. That is, 1 in 9 elderly experience a decline in cognitive function. This decline in cognitive function is a form of impaired cognitive function and is the beginning of symptoms of Alzheimer's disease and other dementias.[8] Decreased cognitive function has experienced neuropsychiatric symptoms and decreased quality of life in the elderly.[9]

Therefore, it is important to investigate severe cognitive decline problems such as dementia from an early stage. It aims to identify any curable conditions and use appropriate medical treatment.[10]

A previous studies demonstrated that in the population, the prevalence of undetected dementia was quite high at

61.7%. One of the possible reasons is that there is no cognitive examination at primary health facilities.[11] This is because MMSE and MoCA assessments require special skills, and training is required to conduct assessments.[7,12] Therefore we need an easier way to measure cognitive function of individuals. If the results of the measurement of cognitive function have been obtained, then treatment can be carried out on individuals with dementia and mild cognitive decline.[13]

There is a relationship between the decline in cognitive function in the elderly with dementia and the occurrence of motor weakness.[14] In more detail, it was demonstrated that motor decline increased rapidly up to 12 years before the onset of cognitive decline or mild cognitive impairment (MCI). In more detail it was demonstrated that motor decline increased rapidly up to 12 years before the onset of cognitive decline or MCI. Thus, the rate of change in motor impairment such as decreased muscle strength can be used to identify individuals who are at risk of developing dementia.[15]

Measurement of muscle strength can be done by measuring hand grip strength using a handheld dynamometer.[16] The advantages of hand-held dynamometers include: inexpensive, easy to carry, non-invasive, fast, reliable, and does not require extensive training to use. Regarding the measurement of handgrip strength in dementia patients with MCI, several studies have shown that the use of a hand-held dynamometer has low variability and high reliability.[17,18]

Based on the foregoing, the decline in cognitive function many go undetected. This is because primary health facilities, including Pos Pelayanan Terpadu (Posyandu), are not involved enough to detect it. There are interesting questions, among others, that it can be a handgrip as an indicator or predictor of cognitive function decline in the elderly. In addition, it is also questionable how the relationship between handgrip strength and cognitive function decline in the elderly.

Furthermore, it is questionable how the mechanisms of decline in cognitive function and handgripth strength in the elderly. Therefore, this review specifically aims to discuss the relationship between handgripth strength and decreased cognitive function in the elderly.

COGNITIVE FUNCTION AND THE ELDERLY IN INDONESIA

There are three levels in human processing information, namely sensation, perception and cognition. Sensation is a direct result of stimulation received from sensory neurons, whereas perception involves the organization and awareness of the sensation. Cognition is a set of interrelated processes, such as memory, language, and problem solving, which will produce structures and strategies that will be applied to perception.[19] Cognitive function is a higher function of the brain to obtain information and is usually related to individual perceptual abilities, memory, language, thinking, reasoning, and awareness.[5]

The elderly in Indonesia increasing year by year. It has been reported that in 2019, the number of elderly people in Indonesia was around 25.64 million, while in 2021 it increased to 29.3 million people. This figure indicates that Indonesia has entered a phase of aging population structure, which is characterized by the proportion of the population aged 60 years and over in Indonesia that has exceeded 10% of the total population. The characteristics of the elderly in Indonesia are dominated by the young elderly with a percentage of 63.82%, followed by the middle-aged elderly at 27.68%, and the elderly at 8.50%.[2]

AGING, MOTOR CONTROL, AND COGNITIVE FUNCTION

As we get older, there are decreases in control and sensorimotor function. Decreased fine motor control, gait (attitude/way of walking) and balance affect their daily activities and independence. The cause of motor deficits in elderly is multifactorial. Among them are the involvement of a decrease in the central nervous system and changes in sensory receptors, muscles, and peripheral nerves.[20] Some changes in cognition appear in the normal aging process. The most important change is the decline in cognitive tasks that require speed in processing and information to make decisions. These include speed of processing, working memory and executive cognitive function.[3]

The cause of declining cognitive function and motor function in the elderly is still unclear. It is possible that neuropathology is the cause of decreased cognitive function as well as motor function in the elderly. The report is in line with the results of research that shows that in the elderly with dementia, several neuropathologies are found that can cause a decline in cognitive and motor function. Moreover, it is also reported that 80-90% of cases of Alzheimer's disease are found pathological lesions on post mortem examination. Pathological lesions found are neurofibrillary tangles (NFTs) and amyloid plaques.[14] NFTs consist of hyperphosphorylated tau proteins (PHF-tau).[21]

Amyloid plaques are caused due to the aggregation of amyloid beta peptide (Aβ) produced by the cleavage of the amyloid precursor protein (APP) due to the proteolytic action of β and γ secretions. In normal processing, what the APP involves is α and γ secretage. On the Aβ-amyloid hypothesis, it is explained that these amyloid plaques can cause synaptotoxicity and neurotoxicity that can proceed into neurodegeneration.

Neurodegeneration in Alzheimer's patients is characterized by deposits of Aβ-proteins of neuron death in large numbers and atrophy of neurons that can lead to the appearance of deficits.[22] The neuropathology also accumulates in the parts of the brain that regulate the

motor, such as the motor cortex, the striatum and also the substantia nigra. This can lead to decreased motor function characterized by muscle weakness.[14]

In vascular dementia, neuropathologies caused by blood vessels are found, one of which is infarction.[23] This infarction causes reduced blood flow to the brain so that symptoms such as forgetfulness, slowing down of thought processes and also motor skills. In vascular dementia, the incidence of chronic hypoperfusion and thromboembolism, causes a decrease in blood flow to the brain, hypoxia, oxidative stress and triggers an inflammatory response. The periventricular alba substantia, basal ganglia, and hippocampus are particularly susceptible to hypoperfusion-induced lesions. This disruption of the prefrontal-basal ganglia circuit causes cognitive deficits in vascular dementia.[24] It is well known that this disorder can also cause deficits in motor function.[25]

Dementia with lewy bodies is pathologically characterized by abnormal aggregation of α-synuclein synapse proteins called 'lewy bodies' in neurons and is associated with brain atrophy.[23] Lewy bodies can cause decreased cognitive and motor functions.[25] Another dementia, namely frontotemporal dementia, is found to have atrophy in the frontal and temporal lobes. This atrophy of certain lobes contrasts with diffusely occurring Alzheimer's disease.

In addition to atrophy, neuronal loss and gliosis were also found, vacuolization of the superficial cortex (spongiosis) and ballooned neurons.[23] Frontotemporal dementia is characterized by the appearance of a decrease in various aspects, including behavior, language and motor function.[26]

DISCUSSION

The strength of the hand grip is thought to be an indicator of cognitive function decline in the elderly.[27-29] Several studies have shown a positive relationship between the strength of the hand grip and cognitive function.[7,30,31] These studies were conducted by calculating the strength of the hand grip using a hand grip dynamometer and measuring cognitive function with instruments such as MMSE and MoCA.[32-34]

Research by McGrath et al showed that every 5 kg decrease in hand grip strength is associated with a 1.10 times the likelihood of a decrease in cognitive function (Table 1).[27] The results of another study demonstrated that weak hand grip strength was associated with a 1.41 times higher probability of MCI occurring. The prevalence of MCI was also found to be high among subjects with low hand grip strength (Table 2).[29] The results of the study are in line with the results of research that shows that physical frailty such as weak hand grip strength is associated with a decrease in cognitive function.[32]

Several studies have shown that a decrease in the strength of the hand grip precedes a decrease in cognitive function.[28,31,34] Likewise, it has been demonstrated that low hand grip strength initiates a decline in cognitive function.[29] It was also demonstrated that the low strength of the hand grip was related to the low MMSE score 4 years later (Table 3).[32] This is supported by a report stating that the discovery of severe dementia neuropathology in post mortem examinations in patients with signs of initial motor weakness without a decline in cognitive function.[25] The results of this study show that a decrease in the strength of the hand grip can predict the decline of cognitive function in the future.

Table 1: The relationship of low strength of hand grips with cognitive function.[27]

Handgrip strength (5 kg lower)	Odds ratio	95% CI	
	1.10	1.04	1.15

Table 2. The relationship between weak grip strength and cognitive function.[29]

Characteristics	OR total	OR (age 50-64 years)	OR (age>65 years)
Weak handgrip strength	1.14***	1.35***	1.54
Age (years)	1.01**	1.02	1.04***
No. of chronic diseases	1.20***	1.24***	1.17***
Low physical activity	1.24**	0.85	1.70**

Note: OR= Odds ratio;*-p<0.05; **-p<0.01; ***-p<0.001.

Table 3: Relationship between measurements and MMSE scores in 4-year follow-ups.[32]

Handgrip strength (kg)	Men	Women
	Unadjusted difference of MMSE score (95% CI) per unit change	
	0.448 **	0.358 **

Note: MMSE score= Mini mental state examination; *-p<0.01; **-p<0.001.

The occurrence of a decline in cognitive function is still unclear, but it is possible that neuropathology in the brain is one of the causes. It has been explained that skilled hand skills and control of handgrip strength involves not only cortical motor areas of the brain, but also higher cognitive performance. This can be seen from the activity in the frontal and parietal cortical areas of brain imaging. The results showed that the complexity of movement and coordination tasks is related to improving cognitive control. It has been proven that the frontal lobe area in healthy elderly has more activity than the unhealthy elderly.[35] The results of the study are in accordance with the theory of the occurrence of atrophy in the frontal lobe in fronto-temporal dementia which can cause a decrease in motor and cognitive functions.[26]

The results of previous studies demonstrated that the results of post-mortem examination of patients with gait impairment were found to be the presence of NFTs in the substantia nigra.[36] The results of this study are in accordance with the theory that the neuropathology of Alzheimer's disease, namely NFTs, can cause neurodegeneration, and if present in susbtansia nigra, it can cause weakness in motor function.[14] In addition, NFTs were also found in patients experiencing gait impairment with subcortical vascular dementia.[37] This result is similar to the theory that ischemia can cause problems with motor function.[25]

The results of previous studies have shown that young and healthy individuals have higher muscle strength compared to the elderly, this is because young individuals have higher testosterone levels than the elderly. This fact is supported by data that shows that during the aging process testosterone deficiency occurs. Decreased muscle strength in elderly is associated with a decrease in testosterone levels.[38]

The results of the study are in line with the results of a study that showed that total testosterone levels were negatively correlated with age.[39] With respect to testosterone levels within the circulation, only free testosterone is available for use by target cells with intermediary sex hormone binding globulin (SHBG).[40,41] It has been demonstrated that SHBG levels in cerebrospinal fluid correlate with decreased cognitive function.[42] Although in the population there is a polymorphism of SHBG, but the results of previous studies have shown that the polymorphism of the SHBG molecule does not affect testosterone levels in circulation.[43] Therefore, we argue that SHBG levels in cerebrospinal fluid are more important than the polymorphism of SHBG molecules in circulation. It is important to note that high levels of SHBG in the circulatory system decrease the bioavailability of testosterone. Therefore, it is necessary to strive so that SHBG levels in the circulation system are in a normal constellation, so that bioavailable testosterone remains high. This opinion is based onour research showing that isoflavone supplementation for the elderly for 6 months reduced SHBG levels by 31.1%.[44]

Other research results show that there is a correlation between testosterone concentration and handgrip strength. It was also shown that the strength of handgrip in the group of non-obese individuals was higher than that of obese individuals.[45] To keep handgrip strength strong, and cognitive function good, it is necessary to strive for a better quality of life for the elderly, for example by paying attention to nutritional intake. A good intake of nutrients will maintain the ideal body mass index. In addition, good nutrient intake also keeps muscle mass, handgrip strength, and cognitive function good. This is in accordance with research that shows that subjects with a BMI of <18.5 kg/m^2 actually have a low intake of macronutrients (proteins, fats, and carbohydrates), resulting in chronic energy deficiency with a low status.[46]

CONCLUSION

Low handgrip strength has been associated with decreased cognitive function in the elderly. Handgrip strength can be an indicator for early detection of cognitive impairment in the elderly. The exact mechanism between the decline in motor strength underlying the decline in handgrip strength and the decline in cognitive function in the elderly remains unclear. The occurrence of neuropathologies such as lewy bodies, amyloid plaques, neurofibrillary tangles, infarction and atrophy of the brain may be the cause of decreased cognitive function in the elderly.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Alyssa NI, Parwanto E. Handgrip strength as an indicator of decreased cognitive function in the elderly. Int J Res Med Sci 2022;10:2978-83.