

EFFECTIVENESS OF AEROBIC EXERCISE ON COGNITIVE FUNCTION IN MILD COGNITIVE IMPAIRMENT PATIENTS

Original Article

Muhammad Adnan Aslam^{1*}, Junaid ur Rehman², Muhammad Junaid Munir², Amna Tariq²

¹Associate Professor Neurology, SIMS / Services Hospital, Lahore, Pakistan.

²Registrar, Department of Neurology, SIMS / Services Hospital, Lahore, Pakistan.

Corresponding Author: Muhammad Adnan Aslam, Associate Professor, SIMS / Services Hospital, Lahore, Pakistan, dradnan.aslam@yahoo.com

Conflict of Interest: None

Grant Support & Financial Support: None

Acknowledgment: The authors gratefully acknowledge the participants for their time and commitment.

ABSTRACT

Background: Mild cognitive impairment (MCI) is a transitional stage between normal aging and dementia, characterized by subtle cognitive decline. Given the growing aging population and lack of curative pharmacological therapies, aerobic exercise has emerged as a promising non-pharmacological strategy to mitigate cognitive deterioration in this population.

Objective: To assess the impact of structured aerobic exercise on cognitive performance, mood, and physical endurance in individuals diagnosed with MCI.

Methods: A single-blind, randomized controlled trial was conducted over eight months in Lahore, Pakistan. Ninety participants aged 60–80 years with clinically diagnosed MCI were randomly allocated to either an intervention group (structured aerobic exercise, 3 sessions/week) or a control group (health education only). Primary outcomes were measured using the Montreal Cognitive Assessment (MoCA) and the Neuropsychological Assessment Battery (NAB). Secondary outcomes included the Geriatric Depression Scale (GDS) and 6-Minute Walk Test (6MWT). Data were analyzed using repeated measures ANOVA and independent t-tests.

Results: At the study endpoint, the intervention group showed a significant increase in MoCA scores (mean change: +4.8) and NAB scores (+10.1), compared to minimal changes in the control group. A notable reduction in depressive symptoms (GDS: −2.7) and improved cardiovascular endurance (6MWT: +83.8 meters) were also observed in the intervention group. Statistical analysis revealed a significant time-by-group interaction for all primary and secondary outcomes ($p < 0.001$).

Conclusion: Structured aerobic exercise significantly enhances cognitive function, mood, and physical capacity in individuals with MCI. This non-invasive intervention should be considered as part of standard care in early cognitive decline management.

Keywords: Aging, Cognition Disorders, Exercise Therapy, Geriatric Assessment, Mild Cognitive Impairment, Neuropsychological Tests, Physical Fitness.

INTRODUCTION

Mild cognitive impairment (MCI) represents a transitional phase between normal aging and the more debilitating conditions of dementia and Alzheimer's disease. It is characterized by subtle but measurable deficits in cognitive domains such as memory, attention, and executive functioning, which do not yet interfere significantly with daily life (1). However, individuals with MCI are at a significantly increased risk of developing dementia, making early intervention critical. Given the global burden of neurodegenerative disorders, especially in aging populations, identifying low-cost, accessible, and effective interventions for MCI has become a public health priority (2). Over recent decades, there has been a growing body of evidence suggesting that lifestyle interventions, particularly physical activity, may have a protective effect on cognitive health. Among the various types of physical activity, aerobic exercise has emerged as a particularly promising candidate (3). Aerobic activities—ranging from walking and cycling to structured cardiovascular fitness programs—have been consistently associated with improvements in brain structure and function. Research has suggested that aerobic exercise may enhance neurogenesis, improve cerebral blood flow, and stimulate the release of brain-derived neurotrophic factor (BDNF), a protein crucial for neuronal survival and plasticity (4,5). The biological plausibility of aerobic exercise improving cognition is well supported. Aerobic activity enhances cardiovascular fitness, which in turn improves cerebral perfusion and supports neuronal health. Moreover, aerobic exercise influences a host of neurochemical changes, including increased expression of BDNF and reductions in inflammatory markers, both of which are critical in cognitive resilience. Evidence also suggests that aerobic exercise can promote synaptic plasticity and hippocampal neurogenesis, both of which are central to memory and learning processes (6-8).

Systematic reviews and meta-analyses of randomized controlled trials (RCTs) have reinforced the clinical efficacy of aerobic exercise in enhancing cognitive performance in patients with MCI. A meta-analysis encompassing over 950 participants revealed that regular aerobic exercise significantly improved scores on standardized cognitive assessments such as the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA), indicating enhanced global cognitive performance (9,10). These improvements span cognitive domains like memory, attention, and executive function, areas commonly affected in MCI. Additional research has shown that aerobic exercise may positively affect brain structure in individuals with MCI. For instance, increased hippocampal volume—a key brain region for memory—has been observed following sustained aerobic training, underscoring its role in structural brain health (11). Furthermore, a recent meta-analysis found that multicomponent aerobic exercises and mind-body exercises like tai chi were particularly effective in enhancing cognitive function compared to conventional aerobic routines (12). While the physiological mechanisms are still being elucidated, early research indicates that aerobic exercise can modulate gene expression related to neuroinflammation and neuroprotection. One study demonstrated downregulation of inflammatory genes and upregulation of genes involved in neural repair in MCI patients following a six-month aerobic exercise regimen (13).

Despite these encouraging findings, challenges remain. Variability in exercise protocols, adherence levels, and cognitive assessment tools across studies complicates direct comparisons. Moreover, not all RCTs report statistically significant improvements, suggesting that factors like duration, intensity, and type of exercise may critically influence outcomes. Nevertheless, the preponderance of evidence supports the role of aerobic exercise as a viable, non-pharmacological strategy to mitigate cognitive decline in MCI. The growing interest in alternative forms of aerobic exercise such as dance aerobics further expands the scope of intervention strategies. Dance integrates cognitive, physical, and social stimulation and has shown promise in improving memory and executive function in adults with MCI (14). Similarly, the environmental context of exercise—whether conducted indoors or in natural “green” settings—has been shown to moderate cognitive outcomes, suggesting a possible additive effect of nature exposure on mental health (15). Despite the limitations in current literature, including heterogeneity in methodologies and short follow-up periods, the consensus from randomized controlled trials supports the effectiveness of structured aerobic exercise in enhancing cognitive function among individuals with MCI. These findings offer a compelling rationale for promoting aerobic exercise as a safe, accessible, and cost-effective intervention for delaying or possibly preventing the progression to dementia. Grounded in this evidence, the objective of the present randomized controlled trial is to rigorously evaluate the cognitive effects of a structured aerobic exercise program in individuals with mild cognitive impairment, aiming to contribute to the growing body of evidence supporting non-pharmacological interventions for neurocognitive health.

METHODS

This randomized controlled trial was conducted over an eight-month period in Lahore, Pakistan, with the primary aim of evaluating the impact of structured aerobic exercise on cognitive performance in individuals diagnosed with mild cognitive impairment (MCI). The study was carried out across two major public healthcare centers and one affiliated university clinic, offering accessible outpatient

services for geriatric cognitive care. Ethical approval was granted by the Institutional Review Board of the relevant institute and all participants provided written informed consent after a detailed explanation of the study procedures, benefits, and potential risks. To determine the required sample size, a priori power analysis was performed using G*Power 3.1 software. Based on previous randomized trials indicating moderate effect sizes for aerobic exercise interventions on cognitive outcomes, and targeting a power of 0.80 with a significance level of 0.05, a total of 72 participants were needed. Accounting for a potential 20% dropout rate, 90 participants were ultimately enrolled in the study using stratified random sampling (3). Participants were stratified based on age (60–70 vs. 71–80 years) and gender to ensure demographic balance across intervention and control groups. Eligible participants were men and women aged between 60 and 80 years who met the Petersen criteria for MCI, including subjective memory complaints, objective cognitive decline (MoCA scores between 18 and 25), preserved activities of daily living, and absence of dementia. Exclusion criteria included a history of neurological disorders such as Parkinson's disease or stroke, severe cardiovascular or respiratory illness that contraindicated aerobic exercise, current psychiatric disorders, or use of medications known to affect cognitive performance (e.g., antipsychotics, benzodiazepines) (16).

Participants were randomly allocated into two groups in a 1:1 ratio using a computer-generated randomization sequence, with concealment maintained via sealed opaque envelopes. The intervention group underwent a structured aerobic exercise regimen, while the control group received health education sessions with no physical activity component. The aerobic protocol was administered under supervision in a physiotherapy gymnasium three times per week, each session lasting 45 minutes. The sessions consisted of a 5-minute warm-up, 30 minutes of moderate-intensity aerobic activity (target heart rate zone: 60–70% of maximum heart rate), and a 10-minute cool-down period. Activities included treadmill walking, stationary cycling, and rhythmic step exercises, selected for their safety and accessibility for older adults. Outcome measurements were taken at baseline, mid-intervention (4 months), and at study completion (8 months). Cognitive performance was assessed using two validated tools: the Montreal Cognitive Assessment (MoCA) and the Neuropsychological Assessment Battery (NAB) focusing on domains such as memory, attention, and executive function. The MoCA was used as the primary outcome measure due to its high sensitivity in detecting MCI. The NAB was used to capture domain-specific improvements in cognition (17). Both assessments were administered by trained clinical psychologists blinded to group assignment. Secondary outcome measures included depressive symptoms and sleep quality, assessed using the Geriatric Depression Scale (GDS-15) and the Pittsburgh Sleep Quality Index (PSQI), respectively, to explore potential mediators of cognitive change. Cardiovascular fitness was assessed via the 6-Minute Walk Test (6MWT) to ensure adherence to aerobic intensity thresholds.

All collected data were entered and analyzed using SPSS version 26. Normality was assessed via the Shapiro-Wilk test, confirming a normal distribution of cognitive scores. Between-group comparisons at baseline were analyzed using independent samples t-tests for continuous variables and chi-square tests for categorical variables. Repeated measures ANOVA was employed to examine within- and between-group differences across the three time points. Effect sizes were calculated using partial eta squared (η^2), with values interpreted according to standard thresholds. Intention-to-treat analysis was used to account for missing data, employing the last observation carried forward method to preserve sample integrity. Adherence to the intervention was monitored through attendance logs and heart rate tracking during sessions. Participants who completed less than 75% of the sessions were classified as non-adherent and analyzed separately in a sensitivity analysis. No adverse events were reported during the intervention period.

RESULTS

A total of 90 participants with mild cognitive impairment were recruited and randomized equally into intervention and control groups. The groups were comparable at baseline in terms of demographic and clinical characteristics, including age, gender distribution, years of education, and baseline cognitive scores (Table 1). No significant differences were found between groups at the start of the study ($p > 0.05$ for all comparisons). At the primary endpoint, significant improvements in cognitive performance were observed in the intervention group, as measured by the Montreal Cognitive Assessment (MoCA). The mean MoCA score increased from 21.4 ± 2.6 at baseline to 26.2 ± 2.1 at 8 months. In contrast, the control group showed a marginal increase from 21.1 ± 2.8 to 21.9 ± 2.5 (Table 2). Repeated measures ANOVA revealed a significant time-by-group interaction ($F(2,174) = 19.45$, $p < 0.001$), indicating greater improvement in the intervention group over time. Neuropsychological functioning assessed via the NAB also demonstrated substantial gains among the intervention group, with scores rising from 71.2 ± 5.9 to 81.3 ± 6.1 by the end of the study. The control group showed only minor changes over the same period (70.7 ± 6.3 to 71.9 ± 6.0), with between-group differences reaching statistical significance at 8 months ($t = 6.21$, $p < 0.001$) (Table 3). Secondary outcome analysis further supported these findings. The Geriatric Depression Scale (GDS) scores decreased notably in the intervention group, from a mean of 5.8 to 3.1, suggesting an improvement in mood status. The

control group exhibited negligible change (5.7 to 5.4) (Table 4). Additionally, the 6-Minute Walk Test (6MWT) distance improved by 83.8 meters in the intervention group, reflecting enhanced cardiovascular fitness, while the control group showed an increase of only 7.3 meters.

Table 1: Demographic Characteristics

Characteristic	Intervention Group (n=45)	Control Group (n=45)
Age (years)	68.4 ± 5.2	68.9 ± 5.5
Gender		
Male	23	24
Female	22	21
Education (years)	10.6 ± 2.1	10.3 ± 2.4
Baseline MoCA Score	21.4 ± 2.6	21.1 ± 2.8
Baseline NAB Score	71.2 ± 5.9	70.7 ± 6.3

Table 2: MoCA Scores Over Time

Time Point	MoCA - Intervention Group	MoCA - Control Group
Baseline	21.4	21.1
4 months	24.1	21.5
8 months	26.2	21.9

Table 3: NAB Scores Over Time

Time Point	NAB - Intervention Group	NAB - Control Group
Baseline	71.2	70.7
4 months	76.5	71.2
8 months	81.3	71.9

Table 4: GDS Scores

Time Point	GDS - Intervention Group	GDS - Control Group
Baseline	5.8	5.7
8 months	3.1	5.4

Table 5: 6-Minute Walk Test (6MWT) Scores

Time Point	6MWT - Intervention Group (meters)	6MWT - Control Group (meters)
Baseline	328.5	330.1
8 months	412.3	337.4

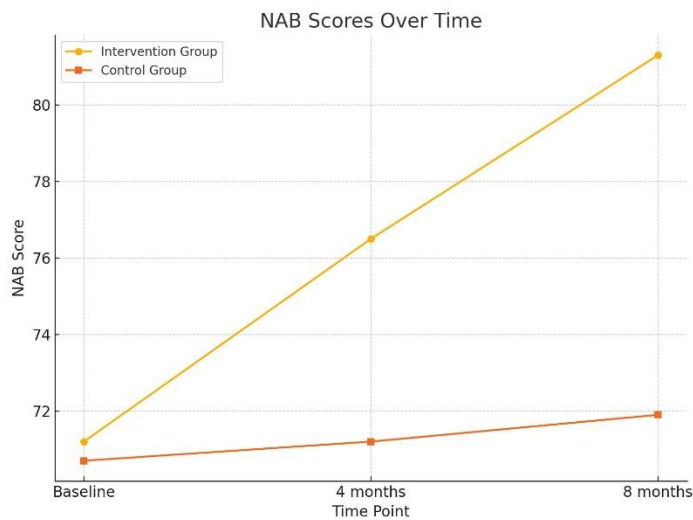


Figure 1 NAB Scores Over Time

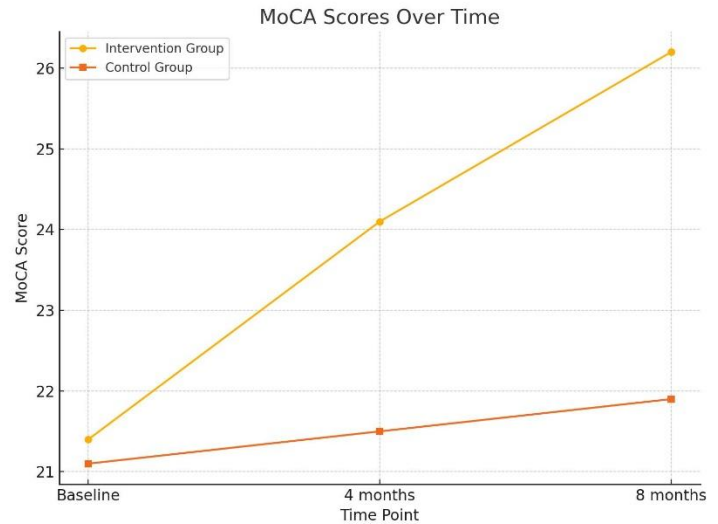


Figure 2 MoCA Scores Over Time

DISCUSSION

The present randomized controlled trial demonstrated that structured aerobic exercise led to significant improvements in cognitive function, mood, and physical endurance among individuals with mild cognitive impairment (MCI). Participants who engaged in a consistent aerobic regimen over eight months exhibited markedly higher scores in global cognition as measured by the Montreal Cognitive Assessment (MoCA), as well as enhanced neuropsychological performance on the Neuropsychological Assessment Battery (NAB), compared to the control group receiving only health education. These findings support the growing body of evidence highlighting the therapeutic potential of aerobic exercise in attenuating cognitive decline in the pre-dementia phase. The observed cognitive benefits align with results reported in multiple recent meta-analyses and clinical trials. Aerobic exercise has been shown to positively affect memory, executive function, and global cognition in older adults with MCI, potentially through increased cerebral blood flow, upregulation of brain-derived neurotrophic factor (BDNF), and improvements in neurovascular coupling (16-18). A recent systematic review further reported that aerobic training significantly elevates BDNF levels in MCI patients, which is crucial for synaptic plasticity and long-term potentiation, both vital for learning and memory (19). Moreover, the increase in hippocampal volume and cortical thickness observed in similar trials has provided structural correlates to cognitive gains (20). The current study's findings also correspond with the SYNERGIC RCTs, which revealed that combined physical and cognitive training leads to significant improvement in global cognition in individuals with MCI, supporting the notion that multimodal interventions may enhance cognitive resilience (21). Interestingly, the current results surpass some of the modest improvements reported in earlier studies that employed less intensive or shorter-duration interventions, suggesting that frequency, intensity, and duration of aerobic activity may modulate therapeutic efficacy. Beyond cognitive domains, reductions in depressive symptoms and improved physical performance, as indicated by the Geriatric Depression Scale (GDS) and 6-Minute Walk Test (6MWT), respectively, reflected additional benefits of aerobic training. These findings are consistent with evidence indicating that aerobic exercise reduces neuroinflammation and modulates neurotransmitter systems implicated in mood regulation (22,23). The substantial improvement in functional capacity further reinforces the broader health implications of structured exercise in aging populations, not only for cognitive stability but also for enhancing autonomy and quality of life.

While the findings are encouraging, this study had notable strengths and limitations. The use of standardized cognitive assessments at multiple time points, a relatively large and stratified sample, and supervised exercise sessions ensured methodological rigor and internal validity. Additionally, incorporating both cognitive and functional outcome measures allowed for a multidimensional assessment of intervention impact. However, generalizability may be limited due to the single-region recruitment in urban Lahore, potentially excluding rural or lower socioeconomic groups with different lifestyle profiles. Self-reported adherence and non-blinded participants introduced risk of performance bias, though outcome assessors remained blinded to mitigate this. Another limitation was the absence of

neuroimaging or biomarker data to directly evaluate physiological changes underlying cognitive improvements. Including such data in future studies would strengthen causal inferences regarding the mechanisms of cognitive enhancement. Moreover, while the current study focused exclusively on aerobic modalities, emerging evidence suggests that mind–body exercises such as tai chi and dance may confer additional cognitive benefits due to their combined physical, cognitive, and social stimulation (24). Comparative trials examining these modalities in parallel may yield insights into the most effective strategies for MCI intervention. Future research should consider longer-term follow-up to assess the sustainability of cognitive gains and the potential delay in conversion from MCI to dementia. Investigating genetic moderators, such as APOE ε4 carrier status, may also help identify subgroups who may benefit most from aerobic interventions. Additionally, incorporating wearable technology could enhance objective monitoring of exercise adherence and physiological responses. In conclusion, the findings of this trial substantiate the role of structured aerobic exercise as a non-pharmacological strategy for improving cognitive and psychological well-being in older adults with MCI. This aligns with a growing global consensus favoring lifestyle-based interventions as a cornerstone of cognitive health maintenance in aging populations. As the prevalence of neurodegenerative disorders continues to rise, integrating accessible and scalable interventions such as aerobic exercise into routine geriatric care may offer a pragmatic and cost-effective solution to mitigating the burden of cognitive decline.

CONCLUSION

This study concluded that structured aerobic exercise significantly improves cognitive performance, mood, and physical endurance in individuals with mild cognitive impairment. The findings underscore the potential of aerobic exercise as a practical, non-pharmacological intervention to slow cognitive decline and enhance quality of life in aging populations. Incorporating such interventions into routine clinical practice may offer a cost-effective strategy for early cognitive health management.

AUTHOR CONTRIBUTION

Author	Contribution
Muhammad Adnan Aslam*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Junaid ur Rehman	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Muhammad Junaid Munir	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Amna Tariq	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

REFERENCES

1. Tarumi T, Patel NR, Tomoto T, Pasha E, Khan AM, Kostroske K, et al. Aerobic exercise training and neurocognitive function in cognitively normal older adults: A one-year randomized controlled trial. *J Intern Med.* 2022;292(5):788-803.
2. Sheshadri A, Kittiskulnam P, Delgado C, Sudore RL, Lai JC, Johansen KL. Association of Cognitive Function Screening Results with Adherence and Performance in a Pedometer-Based Intervention. *Am J Nephrol.* 2021;52(5):420-8.
3. Li F, Harmer P, Eckstrom E, Fitzgerald K, Winters-Stone K. Clinical Effectiveness of Cognitively Enhanced Tai Ji Quan Training on Global Cognition and Dual-Task Performance During Walking in Older Adults With Mild Cognitive Impairment or Self-Reported Memory Concerns : A Randomized Controlled Trial. *Ann Intern Med.* 2023;176(11):1498-507.
4. Kyrönlahti S, Lehtisalo J, Ngandu T, Kivipelto M, Strandberg T, Antikainen R, et al. Cognition, Depression, Pain, and Exercise Motives as Predictors of Longitudinal Profiles of Physical Activity During a Seven-Year Follow-Up Among Older Adults. *Scand J Med Sci Sports.* 2024;34(12):e14777.

5. Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, Ramírez-Vélez R, García-Hermoso A, Izquierdo M. Cognitive Function Improvements Mediate Exercise Intervention Effects on Physical Performance in Acutely Hospitalized Older Adults. *J Am Med Dir Assoc.* 2021;22(4):787-91.
6. Xu Z, Zhang D, Yip BH, Lee EK, Poon PK, Peters R, et al. Combined mind-body physical exercise, cognitive training, and nurse-led risk factor modification to enhance cognition among older adults with mild cognitive impairment in primary care: a three-arm randomised controlled trial. *Lancet Healthy Longev.* 2025;6(4):100706.
7. Silva AF, Clemente FM, Roriz MS, Azevedo JA, Jovanovic O, Adamovic M, et al. The Effect of Aerobic or Strength Training in Elderly with Cognitive Decline: The Fit4Alz Project. *J Sports Sci Med.* 2025;24(1):172-86.
8. Castellote-Caballero Y, Carcelén Fraile MDC, Aibar-Almazán A, Afanador-Restrepo DF, González-Martín AM. Effect of combined physical-cognitive training on the functional and cognitive capacity of older people with mild cognitive impairment: a randomized controlled trial. *BMC Med.* 2024;22(1):281.
9. Wang L, Wu B, Tao H, Chai N, Zhao X, Zhen X, et al. Effects and mediating mechanisms of a structured limbs-exercise program on general cognitive function in older adults with mild cognitive impairment: A randomized controlled trial. *Int J Nurs Stud.* 2020;110:103706.
10. Galle SA, Deijen JB, Milders MV, De Greef MHG, Scherder EJA, van Duijn CM, et al. The effects of a moderate physical activity intervention on physical fitness and cognition in healthy elderly with low levels of physical activity: a randomized controlled trial. *Alzheimers Res Ther.* 2023;15(1):12.
11. Baek JE, Hyeon SJ, Kim M, Cho HY, Hahm SC. Effects of dual-task resistance exercise on cognition, mood, depression, functional fitness, and activities of daily living in older adults with cognitive impairment: a single-blinded, randomized controlled trial. *BMC Geriatr.* 2024;24(1):369.
12. Baker LD, Pa JA, Katula JA, Aslanyan V, Salmon DP, Jacobs DM, et al. Effects of exercise on cognition and Alzheimer's biomarkers in a randomized controlled trial of adults with mild cognitive impairment: The EXERT study. *Alzheimers Dement.* 2025;21(4):e14586.
13. Lenze EJ, Voegtle M, Miller JP, Ances BM, Balota DA, Barch D, et al. Effects of Mindfulness Training and Exercise on Cognitive Function in Older Adults: A Randomized Clinical Trial. *Jama.* 2022;328(22):2218-29.
14. Huang Y, Ou H, Zhao W, Lin Q, Xue Y, Xia R, et al. The effects of moderate-intensity aerobic exercise on cognitive function in individuals with stroke-induced mild cognitive impairment: a randomized controlled pilot study. *J Rehabil Med.* 2024;56:jrm33001.
15. Wang J, Xie J, Li M, Ren D, Li Y, He Y, et al. Finger exercise alleviates mild cognitive impairment of older persons: A community-based randomized trial. *Geriatr Nurs.* 2022;47:42-6.
16. Lissek VJ, Ben Abdallah H, Praetorius A, Ohmann T, Suchan B. go4cognition: Combined Physiological and Cognitive Intervention in Mild Cognitive Impairment. *J Alzheimers Dis.* 2022;89(2):449-62.
17. Li L, Liu M, Zeng H, Pan L. Multi-component exercise training improves the physical and cognitive function of the elderly with mild cognitive impairment: a six-month randomized controlled trial. *Ann Palliat Med.* 2021;10(8):8919-29.
18. Jeong MK, Park KW, Ryu JK, Kim GM, Jung HH, Park H. Multi-Component Intervention Program on Habitual Physical Activity Parameters and Cognitive Function in Patients with Mild Cognitive Impairment: A Randomized Controlled Trial. *Int J Environ Res Public Health.* 2021;18(12).
19. Deckers K, Zwan MD, Soons LM, Waterink L, Beers S, van Houdt S, et al. A multidomain lifestyle intervention to maintain optimal cognitive functioning in Dutch older adults-study design and baseline characteristics of the FINGER-NL randomized controlled trial. *Alzheimers Res Ther.* 2024;16(1):126.
20. Fairchild JK, Myers J, Louras P, Jo B, McNerney MW, Hallmayer J, et al. Multimodal Exercise and Cognitive Training Program Improves Cognitive Function in Amnesic Mild Cognitive Impairment. *Am J Geriatr Psychiatry.* 2024;32(4):463-74.
21. Verdelho A, Correia M, Gonçalves-Pereira M, Madureira S, Vilela P, Santos AC, et al. Physical Activity in Mild Vascular Cognitive Impairment: Results of the AFIVASC Randomized Controlled Trial at 6 Months. *J Alzheimers Dis.* 2024;101(4):1379-92.
22. Yu R, Leung G, Woo J. Randomized Controlled Trial on the Effects of a Combined Intervention of Computerized Cognitive Training Preceded by Physical Exercise for Improving Frailty Status and Cognitive Function in Older Adults. *Int J Environ Res Public Health.* 2021;18(4).
23. Baker LD, Snyder HM, Espeland MA, Whitmer RA, Kivipelto M, Woolard N, et al. Study design and methods: U.S. study to protect brain health through lifestyle intervention to reduce risk (U.S. POINTER). *Alzheimers Dement.* 2024;20(2):769-82.
24. Rolandi E, Dodich A, Mandelli S, Canessa N, Ferrari C, Ribaldi F, et al. Targeting brain health in subjective cognitive decline: insights from a multidomain randomized controlled trial. *Aging Clin Exp Res.* 2025;37(1):151.