

Effect of Exercise on Cognitive Ability, Cardiovascular Fitness, and Quality of Life in Post-Stroke Patients: Systematic Review and Meta-Analysis

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ABSTRACT

Background: Following a stroke, cognitive ability, and cardiovascular fitness decline, exerting a substantial influence on physical rehabilitation and overall quality of life. Stroke management encompasses a multidisciplinary approach, with emerging studies highlighting the role of exercise in enhancing cognitive ability and cardiovascular fitness post-stroke. This study aims to analyze the effects of exercise on cognitive ability, cardiovascular fitness, and quality of life in stroke survivors, shedding light on potential therapeutic benefits.

Subject and Methods: The PICO Model eligibility criteria were employed to execute the article search including P= post-stroke patients; I= exercises C= standard care, O= cognitive ability OR cardiovascular fitness OR quality of life. The study extracted articles from PubMed and Science-Direct databases, with keywords "exercises" AND "cognitive ability" OR "cardiovascular fitness" OR "quality of life" AND "post-stroke patients". Inclusion criteria required full-text articles with randomized controlled trial (RCT) designs, focusing on post-stroke patients and evaluating improvements in cognitive ability, cardiovascular fitness, or quality of life. PRISMA diagram and Review Manager 5.4.1 tool were used to analyse the selected articles.

Results: 25 studies included in the review had 2,110 participants, across Asia; Australia, Europe, North America, and South America eligible for meta-analysis. The result indicated a positive effect of exercise on cognitive ability (SMD=0.68, CI 95% (0.21 to 1.16); p=0.005); cardiovascular fitness (SMD=0.63, CI 95% (0.17 to 1.08); p=0.007) and quality of life (SMD=0.60, CI 95% (-0.08 to 1.27); p=0.080).

Conclusion: Engagement in diverse forms and durations of exercise emerges as a crucial element in post-stroke rehabilitation. This intervention signifies a promising avenue toward enhancing cognitive abilities, and cardiovascular fitness, and potentially elevating quality of life among stroke survivors.

Keywords: stroke, exercise, cognitive ability, cardiovascular fitness, quality of life

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BACKGROUND

Stroke, a neurological and cardiovascular disease (Kusznir Vitturi & José Gagliardi, 2020); (Shakir, 2018); (Lopez et al., 2022) with complex and multifactorial pathophysiology (Ciarambino et al., 2022) affecting more than 15 million people annually causing long-lasting impairment to stroke victims (Bonkhoff et al., 2021) such as paralysis, leaving a patient in a coma, permanent disabilities, or death. As the second leading cause of mortality, in 2019 stroke claimed about 6.55 million lives, which is still increasing, thus pausing global health concerns (Feigin et al., 2021).

Stroke has detrimental impacts on cognitive ability, often leading to deficits in memory, attention, and executive functions due to brain tissue damage (Rizvi et al., 2023), (Morrison et al., 2022). Additionally, it affects cardiovascular fitness by both reducing oxygen supply to the brain and causing physical impairments that limit mobility and activity levels (McDonald et al., 2021). This dual impact severely diminishes the quality of life, manifesting as challenges in daily activities, social interactions, and emotional well-being, necessitating comprehensive rehabilitation strategies for optimal recovery (El Husseini et al., 2023).

Stroke affects people across all age groups (Soto-Cámara et al., 2020) and it arises from an intricate amalgamation of risk factors including but not restricted to hypertension, diabetes, smoking, obesity, and sedentary lifestyle as well as genetics and age (Boehme et al., 2017), (Roy-O'Reilly & McCullough, 2018).

Stroke management involves a multidisciplinary approach; including pharmacological interventions where antiplatelet agents like aspirin, anticoagulants, and neuroprotective drugs are administered (Baig & Bodle, 2023), (Gauberti et al.,

2021). Nevertheless, exercises are tailored to individual capabilities and medical considerations to improve mobility, and strength as well as promote neuroplasticity, fostering neuronal regeneration and rewiring damaged circuits, thereby improving cognitive abilities after stroke (Geidl et al., 2018). On the other hand, exercise boosts cardiovascular fitness, reducing the risk of recurrent strokes and improving overall cardiovascular health (Pinckard et al., 2019). Additionally, exercise enhances psychological well-being, positively impacting mood and self-esteem, thereby enhancing the quality of life for stroke survivors (Hyun et al., 2021). This meta-analysis aims to analyse the effects of exercise on cognitive ability, cardiovascular fitness and quality of life in post-stroke patients.

SUBJECTS AND METHOD

1. Study design and search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adhered by the systematic review (Macleod et al., 2020). The PICO Model eligibility criteria were included in articles selection, P= Post-stroke patients, I= Exercises, C= usual or standard care, and O= Cognitive ability, Cardiovascular Fitness, and Quality of Life. Two electronic databases (PubMed and ScienceDirect) were subjected to a systematic search for articles published from 2016 onwards. The search terms utilized comprised "exercise" AND "cognitive ability" OR "cardiovascular fitness" OR "quality of life" AND "post-stroke patients".

2. Inclusion and exclusion study criteria

Randomized controlled trials (RCTs) examining the effect of exercise on post-stroke patients relative to standard care were included in the systematic review. Regular, recommended, or usual physical

activity/exercise were classified as routine physical activity. Inclusion criteria comprised full research articles detailing RCTs with post-stroke patients as participants. The standard mean difference (SMD) was employed as the relationship's metric, whilst the primary research outcomes analysed improvements in cognitive ability, cardiovascular fitness, and quality of life. Articles that did not adhere to controlled trial methodologies, or with other intervention besides from exercises, or published in other languages other than English were excluded from consideration.

3. Definition of Operational Variables

Exercises; are structured and planned physical activities designed to improve or maintain the overall health and well-being of individuals who have experienced a stroke in terms of cognitive, cardiovascular, and quality of life.

Cognitive ability; is the overall mental capacity involving reasoning, problem-solving, planning, abstract thinking, complex idea comprehension, and learning from experiences.

Cardiovascular fitness; is the body's capacity to absorb oxygen and transfer it to the muscles and organs without being overly tired during extended exercise sessions.

Quality of life; is a subjective measure or standard of health, happiness, or comfort experienced by individuals or groups.

4. Study Instrument

A critical assessment tool derived from the randomized controlled trial checklist was utilized for evaluating study quality. The checklist comprises 7 questions, each with responding to "Yes," "No," or "Unclear." Scores of "2, 1, and 0" are assigned to these responses, respectively. Cumulative scores of each study were calculated based on the responses, with a total score of ≥ 14 indicating minimal bias regarding statistical power, relevance, outcome consistency, quality, and reliability in the primary

studies. Conversely, a score of < 14 suggests the presence of bias in these aspects (Supplementary file).

5. Data Analysis

The study selected articles based on specific criteria and adhered to PRISMA flowchart guidelines. Data analysis utilized Rev-Man 5.4.1 software to determine effect sizes and evaluate heterogeneity consistency (I^2) among the selected research findings.

RESULTS

The preliminary search yielded 4,649 articles. 685 duplicate articles were removed after undergoing title and abstract scanning. Following the application of inclusion and exclusion criteria, 660 articles were exempted due to unrelated interventions, unrelated outcomes, or unclear indication of pre- and post-group comparison leaving 25 articles which met an inclusion criteria for the meta-analysis (Figure 1).

An extensive examination of primary research was conducted to assess the effect of exercise on cognitive ability, cardiovascular health, and quality of life in post-stroke patients. This assessment involved a meta-analysis of 25 articles sourced from diverse locations, including Asia with contributions from China (4), Korea (7), Pakistan (1), Taiwan (1), and Turkey (1), and Australia (1). Europe with publications from Italy (1), Netherlands (1), Norway (2), Sweden (1), and the United Kingdom (1), North America with contributions from Canada (1) and the USA (1), and South America with publications solely from Brazil (2) (Figure 2). Commonalities identified in these studies comprised the use of randomized controlled trial (RCT) design, the inclusion of post-stroke patients as study participants, and the implementation of exercise interventions. Notably, there were variations in sample sizes across the studies, ranging from 15 participants to a

maximum of 362. The intervention period of each research ranged between 30 to 60 minutes, with a frequency of 3 to 5 times a week across the studies. Nevertheless, the

intervention period varied with the shortest period being 4 weeks and some up to 96 weeks (Table 1).

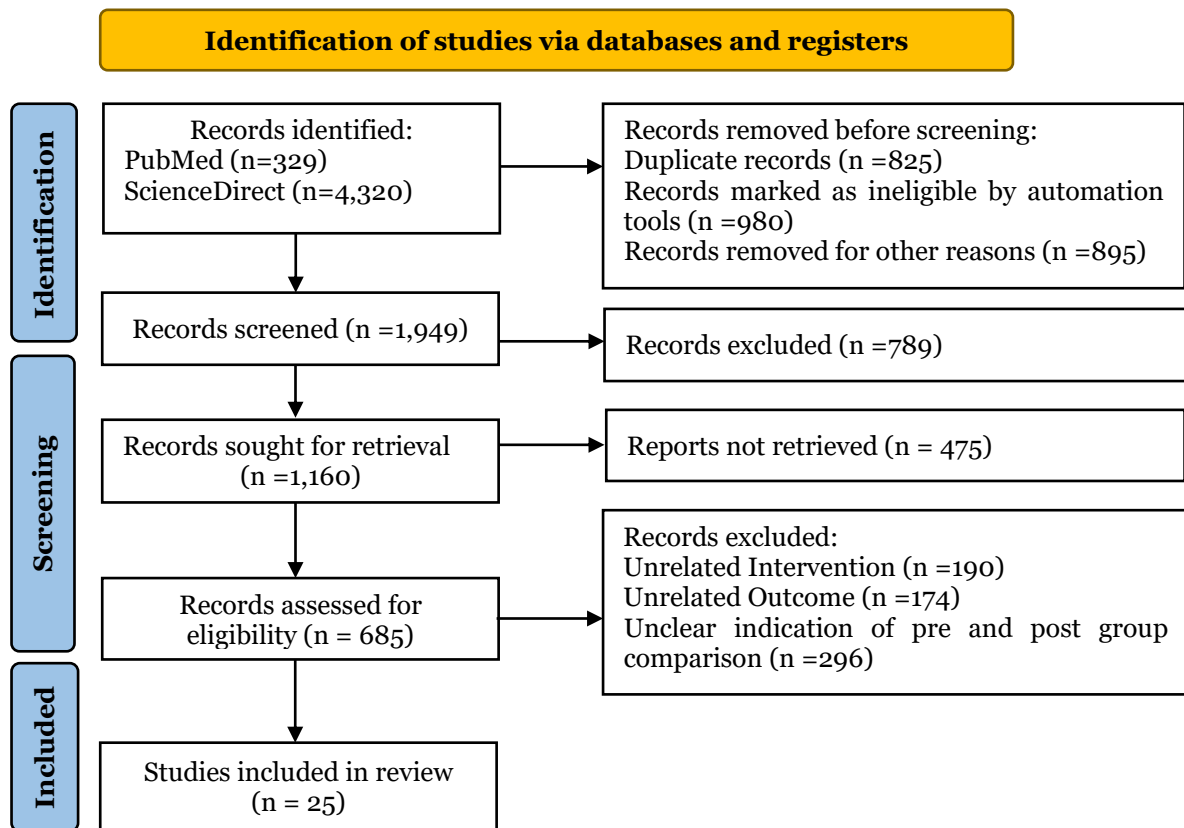


Figure 1. PRISMA Flow Diagram on the effect of exercise on cognitive ability, cardiovascular fitness, and quality of life in post-stroke patients



Figure 2. Study region map of research area on the effect of exercise on cognitive ability, cardiovascular fitness, and quality of life in post-stroke patients

Table 1. Description of the primary studies on effect of exercise on cognitive ability, cardiovascular fitness, and quality of life in post-stroke patients

Author (Year)	Study period	Country	Study design	Sample size	(P) Population		(I) Intervention	(C) Comparison	(O) Outcome
				Total	Post-stroke patient		Exercise	Standard care	
					Age	Diagnosis			
Jiang et al., (2016)	12 weeks	China	RCT	n=100	18-75	within 6 months	1. Conventional therapy (acupuncture) 2. Reha-Com cognitive training (restore attention, and memory, execute function, and improve visual field)	1. Traditional rehabilitation therapy including basic treatment and health education	Cognitive function
Han and Im, (2017)	6 weeks	Korea	RCT	n=20	M/SD	3 months	1. Aquatic treadmill exercise per 6 weeks (water-based aerobic exercise on a motorized aquatic treadmill) 2. Aerobic exercise	1. Land-based exercise per 6 weeks (performed land-based aerobic exercise on a cycle ergometer) 2. Aerobic exercise aerobic exercise	Cardiovascular fitness
Lim et al., (2017)	8 weeks	Korea	RCT	n=20	M/SD	Suffered stroke 2 years previously	1. Conventional stroke rehabilitation program (joint mobility, muscle strengthening, walking exercises) (30 minutes, once a day, 5 days in a week over 8 weeks) 2. Pilates exercises (60 mins, 3 times a week over 8 weeks)	1. Conventional stroke rehabilitation program (joint mobility, muscle strengthening, walking exercises) (30 minutes, once a day, 5 days in a week over 8 weeks)	Cardiovascular fitness
Vahlberg et al., (2017)	3 months	Sweden	RCT	n=67	65-85 years	12 months ago	1. Physical exercises (High-Intensity Functional exercises) 2. Circuit exercises (static and dynamic balance exercises) (75 mins 2-3 times a week)	1. Ordinary exercises with no limitation in persuasion of physical exercise and rehabilitation program	Quality of life

Author (Year)	Study period	Country	Study design	Sample size	(P) Population		(I) Intervention	(C) Comparison	(O) Outcome
				Total	Post-stroke patient		Exercise	Standard care	
					Age	Diagnosis			
Lee et al., (2018)	4 weeks	Korea	RCT	n=32	M/SD	≤3 months	1. Water-based aerobic exercise on a motorized aquatic treadmill 2. Physiotherapy 3. Occupational therapy	1. Land-based aerobic exercise using upper- and lower-body ergometers 2. Physiotherapy 3. Occupational therapy	Quality of life
Munari et al., (2018)	3 months	Italy	RCT	n=15	18-75	At least 6 months before study	1. High-intensity treadmill training	1. Low-intensity treadmill training	Cardiovascular fitness
Chung et al., (2019)	5 weeks	Korea	RCT	n=35	>20	6 months after stroke	1. Task Specific Lower Extremity training for 30min and 1 session of conventional physical therapy for 30 min 5 days a week in 3 weeks 2. Conventional Physical therapy for 30min 5 days a week in 2 weeks	1. 2 sessions of Conventional Physical therapy each 30min,5 days a week in 3 weeks 2. Conventional Physical therapy for 30min 5 days a week in 2 weeks	Cognitive function
Ihle-Hansen et al., (2019)	18 months	Norway	RCT	n=362	>18	first time stroke	1. Regular individualized coaching performed by physiotherapists to achieve physical activity 30 min daily 2. 45–60 min physical exercise including 2–3 bouts of vigorous activity every week. 3. physiotherapists did home visits to provide education and tailored training programs, based on the patient's preferences and goals	1. Usual care	Cognitive function
Hsu et al., (2019)	4 weeks	Taiwan	RCT	n=30	≥20	≥3 months	1. Exercise Training 2. Traditional rehabilitation program	1. Traditional rehabilitation program	Cardiovascular fitness

Author (Year)	Study period	Country	Study design	Sample size	(P) Population		(I) Intervention	(C) Comparison	(O) Outcome
				Total	Post-stroke patient		Exercise	Standard care	
					Age	Diagnosis			
Yeh et al., (2019)	12-18 weeks	Taiwan	RCT	n=30	M/SD	6 months before enrollment	1. Aerobic exercises (30 mins) 2. Computer based cognitive training (30 mins) (2-3 times a week for 12-18 weeks)	1. Non aerobic training (flexibility exercises, muscles strengthening, balance training) for 30 mins 2. Unstructured mental activities (30 mins)	Quality of life
Aguiar et al., (2020)	12-16 weeks	Brazil	RCT	n=22	≥ 20 years	> 6 months stroke within 1 year	Aerobic treadmill training (40 mins, 3 session a week)	Walking over ground (40 mins, 3 session a week)	Quality of life
Koch et al., (2020)	3 months	USA	RCT	n=131	>18		1. A 3 weekly 40 to 60 minutes CARET and 40 minutes CTI sessions. (supervised by trained personnel who assisted with physical (combined Aerobic and Resistance Training) and computer-based cognitive exercises)	1. A 3 weekly 40 to 60 minutes CARET and 40 minutes CTI sessions (supervised training of mild stretching and range of motion exercises, for three 40-minute sessions a week) (The sham cognitive intervention involved computer games such as hang-man, anagrams, and word search for 40 minutes three times weekly)	Cognitive function
Soh et al., (2020)	12 weeks	Korea	RCT	n=36	20-65 years	nil	1. Skater exercise were	1. Conventional treadmill aerobic exercise was	Cardiovascular fitness
Wu et al., (2020)	12 weeks	China	RCT	n=61	18-80 years	Patient treated from Dec 2016 -Dec 2017	Rehabilitation and guidance during inpatient and OPD under collaborative care team (twice a week, not more than 2 hrs)	Rehabilitation guidance and routine nursing measures during inpatient and OPD (once a week)	Quality of life
Zheng et al., (2020)	24 weeks	China	RCT	n=48	45-75	3 months after first ever stroke	1. Bandu Anjin training (40 min a day, 3 days a week) 2. Original medication and rehabilitation	1. Original medication and rehabilitation training	Cognitive function
Gjellesvik et al., (2021)	8 weeks	Norway	RCT	n=70	>18	>3 month; ≥5 years	1. High Intensity Interval Training	1. Standard care	Cognitive function

Author (Year)	Study period	Country	Study design	Sample size	(P) Population		(I) Intervention	(C) Comparison	(O) Outcome
				Total	Post-stroke patient		Exercise	Standard care	
					Age	Diagnosis			
Hyun et al., (2021)	6 weeks	Korea	RCT	n=30	N/A	3-6 month after stroke	1. Trained to sit-to-stand with real-time visual feedback	2. Sit to stand	Quality of life
Ozen et al., (2021)	4 weeks	Turkey	RCT	n=30	18-85	≥3 months since stroke	1. Conventional neurorehabilitation physical therapy (60 mins, 5 days a week for 5 weeks) 2. Computer Game Assisted Task Specific Exercises (30 mins, 5 days per week) under occupational therapist 3. 1 hr physical training	1. Conventional neurorehabilitation physical therapy (60 mins, 5 days a week for 5 weeks) 2. Occupational therapy (30 mins, 5 days a week)	Quality of life
Reynolds et al., (2021)	12 weeks	Australia	RCT	n=20	≥ 18 years	6 months ago	1. Progressive fitness training per ACSM guide 2. Cardiovascular fitness training under a trained physiotherapist 3. Home exercise program (30 mins session per week)	1. Low intensity conventional exercises program 2. Home exercise program (30 mins session per week)	Cardiovascular fitness
Rocha et al., (2021)	3 weeks	Brazil	RCT	n=30	45-80		1. Constraint Induced Movement Therapy	1. Conventional physiotherapy group	Quality of life
Song et al., (2021)	15 months	Korea	RCT	n=34	M/SD		1. Tai-chi (2 a week for 6 months) in 50 mins (contact with instructor)	1. Symptom management program (no contact)	Cognitive function
Deijle et al., (2022)	24 months	Netherlands	RCT	n=119	>18	1 month ago	1. Standard post stroke care 2. Exercises intervention (aerobic and strength training) 1hr per week	1. standard post stroke care	Cognitive function

Author (Year)	Study period	Country	Study design	Sample size	(P) Population		(I) Intervention	(C) Comparison	(O) Outcome
				Total	Post-stroke patient		Exercise	Standard care	
					Age	Diagnosis			
Guillaumer et al., (2022)	12 weeks	Britain	RCT	n=356	≥ 18 years	6-36 months post stroke	1. P2S program is a modularized, tailored program providing evidence-based techniques and information in 6 core modules:(1) blood pressure, (2) smoking, (3) alcohol consumption, (4) physical activity, (5) nutrition, and (6) feelings and mood, as well as a 'my progress' section with each tailored to accommodate stroke-related symptoms	1. An emailed copy of a letter containing links to internet addresses with readily available, generic online health programs and guidelines designed for the general population was sent	Quality of life
Mahmood et al., (2022)	8 weeks	Pakistan	RCT	n=41	45-65	≥6 months	1. Core stability training and conventional therapy	1. Conventional physical therapy 40 min/day, 5 times a week/ 8 weeks (motion exercises, mobility exercises)	Quality of life
Marilyn et al., (2022)	12 months	Canada	RCT	n=138	≥ 17 years	3 months after stroke	1. Attended an outpatient neurovascular clinic for: therapeutic interventions 2. Group exercise 3. Interactive Education sessions	Usual care (Attended an outpatient neurovascular clinic for: therapeutic interventions; follow-up care through 1–3 return clinic visits then referred to their primary care physician for further ongoing care and management.	Cardiovascular fitness

Cognitive ability. Using the Mini-Mental State Examination (MMSE), which measures multiple domains including memory, attention, and executive function, and the Montreal Cognitive Assessment (MoCA), ten studies analysed the effectiveness of exercise on cognitive performance in post-stroke patients. Better cognitive performance is indicated by higher MMSE and MoCA scores. Patients who opted for exercise after a stroke scored higher overall on the MMSE and MoCA by 0.68 units compared to those who chose standard treatment. The difference between the average determined by the random effect model and the heterogeneity effect of the studies estimates ($I^2=90\%$; $p<0.001$) is statistically significant (SMD=0.68, CI 95% (0.21 to 1.16); $p=0.005$) (Figure 3).

Cardiovascular fitness: The effectiveness of exercise on cardiovascular fitness in post-stroke patients was measured by VO₂ peak (peak or maximum oxygen consumption), expressed in ml/kg/min or VO₂ max per ml.kg.min, which indicates the maximum oxygen utilization during peak exercise. Contrast to standard treatment, post-stroke patients opting for exercise showed a significant increase of 0.63 units higher in VO₂peak or VO₂ max, signifying enhanced cardiovascular fitness. The difference is statistically significant (SMD=0.63, CI 95% (0.17 to 1.08); $p=0.007$). The heterogeneity effect of the studies estimates ($I^2=78\%$; $p<0.001$) with the average calculated by a random effect model, (Figure 5).

Quality of life. Ten articles analyzed the quality of life using measures such as EQ-5D, EQ-5D-5L, and SS-QoL. A higher score

in these metrics indicates a better quality of life. This reinforces the significance of the observed increase of 0.60 units in quality of life among post-stroke patients opting for exercises compared to those opting for usual care. The difference is marginally statistically significant (SMD=0.60, CI 95% (-0.08 to 1.27); $p=0.080$), with the heterogeneity effect of the studies estimates ($I^2=92\%$; $p<0.001$) using the average calculated by the random effect model (Figure 7).

RESULTS

Results from this meta-analysis indicate multifaced significance of tailored exercises of different modalities across all domains of post-stroke rehabilitation, suggesting a potential paradigm shift in post-stroke management.

25 randomized controlled trials from Asia, Australia, Europe, North America and South American continent collectively signify the importance of integrating tailored exercise programs into post-stroke rehabilitation protocols within public health management frameworks.

Cognitive ability was analysed under MoCA and MMSE metrics and the result was statistically significant (SMD=0.68, CI 95% (0.21 to 1.16); $p=0.005$). An increase in these metrics indicate that exercise stimulates neuroplasticity, fostering new neural connections and mitigating impairments, leading to enhanced cognitive function. Regular exercise reduces the risk of cognitive decline, thereby improving quality of life and functional independence, (Zhang et al., 2023).

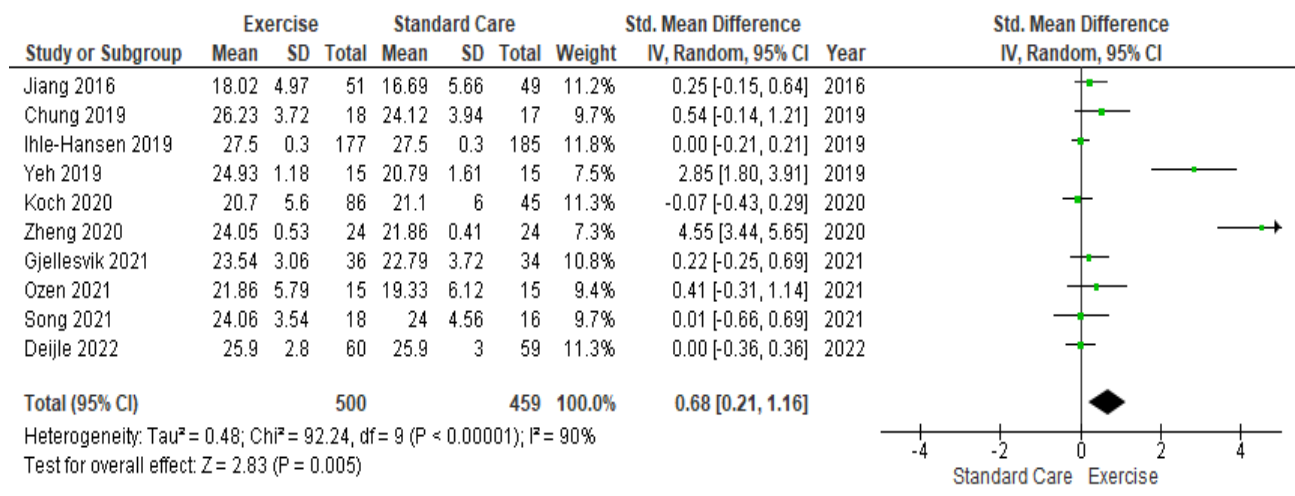


Figure 3. Forest plot on effect of exercise on cognitive ability in post-stroke patients

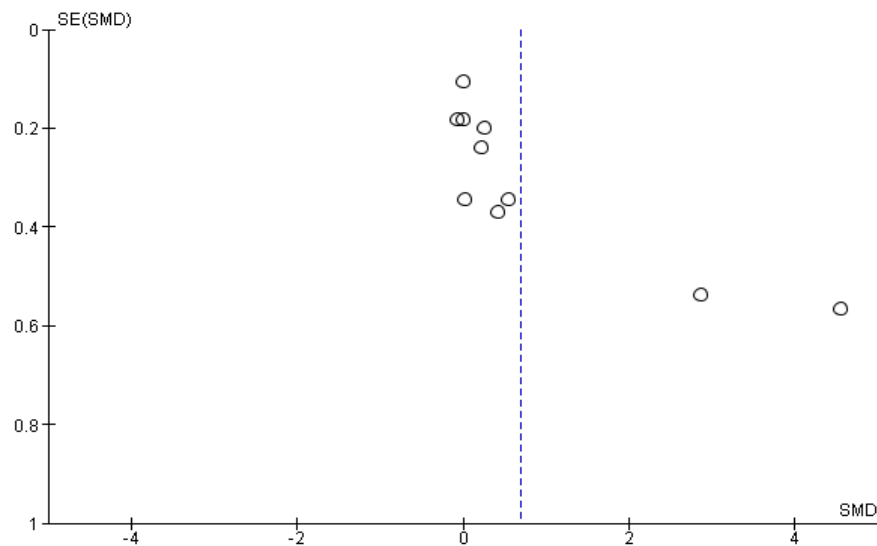


Figure 4. Funnel plot of the effect of exercise on cognitive ability in post stroke patients

In **cardiovascular fitness**, exercise attributed to improved oxygen utilization and vascular health as measured by VO₂peak or VO₂ max. The results were statistically significant (SMD=0.63, CI 95% (0.17 to 1.08); p=0.007). This improvement contributes to endurance, reduced fatigue, and enhanced overall cardiovascular health

in post-stroke patients. Regular exercise helps to mitigate the adverse effects of stroke-related impairments on the cardiovascular system, thereby improving functional capacity and reducing the risk of recurrent cardiovascular events, (Billinger et al., 2014).

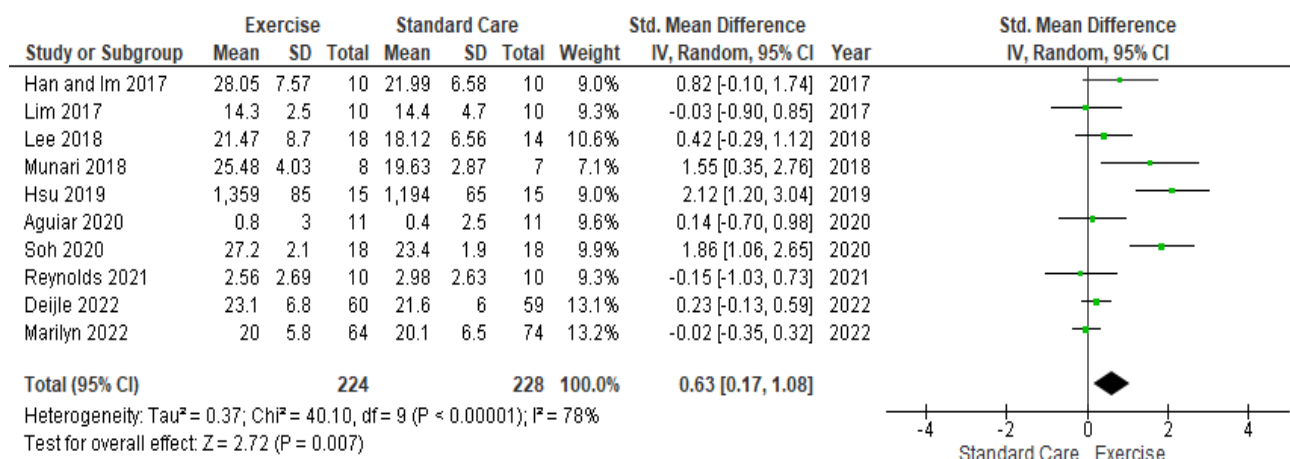


Figure 5. Forest plot of the effect of exercise on Cardiovascular fitness in post stroke patients

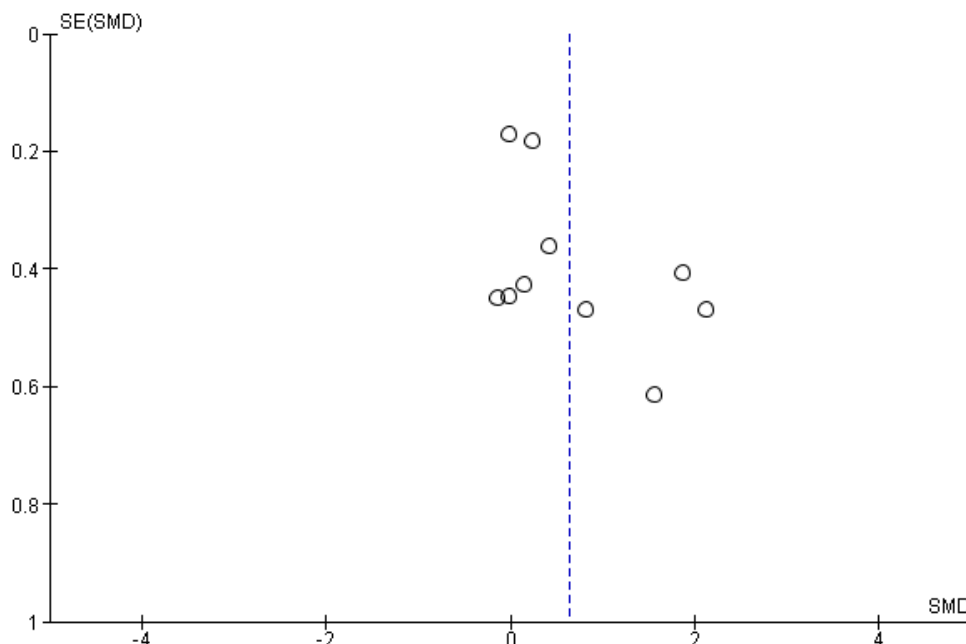


Figure 6. Funnel plot of the effect of exercise on Cardiovascular fitness in post stroke patients

Stroke survivors tend to experience a decrease in their quality of life, (Kwakkel et al., 2019) due to reduced activities as well as impact on cognitive domains, however, exercises have led to improvement in quality-of-life scores with marginally statistically significant results (SMD=0.60, CI 95% (-0.08 to 1.27); p=0.080).

Li et al. (2022) reported on the improvement of global cognition in post-stroke

patients after aerobic exercise intervention (0.51; CI 95% (0.16-0.86); p= 0.004); (Luo et al., 2020) concluded, high-intensity exercise (70-85% HRR/ VO₂peak, 3 to 5 times/week lasting 30 to 40 min for 8 to 12 weeks) may be beneficial for improving VO₂peak and 6MWT in sub-acute and chronic stroke survivors with (SMD = 0.56, CI 95% (0.40; 0.72), p=0.01, I²= 8%; n= 601, WMD= 2.53 mL/kg/min). Ali et al. (2021) concluded

that exercise can have a moderately positive influence on HRQoL and should be regarded an essential aspect of stroke

rehabilitation (SMD= -0.23 CI 95% (-0.40 to -0.07).

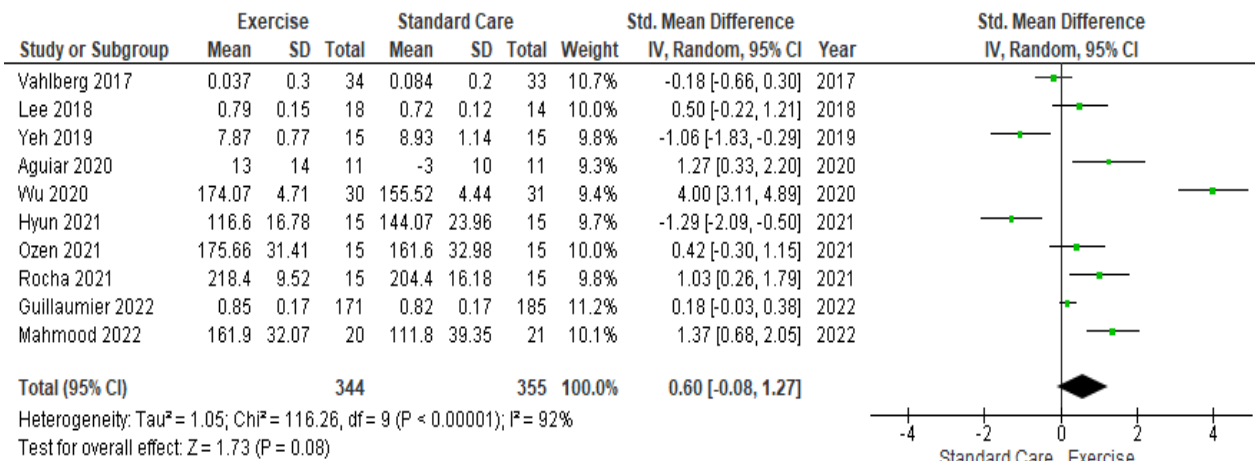


Figure 7. Forest plot of the effect of exercise on Quality of life in post stroke patients

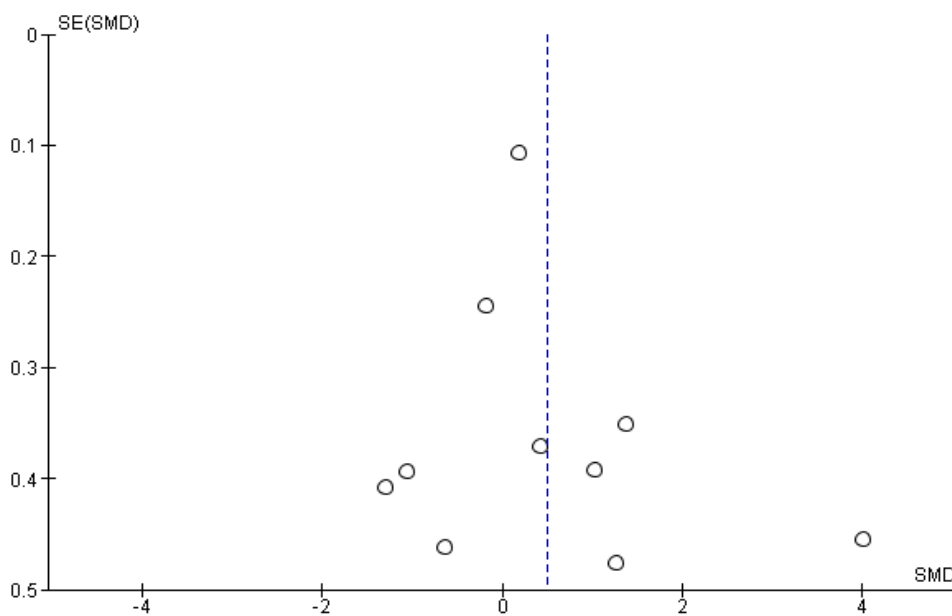


Figure 8. Funnel plot of the effect of exercise on Quality of life in post stroke patients

Exercise was linked to moderate gains in and mental health (SMD= -0.29, CI 95% (-0.49 to -0.09) domains of HRQoL.

Further research is recommended to understand stroke incidence, treatment disparities in terms of intensity and duration, and develop more effective interven-

tions. Policy measures to enhance stroke prevention programs and healthcare infrastructure are crucial, alongside health recommendations for professionals to focus on preventive measures and early diagnosis in stroke management.

AUTHOR CONTRIBUTION

Bertha Sylvester Mangu; lead researcher responsible for topic selection, search, and collection of research data. Bhisma Murti and Dr. Vitri Widyaningsih; analyzed the data, reviewed the research documentation, and interpreted the results in Revman 5.4.1

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The study was self-funded.

CONFLICT OF INTEREST

No conflict of interest.

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