Original article

Rehabilitation through high-intensity exercise in early stages of stroke: Systematic review and meta-analysis

Pedro Diez Solórzano[1,2], Iria Causín Fórneas[3], Iris Ontanilla Bayón[3], Ana Pedruelo Fraile[3], María Medina-Sánchez[2,4], Hugo Olmedillas[1,2]

[1]Functional Biology Department. University of Oviedo. Oviedo. [2]Research Group on performance, physical-sports re-adaptation, training and health (AstuRES). Oviedo. [3]University of Oviedo. Oviedo. [4]Surgery Department. University of Oviedo. Oviedo.

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Summary

Introduction: High intensity training (HIT) has been shown to be safe and feasible, and to report many health related benefits to stroke patients. The objective of this review was to examine the effects of high intensity exercise on functional recovery and health related quality of life in the acute and subacute phases of stroke.
Material and method: Six databases were searched up to october 2023, looking for studies that compared the effect of HIT to other exercise interventions in the first six months after having a stroke.
Results: Seven papers were identified 163 patients were studied with a mean age of 65 years. Statistically significant differences were found for the variables of quality of life and health (average standardized mean difference [SMD] 1,07, with a 95% Confidence Interval [95%CI] of 0,94-1,33; p<0,001), and balance (SMD 0,86, 95%CI 0,41-1,30; p=0,0002); while for the variable mental health (SMD 0,05, 95%CI -0,33-0,44; p=0,79) and cardiorespiratory fitness (SMD 0,56, 95%CI -0,01-1,14; p=0,055) the results of the meta-analysis were not significant.
Conclusions: These results suggest that the implementation of HIT protocol has positive results on quality of life and health of stroke patients, and is safe during the acute and subacute stages of stroke.

Key words:
Physical Condition. Therapeutic exercise. Quality of life. Health.

Rehabilitación mediante ejercicio de alta intensidad en las fases tempranas del ictus: revisión sistemática y metaanálisis

Resumen

Introducción: El ejercicio de alta intensidad (HIT) ha demostrado ser un modelo seguro y factible que ofrece beneficios en la salud de los pacientes con ictus. El objetivo de este metaanálisis fue examinar los efectos del ejercicio de alta intensidad sobre la recuperación funcional y la calidad de vida relacionada con la salud en las fases aguda y subaguda del ictus.
Material y método: Se realizó una búsqueda en seis bases de datos de hasta octubre de 2023 de ensayos clínicos que investigaron los efectos de HIT comparado con otras intervenciones de ejercicio en los primeros seis meses tras haber sufrido un accidente cerebrovascular.
Resultados: Se identificaron siete artículos en los que se estudió a 163 pacientes con una media de edad de 65 años. Se hallaron diferencias estadísticamente significativas para las variables de calidad de vida y salud (diferencia de medias estandarizadas [DME] promedio 1,07, con un intervalo de confianza del 95% [IC95%] de 0,94-1,33; p<0,001), y para el equilibrio (DME 0,86, IC95% 0,41-1,30; p=0,0002); mientras que para la variable salud mental (DME 0,05, IC95% -0,33-0,44; p=0,79) y capacidad cardiorrespiratoria (DME 0,56, IC95% -0,01-1,14; p=0,055) los resultados del metaanálisis fueron no significativos.
Conclusiones: Estos resultados sugieren que la implementación de un protocolo HIT es beneficioso para la mejora de la calidad de vida y la salud, así como mostrarse como una estrategia segura en pacientes en fases aguda y subaguda del ictus.

Palabras clave:
Condición física. Ejercicio terapéutico. Calidad de vida. Salud.

Correspondence: Hugo Olmedillas
E-mail: olmedillashugo@uniovi.es

Introduction

Progressive and significant ageing has been observed in western populations over recent decades. This has led to an increased incidence of age-related disorders, with strokes being the third most relevant pathology within that group in 2019[1]. Over 12 million new cases of stroke were recorded worldwide in that same year, as well as seven million deaths[2]. Both in Spain and throughout Europe, stroke is the second most widespread cause of dementia, behind Alzheimer's Disease, and the most widespread cause of disability[3].

The main consequences in patients who have suffered a stroke are reduced motor control and changes in sensitivity[4]. Furthermore, their cardiorespiratory capacity is reduced by 50%[5], which leads to greater physical inactivity[6] and therefore increased risk of a recurrent stroke[7].

High-intensity exercise includes any type of exercise that achieves at least 70% of the heart rate reserve (HR reserve) or maximal oxygen uptake (VO_2max), 75% of the maximum heart rate (HRmax) or a score of 14 on the Borg perceived exertion scale (RPE)[8]. It can be applied continuously or in intervals, through short high exertion bursts alternated with periods of low activity[9].

At present, rehabilitation programmes for stroke patients place limited emphasis on the recovery of aerobic capacity[10]. However, owing to the benefits and safety reported by HIT protocols in healthy individuals and patients with other chronic diseases[11,12], the inclusion of this type of exercise has been proposed with a view to reducing morbidity in stroke patients[10]. Moreover, there is also evidence to show that its use would be safe and beneficial for the cardiopulmonary health of these patients[13-15], although the best exercise protocol to use is still being discussed[10,16].

It has been shown that functional recovery potential is greater in the first months following the appearance of stroke[4], but the majority of existing evidence studies the impact of high-intensity exercise in the rehabilitation from this disease while including all its stages or the chronic stage only. Hence, the goal of this review was to study the effect of HIT during the acute and sub-acute stages in stroke patients.

Material and method

This systematic review with meta-analysis was carried out according to the PRISMA guide - *"Preferred Reporting Items for Systematic Reviews and Meta-Analyses"*[17].

Search Strategy

All those clinical trials that studied the effects of HIT in patients in the acute and sub-acute stages were included. The studies were considered for inclusion regardless of size, provided that they included a control group for the comparison of results.

The search for articles was conducted using the following databases: *Medline vía PubMed, Cochrane Library (Willey), Web of Science (Clarivate), Embase vía embase.com (Elsevier), SportDiscus (EBSCOhost)* and *BVSalud (Literatura Latino Americana e do Caribe em Ciências da Saúde-LILACs),* up to October 2023. Controlled vocabulary was used (MeSH terms), based on keywords and their synonyms, to refine the search. The references in articles included in systematic reviews were checked in order to identify other potentially eligible studies. A combination of the following terms was used: *"stroke", "ischemic stroke", "haemorrhagic stroke", "cerebrovascular accident", "cerebrovascular disorder", "intensity training", "intensity exercise", "aerobic intensity", "physical therapy", "high intensity training", "high intensity exercise", "aerobic interval training", "continuous moderate exercise".*

This study was registered in PROSPERO *International Prospective Register of Systematic Reviews* (CRD42023432785). Study titles and summaries that could be relevant to this review were obtained. Two authors checked the criteria for inclusion of the studies that were found. Whenever discrepancies arose regarding this matter, a consensus was reached based on a joint agreement. The complete text of the articles was subsequently assessed by using the criteria for inclusion and exclusion.

Selection of the Studies and Eligibility Criteria

The following criteria for inclusion were established: 1) clinical trials; 2) with described intervention that included high intensity based on ESC criteria; and 3) stroke in acute and sub-acute stages.

The following criteria for exclusion were chosen: 1) stroke in chronic stage; 2) measurement of intensity using another variable besides VO_2, HR or RPE; and 3) interventions that did not include aerobic exercise, defined as any activity that uses large muscle groups, can be maintained continuously and is of a rhythmic nature[18].

Extraction of Data and Bias and Quality Risk Analysis

The following information was gathered from the original studies selected: authors, year of publications, characteristics of the patients (age and average time since the appearance of the CVA), characteristics of the intervention (duration and intensity of the sessions) and the measurements of result with their statistical significance (Table 1).

The quality of the studies was assessed using the PEDro[19] scale, as well as the level of evidence using the tool from the University of Oxford Centre for Evidence-Based Medicine (OCEBM)[20].

Statistical Analysis

Jamovi v2.3.21 was used to carry out this meta-analysis. In all the studies that presented continuous data variables, the standardised mean difference (SMD) between the pre- and post-intervention values was chosen with a confidence interval of 95% as measured result (Table 2). For the variable present in more than two studies, the random effects model with statistical approach was used. As for all the other variables, the fixed effects model was used for analysis when comparing between only two studies[21].

Table 1. Comparison of studies.

Authors/ Year/Study Type	Sample	Experimental Intervention	Control	Objective	Conclusions	Measurement
Hornby *et al.* 2022 Secondary analysis	n=44 (HIT n=27 / conventional physiotherapy control n=17) Subjects with locomotive deficiencies of 1-6 months post CVA 18-75 years	Walking (steps, floor, treadmill) reaching 80% of HR res 40 sessions, over 10 weeks. 40 min of walking per session	Functional tasks at lower intensities (<40% of HR res)	To conduct an economic analysis by comparing the costs and efficacy of the HIT programme with conventional physical therapies in subjects with sub-acute CVA	The costs were higher with the HIT protocol, although the benefits obtained by the subjects (AVAC and SSS) favoured this group, which would justify its application	ICERs AVAC (Physical SF-36) SSS
Leddy *et al.* 2016 Secondary analysis	n= 33 (HIT n=21 / conventional intervention n=12)	Practice of continuous walking in multiple environments maintaining 70-80% of HRR/RPE of 15-17 (Borg Scale) Treadmill, floor and steps 40 sessions, 8-10 weeks 1 hour sessions (40 min of walking)	Standard physiotherapy	To assess changes in the performance of aerobic exercise in patients with sub-acute CVA after high-intensity training when compared with conventional therapy	Significant improvements in VO_2submax after the experimental training, with lower reductions, insignificant, in the VO_2peak and VO_2max, in favour of the intervention group Substantial gains in metabolic and locomotive functions in favour of the HIT group	Pulse oximeter 6MWT Portable indirect calorimeter
Sandberg *et al.* 2016 Randomised controlled trial	n= 56 (HIIT n=29 / control n=27) Median of 20 days post CVA Average age 70 years (53-87) Sessions in hospital (not admitted)	60 min of aerobic exercise 2/week, over 12 weeks Cycle ergometer Intervals: to reach ≥75% VO_2max / 80% HR max 14-15 Borg Scale	No kind of rehabilitation. General advice on trying to regain pre-CVA capabilities Low intensity: walking/ stretching	To examine the effects of intense aerobic activity 2/ week over 12 weeks on physical function and quality of life in subjects with sub-acute CVA	Improvement in aerobic capacity and the distance travelled in favour of the intervention group Improvement in the self-perceived measurements (EQ-5D and SIS) in favour of the intervention group	GCTT-TT 6MWT MWS10m TUG SLS EQ-5D SIS HR
Mahtani *et al.* 2017 Secondary analysis	n= 36 (HIT n=23 / control n=13) 1-6 months post CVA 18-75 years Outpatient	40 sessions, 60 min/ session over 10 weeks, 4-5 sessions/week 70-80% HR res or 15-17 Borg scale Continuous exercise Treadmill	Conventional physiotherapy interventions 40 sessions over 10 weeks	To assess the effect of 10 weeks of high-intensity walking training compared with conventional interventions on gait kinematics in individuals with sub-acute CVA	Significant improvement in speed, symmetry and kinematics on the sagittal plane in favour of the intervention group Associated increase in compensatory conduct	Speed, cadence, stride length, spatial and temporal symmetry ROM in the joints Motion capture system with 8 cameras and 32 reflective markers
Wijkman *et al.* 2017. Secondary analysis	n= 53 (HIIT n=29 / control n=27 / 3 subjects excluded during the process) Average age 70 years (53-87) Median of 22 days post CVA Sessions in the hospital (not admitted)	60 min sessions, 2/week, over 12 weeks HIIT: 14-15 Borg scale / 75% VO_2max / 80% HR max Cycle ergometer	General advice on physical activity, no specific programme	To determine whether the exaggerated increase in blood pressure from exercise in subjects with CVA is modulated by aerobic activity	The subjects in the intervention group reach higher working levels, and their aerobic and functional capacity is benefited when compared with the control group Systolic BP remains unchanged after 12 weeks of programme	HR BP WR

(continues)

Table 1. Comparison of studies *(continued)*.

Authors/ Year/Study Type	Sample	Experimental Intervention	Control	Objective	Conclusions	Measurement
Hornby *et al*. 2016 Randomised controlled trial	n=32 (HIT n=15 / control n=17) 1-6 months post CVA (average of 101 days) Outpatient	40 sessions, 60 min/ session over 10 weeks, 4-5 sessions/week 70-80% de HR res / Borg scale ≥14 Continuous exercise Initially treadmill. Later treadmill / floor / steps	Conventional physiotherapy, 40 sessions over 10 weeks Walking on treadmill or floor 30-40% HR res	To examine the effectiveness of walking-based high-intensity training on the ability to walk and other functional areas in subjects 1-6 months post CVA, compared with conventional therapy	Greater improvement in ability to walk and participation for HIT Significant differences in SSS and 6MWT for HIT Differences in spatial-temporal symmetry Balance in bipedalism and STS present similar results between groups	6MWT SSS STS
Krawcyk *et al*. 2019 Randomised controlled trial	n= 71 (HIIT n=40 / control n= 31) 1-21 days post CVA	Conventional care, HIIT protocol 3x3 min + 2 min of active recovery 5 sessions/week, over 12 weeks 77-93% HRmax / 14-16 Borg scale / TT Own choice method To encourage completion, a static bicycle was provided if necessary	Motivational talk on changes to life habits, suggestion of different types of aerobic exercise, measurement (secondary prevention), monitoring of activity	To know whether HIIT training is effective and safe for patients with lacunar CVA	HIIT is safe and effective for patients with lacunar CVA The patients can engage in this activity early in their own home when they choose the type of exercise In 3 months, there were no effects on cardiorespiratory capacity The increase in physical activity did not lead to improvement in GCT-TT power production HIIT did not significantly improve overall wellbeing (depression, chronic stress, fatigue, cognition and quality of life) or cardiovascular function (blood pressure and endothelial function)	CRF with GCT-TT MFI-20 MDI WHO-5 MoCA PAS2 Venous blood biomarkers Blood pressure monitor (EndoPAT 2000) Body composition monitor (OMRON IMC) Accelerometer (AX3) Algometer

n: number of subjects; CVA: cerebrovascular accident; HIT: high-intensity training; HIIT: high-intensity interval training; HR: heart rate; HR max: maximal heart rate; HR res: heart rate reserve; BP: blood pressure; VO2 max: maximal oxygen uptake; VO2 submax: submaximal oxygen uptake; AVAC: years of life adjusted by quality of life; SSS: self-selected speed; ICERs: incremental cost-effectiveness ratios; Physical SF-36: health questionnaire SF-36; EQ-5D: health questionnaire EuroQol-5D; SIS: stroke impact scale; RPE: rate of perceived exertion; h: hours; min: minutes; ROM: range of movement; STS: sit-to-stand test; CRF: cardiorespiratory function; 6MWT: 6-minute walk test; GCT: cycle ergometer stress test; TT: talking test; MWS10m: maximum walking speed 10 m; WR: work rate; TUG: getting up and walking test; SLS: single leg stance test; WHO-5: general wellbeing test WHO-5; MFI-20: multidimensional fatigue inventory; MDI: major depression inventory; MoCA: Montreal cognitive assessment; PAS2: physical activity scale version 2.1.

Secondary studies on the same trial are included in this meta-analysis in such a way that they cannot be analysed despite the existence of comparable variables between them, thereby limiting the scope of this work. This is a hindrance to analysis because, having taken them into consideration would have magnified the effect given that they are variables measured in the same patients.

Results

Systematic Review

As can be seen in the PRISMA flowchart (Figure 1), 2,052 studies were identified and seven articles were finally included in the review.

Characteristics of the Studies Included

Of the seven articles, three of them are randomised controlled trials (RCT)[22-24] and the remaining four are secondary analyses of those trials[25-28]. Hornby *et al.* 2022[28], Leddy *et al.*[26] and Mahtani *et al.*[27] are secondary analyses of Hornby *et al.* 2016[23]; Wijkman *et al.*[25] is a secondary analysis of Sandberg *et al.*[24]; and Krawcyk *et al.*[22] is independent.

The studies were published between 2016 and 2022. They were carried out in different countries, including Denmark, Sweden and the United States.

Characteristics of the Participants

The participants who formed part of the studies analysed were aged between 18 and 75. The participants were required to have a minimum

Table 2. Standardised measurements for the meta-analysis variables.

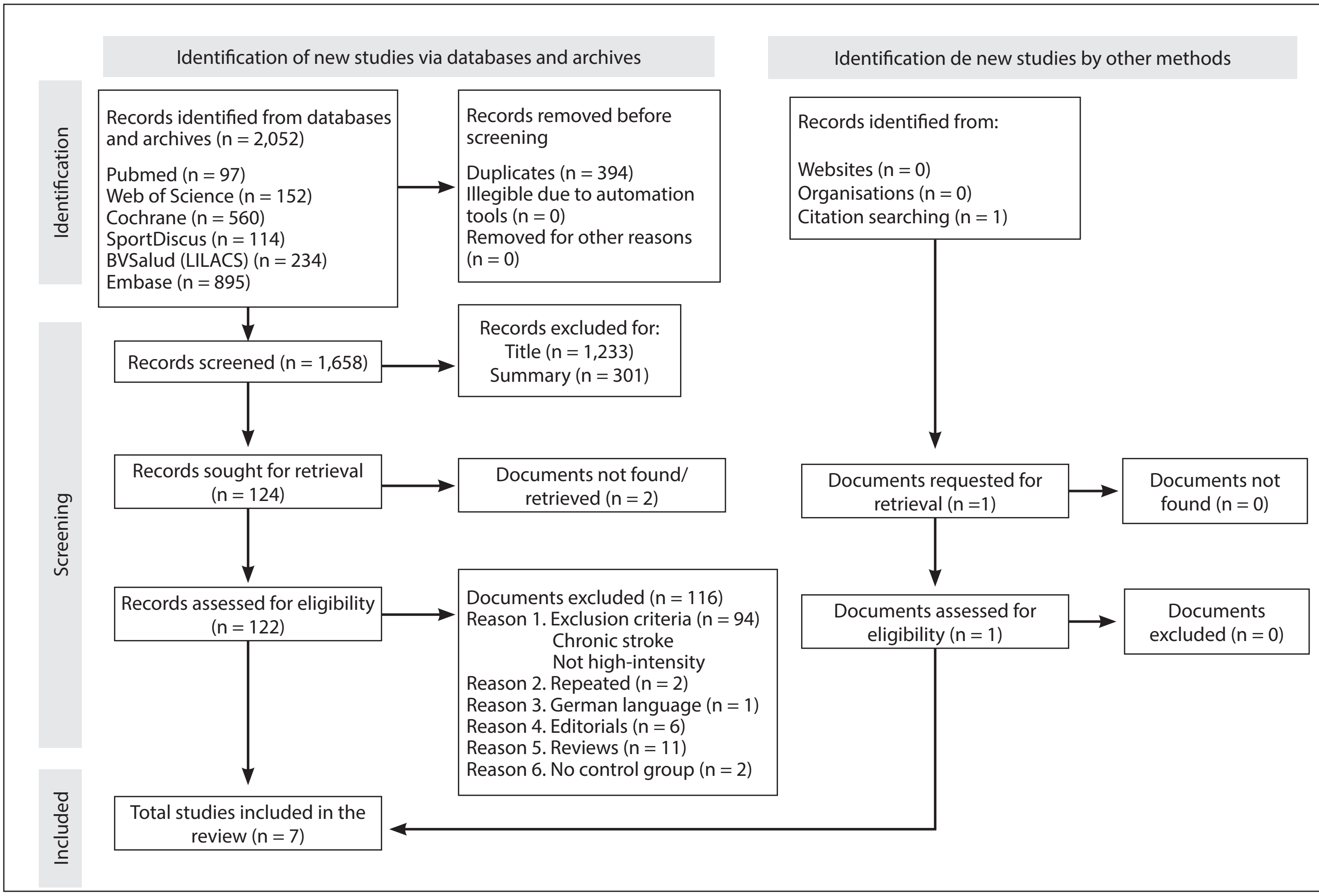
Variables	Article	Result to measure	Nº of subjects	Intervention group			Control group		
				Ni	DMi	DE DMi	Nc	DMc	DE DMc
Cardiorespiratory capacity	Sandberg *et al.* 2016	6MWT (m)	56	29	105.1	76.2	27	35.9	93.2
	Hornby *et al.* 2016	6MWT (m)	32	15	116.0	101.4	17	29.0	77.5
	Krawcy *et al.* 2019	GCT-TT (Watts)	63	31	7.7	31.7	32	6.7	32.7
Quality of life and health	Sandberg *et al.* 2016	EQ5D VAS	56	29	14.9	16.6	27	0.7	12.9
	Hornby *et al.* 2016	Physical SF36	32	15	9.0	4.9	17	2.0	5.3
Mental health	Krawcyk *et al.* 2019	WHO-5	63	31	4.0	15.3	32	5.0	12.4
	Hornby *et al.* 2022	Subdomain mental health	44	27	3.0	13.1	17	0.0	10.6
Balance	Sandberg *et al.* 2016	SLS	56	29	10.4	7.4	27	0.9	7.6
	Hornby *et al.* 2016	Berg scale	32	15	8.0	10.6	17	5.0	10.8

Variables	Article	Result to measure	Ni	Intervention group					
				PREi value	DE PREi	POSTi value	DE POSTi	DMi	DE DMi
Cardiorespiratory capacity	Sandberg *et al.* 2016	6MWT (m)	29	394.7	114.7	499.8	93.1	105.1	76.2
	Hornby *et al.* 2016	6MWT (m)	15	116.0	88.0	232.0	149.0	116.0	101.4
	Krawcyk *et al.* 2019	GCT-TT (Watts)	31	118.5	43.1	126.2	46.3	7.7	31.7
Quality of life and health	Sandberg *et al.* 2016	EQ5D VAS	29	72.3	22.3	87.2	9.1	14.9	16.6
	Hornby *et al.* 2016	Subdominio mental health	15	35.0	7.3	44.0	6.1	9.0	4.9
Mental health	Krawcyk *et al.* 2019	WHO-5	31	65.0	23.0	69.0	16.0	4.0	15.3
	Hornby *et al.* 2022	Physical SF36	27	51.0	19.0	54.0	18.0	3.0	13.1
Balance	Sandberg *et al.* 2016	SLS	29	9.6	10.3	20.0	10.6	10.4	7.4
	Hornby *et al.* 2016	Berg scale	15	32.0	16.0	40.0	11.0	8.0	10.6

Variables	Article	Result to measure	Nc	Control group					
				PREc value	DE PREc	POSTc value	DE POSTc	DMc	DE DMc
Cardiorespiratory capacity	Sandberg *et al.* 2016	6MWT (m)	27	384.3	131.9	420.2	131.6	35.9	93.2
	Hornby *et al.* 2016	6MWT (m)	17	131.0	108.0	160.0	111.0	29.0	77.5
	Krawcyk *et al.* 2019	GCT-TT (Watts)	32	119.5	44.0	126.2	47.9	6.7	32.7
Quality of life and health	Sandberg *et al.* 2016	EQ5D VAS	27	80.4	18.9	81.1	17.5	0.7	12.9
	Hornby *et al.* 2016	Physical SF36	17	36.0	7.5	38.0	7.4	2.0	5.3
Mental health	Krawcyk *et al.* 2019	WHO-5	32	64.0	18.0	69.0	17.0	5.0	12.4
	Hornby *et al.* 2022	Subdomain mental health	17	63.0	12.0	63.0	16.0	0.0	10.6
Balance	Sandberg *et al.* 2016	SLS	27	11.8	10.8	12.7	10.7	0.9	7.6
	Hornby *et al.* 2016	Berg scale	17	33.0	16.0	38.0	14.0	5.0	10.8

Ni: sample size in intervention group; DMi: standardised average difference in intervention group; DE DMi: standard deviation of the standardised average difference of the intervention group; Nc: sample size in control group; DMc: standardised average difference in control group; DE DMc: standard deviation of the standardised average difference of the control group; PREi value: pre-intervention average of the experimental group; DE PREi: standard deviation of the pre-intervention of the experimental group; PREc value: pre-intervention average of the control group; DE PREc: standard deviation of the pre-intervention of the control group; 6MWT: 6-minute walking test; GCT-TT: stress test on cycle ergometer with talking test; EQ5D VAS: questionnaire EuroQol-5D; Physical SF36: health questionnaire SF36; Subdomain mental health: health questionnaire SF-36, subdomain mental health; WHO-5: general wellbeing index WHO-5; SLS: single leg stance test; m: metres; Watts: watts.

Figure 1. PRISMA flowchart.



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level of stability and mobility that would enable the exercise (ability to walk five metres with minimal or moderate assistance), as well as the ability to understand written and spoken instructions, including the capacity to give informed consent[22-28].

Characteristics of the Interventions and Conditions of the Control Groups

Table 3 shows the information gathered on the intervention in the studies for this work, including RCTs and secondary analyses. An intervention model based on exercise at intervals was used in three studies[22,24,25], while the other four used continuous exercise. Different instruments were used for the rehabilitation: a treadmill was used in four of the studies[23,26-28], an ergometer in three[22,24,25] and steps or walking on flat ground was also used in another three[23,26,27].

Different parameters were used to measure the intensity of the exercise, it being possible to use several of them in each study:

VO_2max and HRmax was used in two studies[24,25], HR reserve in five[23,26-29] and the RPE score in another five[22,23,25-27].

The intervention was spread over between eight and twelve weeks. In terms of the session frequency, this was two days a week in two publications[24,25] and between four and five days a week in the others. Only one of the studies had a duration of less than 40 minutes[22]. Finally, six studies were carried out in an outpatient environment and only one in a hospital environment[25].

A "(+12)" is added in brackets in certain sections. This corresponds to patients of the Holleran *et al.*[29] protocol, a preliminary study that was carried out to know whether it was possible to carry out the Hornby *et al.*[23] study and which therefore follows the same intervention but the patients of which were not added to the tables because there is no control group.

Quality Assessment

The methodological quality of each study is represented in Table 4. It can be seen that five of the publications included present a good quality[22-25,28] given that they obtained a rating of between 6 and 8 points out of 10. Of the remaining two, one obtained a score of 5[27] and

Table 3. Comparison of interventions.

Intervention	Subtype	RCTs and secondary analyses	Participants
Type	HIT	4	86(+12)
	HIIT	3	98
Method	Treadmill	4	86(+12)
	Cycle ergometer	3	98
	Floor/steps	3	63(+12)
Intensity measurement	VO_2max	2	58
	RHmax	2	85
	HR res	5	99(+12)
	RPE (Borg)	5	128(+12)
Time	≤40 min	1	40
	≥40 min	6	144(+12)
Frequency	≤4 days/week	2	58
	4-5 days/week	5	126(+12)
Programme duration	8-12 weeks	7	184(+12)
Environment	Hospital	1	29
	Outpatient	6	155(+12)

HIT: high-intensity training; HIIT: high-intensity interval training; VO_2max: maximal oxygen uptake; HRmax: maximal heart rate; HR res: heart rate reserve; RPE (Borg): rate of perceived exertion (Borg scale); "(+12)" corresponds to the subjects in the Holleran *et al,* protocol.

the other obtained a score of 4[26], this being considered an acceptable level of evidence.

The selection criteria were specified in all the studies and they began with groups of patients who presented similar baseline characteristics.

Except in one[26], all the subjects were given a random and concealed allocation. The assessors were blinded in some[22-24,26]. Except in two[26,27], results were presented from all the participants to whom the intervention was allocated or who were allocated to the control group. When this was not possible, the data were analysed on an "intention-to-treat" basis. Finally, in none of the studies were the measurements of the results obtained in more than 85% of the patients. This was because they did not reach that percentage or because no explicit mention was made of it.

On the other hand, all the trials met the requirements of a randomised clinical trial and were classified as level 1b.

Meta-analysis

- *Cardiorespiratory capacity.* A total of three studies reported pre- and post-intervention data for cardiorespiratory capacity. The SMDs varied between 0.03 and 0.95, with all the estimates being positive. The average estimated SMD based on the random effects model was 0.56, with a confidence interval of 95% (CI95%) of between -0.01 and 1.14. The average result presented no significant differences ($z = 1.92$, $p = 0.055$). The Q test for heterogeneity was not significant. However an average heterogeneity in the results was observed ($Q(2) = 5.83$, $p = 0.05$, $tau^2 = 0.16$, $I^2 = 64.8\%$). The prediction interval of 95% given for the results varies between -0.42 and 1.54 (Figure 2).
- *Quality of life and health.* A total of two studies reported pre- and post-intervention data for quality of life and health. The SMDs varied between 0.94 and 1.33, with all the estimates being positive. The average estimated SMD based on the fixed effects model was 1.07, with a CI95% of between 0.62 and 1.52. The average result presented no significant differences ($z = 4.69$, $p <0.0001$). According to the Q test, there was no significant amount of heterogeneity in the true results ($Q(1) = 0.67$, $p = 0.41$, $I^2 = 0.00\%$) (Figure 3).
- *Mental health.* A total of two studies reported pre- and post-intervention data for mental health. The SMDs varied between -0.07 and 0.24, with half of the estimates being negative (50%). The average estimated SMD based on the fixed effects model was 0.05, with a CI95% of between -0.33 and 0.44. The average result presented no significant differences ($z = 0.27$, $p = 0.79$). According to the Q test, there was no significant amount of heterogeneity in the true results ($Q(1) = 0.61$, $p = 0.44$, $I^2 = 0.00\%$) (Figure 4).
- *Balance.* A total of two studies reported pre- and post-intervention data for balance. The SMDs varied between 0.27 and 1.25, with all the estimates being positive. The average estimated SMD based on the fixed effects model was 0.86, with a CI95% of between 0.41 and 1.3. The average result presented no significant differences ($z = 3.79$, $p = 0.0002$). According to the Q test, the true results are apparently heterogeneous ($Q(1) = 4.49$, $p = 0.03$, $I^2 = 77.75\%$) (Figure 5).

Table 4. PEDro scale *(Physiotherapy Evidence Database)*.

Studies	1	2	3	4	5	6	7	8	9	10	11	Total PEDro scale
Hornby *et al.* 2022	X	X	X	X					X	X	X	6/10
Leddy *et al.* 2016	X			X			X			X	X	4/10
Krawcyk *et al.* 2019	X	X	X	X			X		X	X	X	7/10
Sandberg *et al.* 2016	X	X	X	X			X		X	X	X	7/10
Mahtani *et al.* 2017	X	X	X	X						X	X	5/10
Wijkman *et al.* 2018	X	X	X	X					X	X	X	6/10
Hornby *et al.* 2016	X	X	X	X			X		X	X	X	7/10

1 selection criteria; 2 random allocation; 3 concealed allocation; 4 baseline comparison of the groups; 5 blinded subjects; 6 blinded therapists; 7 blinded assessors; 8 key outcome measurements in >85% subjects; 9 "intention to treat" monitoring and analysis; 10 comparison between groups; 11 point estimates and variability. An "X" indicates a "yes" score and its absence a "no".

Figure 2. Forest plot for cardiorespiratory capacity.

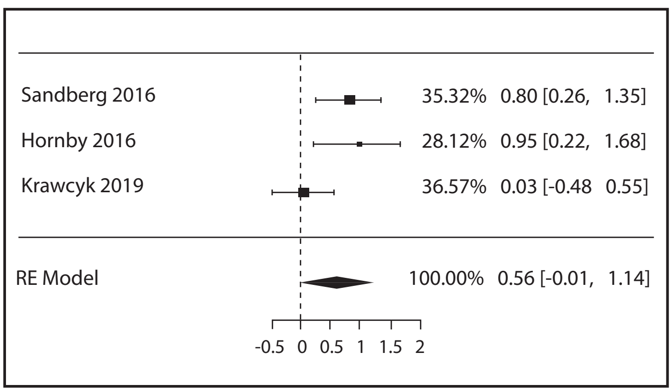


Figure 4. Forest plot for mental health.

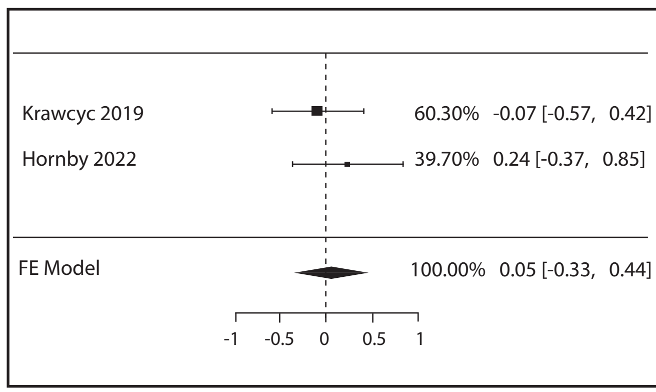


Figure 3. Forest plot for quality of life and health.

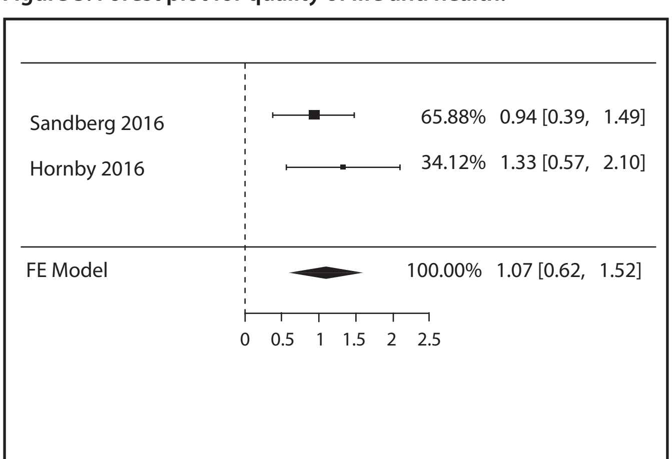
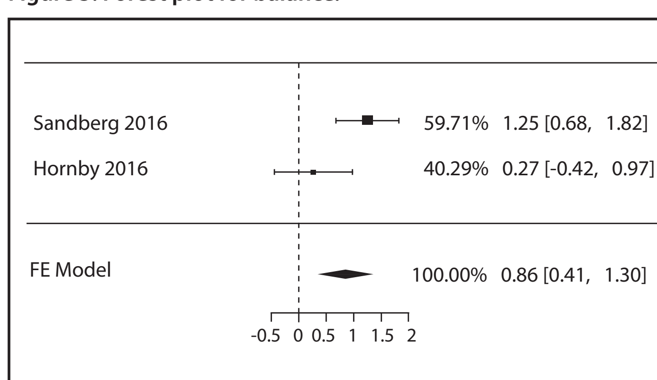


Figure 5. Forest plot for balance.



Publication bias tests were observed using the Egger test for the balance variable only (p = 0.03).

Adverse Events

The adverse episodes found were analysed in depth, with no significant differences observed between groups. The groups were similar in terms of the number of events. The events included fractures, wounds, falls without damage, joint and muscle pain, as well as cardiorespiratory events (high blood pressure, angina and bronchoaspiration), which required hospital admission[23,26]. Two articles do not record this information[27,28], one article presented no adverse events related to the intervention[22] and another two presented no serious adverse events throughout the full duration of the trial[24,25].

Discussion

Based on the data presented in this meta-analysis, we suggest that a protocol of high-intensity exercise has beneficial effects on quality of life and health, as well as balance, but not significant in terms of mental health and cardiorespiratory capacity in the early stages of patients with stroke when compared with conventional interventions. It was possible to include four of the seven articles in the quantitative analysis section, with good evidence quality.

Cardiorespiratory Capacity and Haemodynamic Variables

We found positive results, albeit insignificant for cardiorespiratory capacity in the intervention group. In a previous meta-analysis, in which chronic patients were included, significant beneficial effects were reported from HIT on cardiorespiratory capacity[13]. This could be because the patients at this stage of recovery usually begin with reduced cardiovascular capacity, meaning they present a greater margin of improvement. However, in the early stages of stroke, the potential for capacity recovery to pre-stroke values is greater given that the patients have not been suffering the consequences of their disease for as long and, therefore, have not deteriorated due to inactivity over such a long time. Furthermore, greater aerobic capacity has been linked to a reduction in cardiovascular and recurrent stroke risk factors, partly due to the decrease it causes in blood pressure and serum cholesterol levels[30]. Our analysis did not study haemodynamic levels, although the original articles by Krawcyk *et al.*[22] and Wijkman *et al.*[25] did observe a significant improvement in the heart rate reduction, in favour of the intervention.

Quality of Life and Health

Previous studies have confirmed that aerobic exercise not only improves cardiorespiratory capacity and disability but also mobility and balance at any stage of recovery with a strong level of evidence[7,16], which has a direct impact on quality of life. In this regard, we were able to confirm that HIT significantly improves quality of life and health in the intervention group when compared with the control group. Nonetheless, this does not correspond to the results described previously by other authors[31]. This discrepancy could be explained by the lower intensity to which the intervention group in said study was subjected (60-80% HR reserve).

Mental Health and Cognition

In terms of mental health, this study did not observe that the HIT model offers any greater benefits than classic rehabilitation protocols. In this regard, the impact had by aerobic exercise on existing depression and mental wellbeing is not conclusive[16]. This could be due to the limited number of patients recruited, meaning that the results produced may not be definitive.

Balance

Our quantitative analysis coincides with the conclusions reached in the review by Saunders *et al.*[16], in which it is established that aerobic exercise produces a greater improvement in balance when compared with conventional rehabilitation interventions at any stage of recovery with a strong level of evidence.

Kinematics

The changes in kinematics were studied from different perspectives. Hence, Holleran *et al.*[29] reported a significant improvement in the speed, cadence and length of stride. This implies that high-intensity exercise may be a factor that improves the prognosis when recovering the capacity of an efficient gait, although the evidence to date is limited due to the number of studies found.

Adverse Events

No serious adverse events were observed in any of the studies included. However, it should be stressed that they were only analysed in depth in two of the seven articles without showing a clear link to the intervention[23,26]. Others mention the lack of serious adverse events during the trial[24,25]; Krawcyk *et al.*[22] found no other kind of adverse event; and this is not mentioned in the last two[27,28].

Other reviews strengthen the safety of HIT in patients with stroke at all stages of recovery, such as Luo *et al.*[13], Anjos *et al.*[15], and Fahey *et al.*[32], in which no significant differences were found between the high-intensity exercise groups and the control groups, there being no increase in the rate of adverse events when compared with conventional rehabilitation.

The available evidence suggests that the model is safe and well tolerated. However, despite the safety of these protocols, Wijkman *et al.*[25] observed a significant elevation in systolic blood pressure in response to the exercise. For this reason, we consider it essential that this model of exercise be prescribed and supervised by trained professionals and carefully adapted to the individual needs of each subject, together with rigorous control of the physiological variables of each patient during the intervention.

Strengths and Limitations

It should be taken into consideration that different terminology is used to define the intensity of exertion. In our case, it was decided to follow the indications of the European Society of Cardiology (ESC). For that reason, a number of studies were rejected under this criteria, mainly because the levels of intensity they proposed were lower than the established. On the other hand, the search was performed in major databases, so we therefore believe that we successfully grouped together the most relevant studies on the topic.

Due to the recent nature of this line of research (the earliest study was conducted in 2016), there is little literature available. This is a limitation and we should be cautious in the contributions presented here. Nonetheless, the analysis of methodological quality confirms that five trials obtained a good level of quality and an acceptable level of evidence in the remaining two.

Conclusions

Our meta-analysis suggests that use of an HIT protocol is beneficial in improving quality of life and health, as well as showing itself to be a safe strategy in patients in acute and sub-acute stages of stroke.

Conflict of Interest

The authors declare no conflict of interest whatsoever.

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