Title: Aerobic Training in Stroke Rehabilitation: What is known and what needs to be addressed – A systematic review**.**

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Abstract

Background: Most stroke survivors live with residual physical impairments that may promote a sedentary lifestyle and resultant secondary complications, especially poor cardio-respiratory fitness. This systematic review was conceived to examine the extent of research on the effect of aerobic exercise on health outcomes of stroke survivors as a prelude to a clinical trial.

Method: Electronic databases were searched with the last search performed in May, 2014. The methodological quality of studies was assessed using the PEDro scale. High-quality randomized controlled trials (RCTs) were considered level 1 evidence while lower-quality RCTs were considered level 2 evidence.

Result: A total of 642 articles were generated from the search strategy; 10 articles fulfilled all criteria and were selected for this review. 50% of these studies recruited stroke survivors with ischaemic type of stroke while 30% had individuals with either ischaemic or haemorrhagic types. 70% of the studies had good scores while 30% had fair scores in methodological quality. The majority of the studies used VO2max as the outcome for assessing aerobic fitness; a few studies (10% each) assessed anthropometric outcomes and biochemical profile. No study assessed a haematological profile nor compared the effects of continuous and interval aerobic exercise on stroke outcomes.

Conclusion: A gap in clinical trials on the effects of aerobic exercise on biochemical, haematological and anthropometric profiles of stroke survivors exists as well as in the comparative effects of continuous and interval training on stroke outcomes.

Key Words: Aerobic, Exercise, Stroke, Review.

Introduction

Stroke is one of the most common chronic conditions seen in older adults, with an incidence approximately doubling each decade after the age of 55 years (Ovbiagele et al, 2013; Feigin et al, 2003). Most stroke survivors continue to live with residual physical impairments, which may promote a sedentary lifestyle and resultant secondary complications (Calmels et al, 2011). One of the secondary complications commonly observed following stroke is poor cardio-respiratory fitness (Chu et al, 2004). Low cardio-respiratory fitness is related to poor functional performance (Mattlage et al, 2013), increased energy cost of ambulation (Hamzat, 2002), and increased risk of stroke and cardiovascular disease (Kurl et al, 2003). Indeed, cardiac events and recurrent stroke are major occurrences in stroke survivors (Hardie et al, 2004). Increasing exercise capacity following a stroke can help prevent deterioration of the cardiovascular system (Sacco et al, 2013). Such effects are important given that cardiovascular disease is the leading prospective cause of death in individuals with stroke, coupled with the fact that cardiovascular fitness in individuals with stroke has been found to be as low as 50–80% of the age and sex-matched values in inactive individuals (MacKay-Lyons and Makrides, 2004; Pang et al, 2005). This implies that the aerobic fitness level of many stroke survivors does not even reach the critical value that is essential for independent living (Cress and Meyer, 2003). Therefore, increasing exercise capacity in persons with stroke to improve their ability to perform functions of daily living, which might be limited by weakness and fatigue secondary to the stroke, is a desired strategy in stroke rehabilitation.

Aerobic exercise training has been known to have an important role in improving cardiovascular fitness and other health outcomes among stroke patients by breaking the vicious cycle of physical inactivity and functional decline. The objective of this systematic review was to examine the extent of research on the effect of aerobic exercise on health outcomes of stroke survivors in order to provide an enabling platform for the justification of a clinical trial on the effect of interval and continuous aerobic exercise training on the physical, anthropometric and haemato-biochemical profiles of stroke survivors.

Methods

The PICO method (CEBM, 2014) was used to define the four major components of the systematic review question:

P (Patient) = Patients with stroke;

I (Intervention) = Exercise programmes that include a substantial aerobic exercise component, with aerobic exercise being defined as ‘a structured exercise programme that involves the use of large muscle groups for extended periods of time in activities that are rhythmic in nature, including but not limited to walking, stepping, running, swimming, cycling and rowing (ACSM, 2010);

C (Comparison) = Control group without intervention or other activities designed to improve aerobic fitness;

O (Outcome) = aerobic fitness and other health indicators in cardiovascular, physical function, anthropometry, haematology and biochemistry.

For an article to be selected, the following inclusion criteria had to be met: a randomised controlled trial that investigated the effects of aerobic exercise in stroke patients between 1990 and 2013; the aerobic training protocol clearly described and the study published in English.

The outcomes of interest in this systematic review are aerobic fitness, e.g., maximal oxygen consumption (VO2max) achieved during a graded exercise test on a bicycle ergometer or treadmill; anthropometric outcomes that included body composition, body weight, body mass index (BMI) and waist girth; and cardiovascular outcomes such as resting heart rate and blood pressure. Other variables are biochemical outcomes such as blood lipid profile, glucose tolerance and insulin sensitivity, haematological outcomes such as full blood count, haemoglobin concentration, red and white blood cell counts; physical outcomes such as motor function, balance, gait speed and functional ability. The comparative effects of interval and continuous aerobic training formed an important research question, and these outcomes were also examined in this systematic review.

The following electronic databases were searched online: MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library Database of Systematic Reviews and Physiotherapy Evidence Database (PEDro), with the last search performed in May, 2014. For these databases, the keyword ‘stroke’ was used for the search. The titles and abstracts of the articles generated by the search strategy were first screened to eliminate irrelevant articles. For the remaining papers, the full text was reviewed to determine eligibility. The reference list of each selected article was checked to identify other potential articles. The PEDro score of each selected study, which is an indicator of the methodological quality (9–10 = excellent; 6–8 = good; 4–5 = fair; 4 = poor), was checked. The PEDro scale is a common tool used to assess the scientific rigor of experimental studies and has been shown to be a more comprehensive measure of methodological quality than the Jadad scale in the stroke rehabilitation literature (Bhogal et al, 2005). Based on the PEDro assessment and sample size used, the level of evidence was assigned to each study. High-quality random controlled trials (RCTs) (rated as good or excellent by PEDro and sample size greater than 50) were considered level 1 evidence, whereas lower-quality RCTs were considered level 2 evidence (rated as fair or poor by PEDro, or sample size < 50) (Warburton et al, 2011; Jamnik et al, 2011).

Results

A total of 642 articles were generated from the search strategy; 10 articles fulfilled all the criteria and were selected for this review. Fifty percent of these studies (Globas et al, 2012;

Tolendano et al, 2011; Ivey et al, 2007; Katz-Leurer et al, 2006 and Macko et al, 2005) recruited stroke survivors with ischaemic type of stroke while 30% (Katz-Leure et al, 2003a; Katz-Leure et al, 2003b and Duncan, 2003) had individuals with either ischaemic or haemorrhagic types participating (as shown in **Table 1**). Table 1 also reveals that over 60% of the studies recruited individuals who have had stroke beyond three months (Globas et al, 2012; Outermans et al, 2010; Ivey et al, 2007; Katz-Leurer et al, 2006; Macko et al, 2005; Duncan, 2003 and Potempa, 1995).

Table 1: Summary of Stroke Characteristics

Item	No.	Percentage
Stroke type		
Ischaemic only	5	50
Haemorrhagic only	0	0
Both	3	30
No report	2	20
Stage of Recovery (months)		
Acute (0-3)	3	30
Sub-acute (3-6)	2	20
Chronic (> 6)	4	40
Acute & sub-acute	1	10

Methodological quality was assessed using the PEDro rating criteria; 70% (Globas et al, 2012; Toledano et al, 2011; Outermans et al, 2010; Katz-Leurer et al, 2006; Duncan, 2003; Katz-Leurer et al, 2003a and Katz-Leurer et al, 2003b) of the studies had good sores and 30% (Ivey et al, 2007; Macko et al, 2005 and Potempa, 1995) had a fair score. 60% of the studies used a sample size between 21 and 40 stroke survivors. Considering both the PEDro ratings and sample size used, three studies provided level 1 evidence (Duncan, 2003; Katz-Leurer et al, 2003a and Katz-Leurer et al, 2003b) while the other seven were considered level 2 studies (as shown in **Table 2**).

Table 3 summarised the aerobic exercise protocols used in the various studies being reviewed. Half of the studies (Katz-Leurer et al, 2006; Duncan, 2003; Katz-Leurer et al, 2003a; Katz-Leurer et al, 2003b and Potempa et al, 1995) used bicycle ergometry as the exercise modality while 30% (Globas et al, 2012; Ivey et al, 2007 and Macko et al, 2005) used treadmill exercise.

Table 2: Summary of Methodological Qualities of Studies

Item	No.	Percentage
PEDro Rating Criteria		
Eligibility criteria specified	9	90
Subjects randomly allocated to group	10	10
Allocation concealed	3	30
Group similar at baseline	10	10
Subject blinding	0	0
Therapist blinding	0	0
Assessor blinding	6	60
Less than 15% drop out rate	5	50
Between group statistical comparison reported	10	100
Point estimate and variability measure reported	10	100
PEDro Total Score		
Excellent (9-10)	0	0
Good (6-8)	7	70
Fair (4-5)	3	30
Poor (0-3)	0	0
Sample Size		
1 – 10	0	0
11 – 20	0	0
21 – 30	2	20
31 – 40	1	10
41 – 50	3	30
Greater than 50	4	40
Level of Evidence		
Level 1	3	30
Level 2	7	70

Fifty percent of the studies (Ivey et al, 2007; Katz-Leurer et al, 2006; Macko et al, 2005; Duncan, 2003 and Potempa et al, 1995) had the participants performing aerobic exercise for 21 to 40 minutes per session and 80% (Globas et al, 2012; Outermans et al, 2010; Ivey et al, 2007; Macko et al, 2005; Duncan, 2003; Katz-Leurer et al, 2003a; Katz-Leurer et al, 2003b and Potempa et al, 1995) had exercise protocols designed such that aerobic exercise was performed 3 to 4 times per week. 60% of the studies had their aerobic exercise spanning between 5 to 12 weeks. **Table 3** also revealed that 80% of the studies used high intensity aerobic exercise; 90% of the articles reported use of continuous mode of aerobic exercise, and 10% (Duncan, 2003) reported use of interval exercise, while no study was found that used or compared continuous and interval aerobic exercise effects on stroke survivors.

Table 3: Summary of Aerobic Exercise Protocol

Item	No.	Percentage
Modality		
Bicycle ergometer	5	50
Treadmill	3	30
Both	1	10
Others	1	10
Duration Per Session (mins)		
1 – 20	2	20
21 – 40	5	50
41 – 60	3	30
> 60	0	0
No. of Sessions per Week		
1 – 2	1	10
3 – 4	8	80
> 4	1	10
Total Exercise duration (weeks)		
1 – 4	2	20
5 – 8	3	30
9 – 12	3	30
> 12	2	20
Intensity		
Low (20-39% HRR; 50-63% HRmax)	1	10
Moderate (40-59% HRR; 64-76% HRmax)	1	10
High (60-84% HRR; 77-93% HRmax)	8	80
Mode		
Continuous	9	90
Interval	1	10
Both (comparison)	0	0

HRR = Heart Rate Reserve
HRmax = Maximum Heart Rate

The majority of the studies used VO2max as the outcome for assessing aerobic fitness, while a few studies (10% each) assessed anthropometric studies such as BMI, body weight, free fat mass and percentage body fat. 30% of the studies assessed resting heart rate and blood pressure as measures of the cardiovascular profile. Most of the studies assessed the following physical profiles in this descending order: walking endurance, balance, walking speed and activities of daily living as shown in **Table 4**.

Table 4: Summary of Outcomes

Item	No.	Percentage
Aerobic Fitness		
VO2max	5	50
Max work load	1	10
Anthropometry		
BMI	1	10
Body weight	1	10
Free fat mass	1	10
% fat	1	10
Cardiovascular Profile		
RHR	3	30
BP (SBP & DBP)	3	30
Physical Profiles		
Walking speed	3	30
Walking endurance	6	60
Balance	4	40
ADL	3	30
Energy cost	1	10
Quality of life	1	10
Adverse effect	1	10
Biochemical Profiles		
Fasting Glucose	1	10
Fasting Insulin	1	10
Haematological Profiles	0	0

ADL = Activities of Daily Living

Discussion

The majority of the studies in this review recruited individuals with ischaemic type of stroke, and the few studies that recruited both ischaemic and haemorrhagic stroke patients still had ischaemic stroke survivors in greater number, e.g., the study by Duncan et al (2003) had 88.1% and 91.7% of participants with ischaemic stroke in the experimental and intervention groups, respectively. This may be attributed to the fact that haemorrhagic subtypes of stroke are less common than ischemic stroke (Sacco et al, 2013) and have higher mortality and morbidity associated with them (Kernan et al, 2014; Gordon et al, 2004) coupled with the fact that intra-cerebral haemorrhage alone has a nearly 40% case-fatality rate at 30 days (Palm et al, 2010; Kleindorfer et al, 2010). It may therefore be possible that very few patients with haemorrhagic stroke were available for the studies. It is also possible that the few available patients with haemorrhagic type of stroke may not have met the inclusion criteria because of the delicate nature of haemorrhagic stroke, especially the intra-cerebral type. Most of the studies recruited fewer participants in the acute phase of stroke except for a few studies that were targeted at patients in the acute phase from the outset. This observation may not be too far from the level of exertion required in the aerobic training, noting that four-fifths of the studies used high intensity exercises. Also, some studies excluded non-ambulatory patients, and this may have excluded some patients in the acute phase because at this phase, few stroke survivors may have been ambulatory.

Almost all the studies used bicycle ergometer and/or treadmill as their aerobic training modality. This could be because treadmill and bicycle ergometers are popular modalities used for aerobic training (Sacco et al, 2013; Gordon et al, 2004), and their use have been shown to have positive effects on ambulation and performance of activities of daily living among stroke survivors (Calmels et al, 2011; Ivey et al, 2007; Macko et al, 2005). Most of the studies used exercise protocols lasting between 20 – 60 minutes per session, 3 – 4 sessions a week for 5 – 12 weeks at high intensity (60 – 84% heart rate reserve or 77 – 93% maximal heart rate). This is in line with the recommendation of the American Heart Association (AHA) for stroke survivors. AHA recommends an optimal dosage according to the individual's needs and limitations. That aerobic training modes may include leg, arm, or combined arm-leg ergometry at 40% to 70% of peak oxygen consumption or heart rate reserve with perceived exertion used as an adjunctive intensity modulator. The recommended frequency of training is 3 to7 days a week, with duration of 20 to 60 min/day of continuous or accumulated exercise, depending on the patient's level of fitness. Also, intermittent training protocols may be needed during the initial weeks of rehabilitation because of the extremely deconditioned level of many convalescing stroke patients (Gordon et al, 2004). All the studies (except Duncan, 2003) used continuous mode only. None of the studies included in this review compared the effects of interval and continuous aerobic exercise modes. The superlative effects of continuous and interval training has been a hot debate in the field of exercise physiology and rehabilitation.

Maximal oxygen consumption (VO2max), walking endurance and speed, balance and a few cardiovascular parameters were the major outcomes assessed, whereas less attention was given to outcomes such as anthropometric, haematological and biochemical profiles. This may be a result of the fact that the majority of the studies had experts in physiotherapy as lead authors, resulting in the tendency to focus on physical profiles of stroke survivors. Aerobic exercise had significant positive effects on VO2max (Globas et al, 2012; Ivey et al, 2007; Macko et al, 2005), walking speed (Globas et al, 2012; Toledano et al, 2011), and activities of daily living and quality of life (Globas et al, 2012). However, no significant effect was found on BMI, free fat mass, percentage body fat, fasting lipid and glucose level. It may therefore be necessary to carry out more studies to assess the effect of exercise on haematological and biochemical profiles.

Conclusion

Most studies assessing the effects of aerobic exercise emphasised the physical and cardiovascular profiles with little or no emphasis on the haematological and biochemical profiles. Also, the majority of studies used either continuous mode only or interval modes only (on very few occasions), and no study seemed to have compared the effects of these two modes on stroke outcomes. We therefore recommend a clinical trial that will assess the effects of continuous and interval training on the physical, anthropometric and haemato-biochemical profiles of stroke survivors.

Conflict of interest: None declared

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