

## Effects of Exercise Training on Cardiovascular and Autonomic Parameters in Stroke Survivors: A Systematic Review

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### Abstract

Negative changes in cardiovascular and autonomic variables in stroke survivors have encouraged the global scientific community to focus on investigating therapeutic strategies to mitigate stroke damage. The objective of the present study was to describe the effects of exercise training on cardiovascular and autonomic variables in stroke survivors. We used the PICO (population, intervention, control/comparison, and outcome variables) model for the search of articles in PubMed and Physiotherapy Evidence Databases from 2009 to December 2018. The following data were also recorded: type of study, author, year of publication, participants (time after stroke, sample size, and age) and benefits of exercise training. A total of 544 articles were initially selected, of which nine peer-reviewed articles met the search criteria. These nine studies enrolled 611 participants (middle-aged or elderly), and pointed to positive effects of training on maximal oxygen uptake, peak aerobic capacity, 6-minute walk test and resting heart rate. However, more well-controlled studies are needed to confirm

the benefits of exercise training on cardiovascular and autonomic variables in this population.

### Introduction

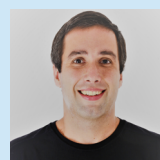
Stroke can be defined as a neurological loss associated with abnormal vascular perfusion due to a vascular cause.<sup>1</sup> It affected 33 million people worldwide in 2010, of which 16.9 million experienced the first stroke.<sup>2</sup>

After stroke, in addition to increased mortality risk due to brain damage, there are impairments in autonomic cardiac control (ACC),<sup>3,4</sup> which are associated with reduced aerobic fitness due to changes in central (reduced central stimulation to the heart) and peripheral (reduction of muscle mass, changes in type II to type I fibers, and reduction of type I fibers) nervous system.<sup>5-8</sup> In this sense, MacKay-Lyons and Makrides<sup>5</sup> observed impaired aerobic capacity (peak  $\text{VO}_2$ ) in stroke survivors.

Additionally, changes in ACC may indicate health impairment, including changes in blood pressure due to reduction of cardiac baroreflex sensitivity and high risk of cardiac death.<sup>9-14</sup> In addition, Dütsch et al.,<sup>15</sup>

### Keywords

Exercise; Physical Fitness; Cardiovascular System; Autonomic Nervous System; Physiotherapy; Rehabilitation; Stroke; Review.



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have observed that, regardless of the side affected by the stroke, the individuals showed impairments in the ACC, such as increased sympathetic and decreased parasympathetic system activities.<sup>3,4,15,16</sup>

Exercise training has been used as a non-pharmacological strategy in the management of stroke survivors. Meta-analyses and review studies have reported an increase in strength and muscle function, as well as improvement in cardiovascular variables of stroke survivors in response to exercise training.<sup>17-23</sup>

Although review studies on the association of exercise training and stroke have been gaining attention, the worldwide epidemic of this disease and its structural and functional consequences on cardiovascular and autonomic variables justify the need for further studies on adequate strategies to mitigate stroke damage. This would provide health professionals with more information on the most appropriate exercise prescription to prevent further stroke complications. Thus, the objective of the present study was to describe the effects of exercise training on cardiovascular and autonomic variables in stroke survivors.

## Methods

### Eligibility criteria

#### Study selection

The PICO (population, intervention, control/comparison, and outcome variables) model was used for study selection. Studies were chosen for inclusion if they met the following four criteria: (A) post-stroke (> 6 months) patients of both genders, aged over 18 years; (B) structured exercise training program (aerobic and/or resistance); (C) randomized controlled trials; (D) cardiovascular (aerobic capacity) and/or autonomic (resting heart rate in beats/min; heart rate variability) benefits of exercise. The reviewers documented the methodological quality of the studies and extracted relevant data. The following quality criteria were documented: baseline comparison of groups, randomization, all assessed outcomes, and details of participants (i.e., age, gender and time after stroke).

The screening was performed by two independent reviewers. For each article, any discrepancy between the reviewers was resolved by re-reading and further analysis. In the first screening stage (titles plus abstracts), studies were selected when both reviewers agreed they were eligible for inclusion or if there were

no disagreements on whether to exclude them. In the second screening stage (full text), studies were included when both reviewers agreed that they met all the inclusion criteria.

### Study identification and selection

Relevant studies were identified through computerized and manual searches. For data collection, PubMed and Physiotherapy Evidence Database (PEDro) databases were systematically searched from 2009 until December 2018 (last 10 years).

The following keywords were used in the search: stroke, cerebrovascular accident, cerebral vascular accident, exercise training, aerobic training, aerobic exercise, resistance exercise and resistance training. This review was written in accordance with some items of the Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### Assessment of article quality

The methodological quality of the studies was evaluated using the PEDro scale. Two independent reviewers completed the checklist based on the PEDro scale.

The PEDro scale evaluates the following aspects of methodological quality: (1) detailed eligibility criteria, (2) random allocation, (3) concealed allocation, (4) baseline prognostic similarity, (5) participant blinding, (6) therapist blinding, (7) outcome assessor blinding, (8) more than 85% follow-up for at least one primary outcome, (9) intention-to-treat analysis, (10) between- or within-group statistical analysis for at least one primary outcome, and (11) point estimates of variability given for at least one primary outcome.

The internal validity of the randomized controlled trials was evaluated. A study with a PEDro score of 6 was considered level-1 evidence (6–8 good, 9–10 excellent) and a study with a score of 5 was considered level-2 evidence (4–5 acceptable, 4 poor).

### Data extraction

The following characteristics were recorded for all articles: type of study, author, year of publication, participants (time after stroke, sample size, and age), cardiovascular and autonomic benefits. This procedure was performed by two reviewers: one reviewer collected the data and the second double-checked it.

## Results

A total of 544 articles were initially selected, of which nine peer-reviewed articles met the search criteria. These nine studies enrolled 611 participants (middle-aged or elderly) stroke survivors. The retrieved studies and population characteristics, intervention, and outcomes are shown in Table 1.

After analysis of the selected studies, we found that aerobic training was the predominant exercise training modality, and the main benefits were observed in the following: maximal oxygen uptake, peak aerobic capacity, 6 minutes' walk test and resting heart rate beats/min (Table 1).

There were no accidents involving the participants during the programs (exercise training) in the nine studies selected. However, 17 patients were excluded for the following reasons: absences from training days, lack

of motivation, kidney disease, alcoholism, epilepsy, knee pain, inability to perform tests, and dropping out of the study. These findings indicate that the exercise training programs used in these studies seemed to be safe.

## Discussion

To our knowledge, this is the first review on cardiovascular and autonomic impairments caused by stroke and the effects of exercise training on these variables in this population.

It is widely recognized that the practice of structured exercise training program may provide several benefits for both healthy individuals and those affected by chronic degenerative diseases.<sup>23-35</sup> Some reviews and meta-analyses have already demonstrated positive effects of exercise training on functional parameters and on the aerobic capacity of poststroke individuals.

**Table 1 - Benefits of exercise training in stroke survivors (n = 9)**

Authors	Sample	Intervention	Main findings	Quality (PEDro Scale)
Quaney et al., <sup>36</sup> 2009	38 subjects (17 men and 21 women) (> 6 months poststroke).	Aerobic training	↑ Maximal oxygen uptake	6/10
Globas et al., <sup>37</sup> 2012	36 subjects (29 men and 7 women) (≥ 6 months poststroke)	Aerobic training	↑ Peak aerobic capacity, ↑ 6 minutes' walk test	7/10
Jin et al., <sup>38</sup> 2012	133 subjects (94 men and 39 women) (≥ 6 months poststroke)	Aerobic training	↑ Peak VO <sub>2</sub> , L/min, ↑ peak VO <sub>2</sub> , mL/kg/min	4/10
Jin et al., <sup>43</sup> 2013	128 subjects (91 men and 37 women) (≥ 6 months poststroke)	Aerobic training	↑ Peak VO <sub>2</sub> , L/min, ↑ peak VO <sub>2</sub> , mL/kg/min, ↓ resting HR beats/min	4/10
Gordon, Wilks, McCaw-Binns, <sup>39</sup> 2013	128 subjects (64 men and 64 women) (> 6 months poststroke)	Aerobic training	↑ 6 minutes' walk test	7/10
Severinsen et al., <sup>40</sup> 2014	48 subjects (men) (≥ 6 months poststroke)	Resistance training	↑ Peak aerobic capacity	5/10
Lee et al., <sup>41</sup> 2015	26 subjects (> 6 months poststroke)	Aerobic training + resistance training	↑ 6 minutes' walk test	7/10
Ivey et al., <sup>41</sup> 2017	30 subjects (21 men and 9 women) (> 6 months poststroke)	Resistance training	↑ 6 minutes' walk test, ↑ peak aerobic capacity	4/10
Marzolini et al., <sup>44</sup> 2018	44 subjects (men) (> 6 months poststroke)	Aerobic training+resistance training	↑ 6 minutes' walk test, ↑ peak VO <sub>2</sub> , mL/kg/min, ↓ resting HR beats/min	6/10

According to Harris and Eng,<sup>17</sup> Mehta et al.,<sup>18</sup> and Wist et al.,<sup>19</sup> it is possible to improve functional components of poststroke individuals through the practice of resistance training. Additionally, Francica et al.,<sup>21</sup> have shown that aerobic exercise can benefit functional and cardiovascular abilities in poststroke individuals. Pang et al.,<sup>22</sup> have also observed improvement in cardiorespiratory capacity of poststroke individuals who underwent aerobic exercise training.

In line with some of the above findings, seven randomized controlled trials showed benefits on aerobic fitness provided by systematized exercise programs.<sup>36-42</sup> However, in the last 10 years, we found only two studies addressing ACC and exercise in stroke survivors.<sup>42-44</sup> Thus, once again, we emphasize the need for further randomized studies to investigate the effects of exercise training on negative changes in ACC caused by stroke.

ACC is performed by the influence of the sympathetic and parasympathetic branches on the myocardial cells promoting either increase or decrease of the heart rate, according to the needs of the organism. Such variation in heart rate moment by moment in response to the body's need is called heart rate variability. When heart rate variability is normal, it indicates the ability of ACC to respond to multiple physiological stimuli, such as exercise training, mental stress, respiration, and metabolic alterations.<sup>45-47</sup> Any negative change in the interaction between central and peripheral nervous systems (afferent and/or efferent pathways) reduces heart rate variability by compromising ACC with consequent health impairment.<sup>9-11</sup>

According to a study by Kleiger et al.,<sup>48</sup> there is a strong relationship between mortality risk and heart rate variability in individuals after acute myocardial infarction. A high heart rate variability represents good functioning of the autonomic nervous system, positively impacting the health status of an individual, whereas the reduction of this variable indicates losses on the ACC and higher risk of cardiac death.<sup>12,13</sup> According to a study conducted by Francica et al.,<sup>49</sup> poststroke individuals had lower heart rate variability when compared to controls. Although few studies have attempted to investigate the effects of exercise on ACC poststroke, it has been demonstrated that non-pharmacological strategies (exercise training) may increase heart rate variability in other populations and consequently reduce the risk for cardiovascular death.<sup>50-57</sup>

## Conclusions

This review found that in the last ten years, few randomized clinical trials involving aerobic training, resistance training, and cardiovascular and autonomic variables after chronic stroke have been performed. Evidence from some studies suggests that exercise training seems effective in improving cardiovascular and autonomic variables in stroke survivors. More randomized controlled trials are needed to assess the role of exercise training in the management of stroke survivors, so that health professionals can make informed choices when prescribing exercise training to improve the impaired variables above mentioned.

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## Author contributions

Conception and design of the research: Gambassi BB, Santos CP, Queiroz C, Schwingel PA, Almeida FJF, Almeida AERAF, Ribeiro JR, Novais TMG, Rodrigues B. Acquisition of data: Gambassi BB, Santos CP, Queiroz C, Schwingel PA, Almeida FJF, Almeida AERAF, Ribeiro JR, Novais TMG, Rodrigues B. Analysis and interpretation of the data: Gambassi BB, Santos CP, Queiroz C, Schwingel PA, Almeida FJF, Almeida AERAF, Ribeiro JR, Novais TMG, Rodrigues B. Writing of the manuscript: Gambassi BB, Santos CP, Queiroz C. Critical revision of the manuscript for intellectual content: Gambassi BB, Schwingel PA, Almeida FJF, Rodrigues B.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any thesis or dissertation work.

## Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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