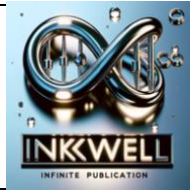




# INTERNATIONAL JOURNAL OF PHYSICAL THERAPY RESEARCH & PRACTICE

AN OFFICIAL JOURNAL OF SAUDI PHYSICAL THERAPY ASSOCIATION



Review Article

## Potential Benefits of Aerobic Walking Exercise on Cardiovascular, Pulmonary, and Bone Health in Non-Ambulatory Stroke Survivors: A Narrative Review

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### Article Info

Received : May 17, 2024  
Accepted : May 23, 2024  
Published : May 31, 2024

**To Cite:** Abdulfattah S. Alqahtani; Ramzi Alajam; Wen Liu. Potential Benefits of Aerobic Walking Exercise on Cardiovascular, Pulmonary, and Bone Health in Non-Ambulatory Stroke Survivors: A Narrative Review. International Journal of Physical Therapy Research & Practice 2024;3(5):237-252

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### Abstract

Stroke is the leading cause of long-term disability worldwide. After stroke, people commonly experience additional cardiovascular disease, cognitive declination, sensorimotor disability, pulmonary dysfunction, psychological problems, and bone health declinations. In stroke rehabilitation research, most of previous studies focused on recovery of sensorimotor function, with few studies examined outcomes in cardiovascular, cardiopulmonary, and bone health, particularly in non-ambulatory individuals who are at even higher risk of secondary complications. In this narrative review, we reviewed the health benefits of aerobic walking exercise on cardiovascular, pulmonary, and bone health in non-ambulatory stroke survivors. We started with a review of health issues in cardiopulmonary system and bones in non-ambulatory stroke survivors. We then reviewed the current state of clinical research findings of aerobic walking exercise in non-ambulatory stroke survivors. We reviewed the aerobic exercise guidelines for non-ambulatory stroke survivors and whether walking exercise was recommended for them. Then, we investigated the exercise position (standing vs. sitting) to see which exercise position would be recommended to improve or at least maintain the health of cardiopulmonary and bone in non-ambulatory stroke survivors. We finally reviewed the walking assistive devices that makes walking exercise feasible for non-ambulatory stroke survivors.

**Keywords:** Stroke; Non-Ambulatory; Walking; Cardiovascular; Cardiopulmonary; Bone

### Introduction

Stroke is the leading cause of long-term disability worldwide.(Feigin et al., 2022) After stroke, people

commonly experience additional cardiovascular disease (metabolic syndrome, coronary artery disease, myocardial infarction, and hypertension), cognitive declination,

sensorimotor disability, pulmonary dysfunction, psychological problems, and bone health declinations.(Fisher, Srikusalanukul, Davis, & Smith, 2013; Globas et al., 2012; T. S. Jorgensen et al., 2016; Lennon, Carey, Gaffney, Stephenson, & Blake, 2008; Quaney et al., 2009; Roth, 1993; Stoller, de Bruin, Knols, & Hunt, 2012; Truelsen, Prescott, Lange, Schnohr, & Boysen, 2001) Previous studies reported that pharmacological and non-pharmacological rehabilitation programs may help stroke survivors improving their motor skills and quality of life (Demaerschalk et al., 2016; Lackland et al., 2014; Stoller et al., 2012). Many of those studies focused on recovery of sensorimotor function, while few studies focused on cardiovascular, cardiopulmonary, and bone health after stroke, particularly in non-ambulatory individuals(Langhorne, Coupar, & Pollock, 2009; M. J. Mackay-Lyons & Makrides, 2002b; D. Wade, 1999) who are at high risk of secondary complications (Delussu et al., 2014; Wang, Wang, Fan, Lu, & Wang, 2014). Cumulative findings of clinical studies have indicated that more than 50% of stroke survivors are disabled to some degree, despite intensive acute care and rehabilitation training.(H. S. Jorgensen, Nakayama, Raaschou, & Olsen, 1999) Regarding to gait impairment, about 57 to 63% of stroke survivors cannot walk independently at stroke onset and 22 to 50% of them remain non-ambulatory after intensive rehabilitation (Chieffo, Comi, & Leocani, 2016; Friedman, 1990; H. S. Jorgensen, Nakayama, Pedersen, et al., 1999; H. S. Jorgensen, Nakayama, Raaschou, & Olsen, 1995; H. S. Jorgensen, Nakayama, Raaschou, et al., 1999; H. S. Jorgensen, Nakayama, Raaschou, Vive-Larsen, et al., 1995; Keenan, Perry, & Jordan, 1984; D. T. Wade, Wood, Heller, Maggs, & Langton Hewer, 1987).

In addition, standard rehabilitation programs for stroke survivors with severe disabilities do not

induce enough aerobic effect.(Ivey, Hafer-Macko, & Macko, 2006; Jin, Jiang, Wei, Chen, & Ma, 2013) Non-ambulatory stroke survivors are physically inactive; and therefore at even higher risk of cardiovascular disease, pulmonary dysfunction, osteoporosis, and metabolic syndrome (Fini, Bernhardt, & Holland, 2017; D. Y. Kim, Jung, & Seo, 2014; Luft et al., 2008). In this narrative review, we focused on health benefits of aerobic walking exercise on cardiopulmonary system and bones in stroke survivors who cannot walk independently. We began with a brief review of health issues in cardiopulmonary system and bones in non-ambulatory stroke survivors. We then reviewed the current state of clinical research findings of aerobic walking exercise in non-ambulatory stroke survivors. We reviewed clinical guidelines as well as possible barriers for walking exercise in non-ambulatory stroke survivors. We further compared pros and cons of mode of exercise (standing vs sitting) in terms of improvement in cardiovascular, cardiopulmonary, and bone health through a review of indirect evidence, focusing on why we think walking exercise would be better for non-ambulatory stroke survivors. Finally, we reviewed recent development in technology that makes a walking exercise feasible to be utilized in the rehabilitation for non-ambulatory stroke survivors.

### **Health issues in cardiopulmonary system and bone in non-ambulatory stroke survivors**

Non-ambulatory stroke survivors commonly present with serious cardiovascular complications. Compared to healthy people with sedentary lifestyle, stroke survivors present with a reduced fitness level by almost 50% and reduced cardiac output, which affect negatively their engaging in daily physical activities.(Chang, Kim, Huh, Lee, & Kim, 2012; Lloyd, Skelton, Mead,

Williams, & van Wijck, 2018; Stoller et al., 2015) The reduced fitness level is often related to an increase in risk of cardiovascular diseases and mortality.(Chang et al., 2012; Stoller et al., 2015; Wang, Wang, Fan, Jiang, et al., 2014) Hypertension is prevalent in almost 80% of stroke survivors after they discharged from the hospital (Kohok et al., 2018). Non-ambulatory stroke survivors are at even higher risk of cardiovascular disease compared to ambulatory stroke survivors.(Lloyd et al., 2018) Non-ambulatory stroke survivors are prone to deep vein thrombosis, which might cause sudden death once it reaches the lungs or heart.(Dennis, Sandercock, Graham, Forbes, & Smith, 2015) Furthermore, non-ambulatory stroke survivors who did not have diabetes before stroke onset are prone to develop diabetes mellitus.(Wang, Wang, Fan, Lu, et al., 2014) Non-ambulatory stroke survivors are at higher risk of glucose intolerance, which can increase the risk of atherosclerosis, myocardial infarction, and recurrent stroke.(Wang, Wang, Fan, Lu, et al., 2014) Although 75% of stroke survivors are prone to cardiovascular disease that is a prominent cause of death post-stroke,(Lennon & Blake, 2009) the information regarding cardiovascular health in non-ambulatory stroke survivors is limited.(Lloyd et al., 2018; M. J. Mackay-Lyons & Makrides, 2002b)

Non-ambulatory stroke survivors often exhibit declination in their lung function. They are physically inactive with a sedentary lifestyle (Fini et al., 2017) that leads to poor lung function (O'Donovan & Hamer, 2018). Impaired lung function in stroke survivors usually hinders performance in daily activities and increases the risk of cardiovascular disease (Truelsen et al., 2001). Abnormal lung function and impaired breathing in stroke survivors may be due to weaknesses in respiratory muscles, sedentary

lifestyle, damage to relevant neural pathways, and diaphragm hemiparesis.(Billinger, Coughenour, Mackay-Lyons, & Ivey, 2012; de Almeida, Clementino, Rocha, Brandao, & Dornelas de Andrade, 2011; Ezeugwu, Olaogun, Mbada, & Adedoyin, 2013; Vingerhoets & Bogouslavsky, 1994) For instance, stroke survivors during subacute stage showed a lower tidal volume during submaximal exercise when compared to sedentary healthy people.(Sisante, Mattlage, Arena, Rippee, & Billinger, 2015) Impairments in lung function predispose stroke survivors to rapid fatigue and exercise intolerance, which significantly limit their functional activities of daily living and their participation in rehabilitaiton programs.(Ezeugwu et al., 2013) It also increases the risk of recurrence of stroke(van der Palen et al., 2004) and risk of pulmonary infection because of inability to clear up lungs efficiently from mucus.(Jang & Bang, 2016; J. Kim, Park, & Yim, 2014)

Non-ambulatory stroke survivors might lose their bone density and bone mass rapidly. Due to decrease in limb loading, non-ambulatory stroke survivors are at higher risk of rapid bone loss when compared to stroke survivors who are able to walk (Huo, Hashim, Yong, Su, & Qu, 2016). In general, stroke survivors often experience deterioration in bone health, especially in the affected limbs, which increases the risk of bone fractures (Pang, Eng, McKay, & Dawson, 2005). In stroke survivors, bone formation markers are significantly lower and bone resorption markers are significantly higher compared to healthy adults (Fisher et al., 2013). Osteoporosis is common in stroke survivors during the first year after stroke onset when compared to healthy individuals (Tomasevic-Todorovic et al., 2016). Loss of bone health is noticed largely within six months of stroke onset and is associated with vascular elasticity, motor impairments, reduced fitness

level, and functional limitations after stroke (K. Borschmann, Pang, Bernhardt, & Iuliano-Burns, 2012; Fisher et al., 2013; Pang, Eng, McKay, et al., 2005; Pang, Yang, & Jones, 2013; Pang et al., 2012). In ischemic stroke female rat's models, bone resorption and osteoclast were increased in the femoral and tibial bones of hemiplegic sides one week post stroke (Chung, Lee, Im, & Park, 2012). N-terminal propertied of type 1 procollagen, a bone formation marker, was significantly decreased in male rats after 28 days of stroke onset, while cortical and total bone volumes were higher in control male rats (K. N. Borschmann et al., 2017).

### **Aerobic exercise in non-ambulatory stroke survivors**

There is limited information about the effects of aerobic exercise on cardiovascular risk, pulmonary function, and bone health in non-ambulatory stroke survivors (Stoller et al., 2014; Wang, Wang, Fan, Lu, et al., 2014). In a Cochrane review published in 2016 (Saunders et al., 2016), only two out of 58 trials focused on non-ambulatory stroke survivors. Those two trials using treadmill and resistance exercise (Richards et al., 1993) and ergometer device (Wang, Wang, Fan, Lu, et al., 2014) did not report any outcome measurements on pulmonary or bone health, and only Wang et al. (Wang, Wang, Fan, Lu, et al., 2014) reported an improvement in glucose tolerance and total triglycerides as cardiovascular health outcome measures. In a recent meta-analysis (2017) looking at the effect of exercise on cardiovascular risk following stroke, only one study included non-ambulatory stroke survivors, and one participant in another study who had severely impaired walking (D'Isabella, Shkredova, Richardson, & Tang, 2017). The only study that targeted non-ambulatory stroke survivors was a pilot trial of a sitting aerobic exercise intervention

using an ergometer device and reported an improvement in functional abilities, (Wang, Wang, Fan, Jiang, et al., 2014) fasting blood insulin, insulin tolerance, and total triglycerides. (Wang, Wang, Fan, Lu, et al., 2014) A pilot study reported an improvement of lung functions in non-ambulatory stroke survivor following an aerobic walking exercise (Alqahtani, Alajam, Eickmeyer, Vardey, & Liu, 2020).

Use of robot-assisted treadmill training may help non-ambulatory stroke survivors in walking exercise. Some of past studies reported improvement in walking performance and fitness level after robot-assisted treadmill walking exercise in severely impaired stroke survivors at subacute stage, (Chang et al., 2012; Morone et al., 2011; Tong, Ng, & Li, 2006; Werner, Von Frankenberg, Treig, Konrad, & Hesse, 2002) as well as measurements of cardiovascular system. (Chang et al., 2012) (Han, Im, Kim, Seo, & Kim, 2016) The study by Chang et al. (Chang et al., 2012) randomly assigned the participants of subacute stroke survivors to a robot-assisted training or conventional physical therapy group undergoing 20 training sessions in two weeks. The robot-assisted training group showed significantly better improvement than control group in peak VO<sub>2</sub>, but not in resting heart rate or blood pressure during stress test. In a different study, non-ambulatory stroke survivors at subacute stage were randomly assigned to an intervention (robot-assisted gait therapy) or a control (conventional therapy) group undergoing 5 sessions/week for 4 weeks. (Han et al., 2016) The intervention group did significantly better than the control group in reversing arterial stiffness and improving peak aerobic capacity, but not in resting heart rate or blood pressure. The lack of better improvement in heart rate and blood pressure in those two studies may be due to following reasons. First, the participants in the

study by Chang et al. were less than one month post stroke while their resting heart rate were still within the normal range.(Chang et al., 2012) Second, it is recommended that a minimum of 8 weeks of aerobic exercise is needed to improve cardiovascular fitness after stroke.(Ivey, Hafer-Macko, & Macko, 2008) The training period in both studies (2 or 4 weeks) may be too short to induce significant differences in those measurements. Third, the robot-assisted gait training might provide insufficient challenge during the training to cardiovascular system of the participants. Fourth, both studies did not monitor the use of hypertension medication which could affect heart rate.

Although aerobic walking exercise may possess the potential for improvement in cardiovascular systems in non-ambulatory stroke survivors, it has not been recommended by exercise guidelines. Current guidelines for adult stroke rehabilitation proposed by the American Heart Association recognize the promising results of walking exercise in non-ambulatory stroke survivors, but did not strongly recommend its clinical application due to currently insufficient supporting evidence (Billinger et al., 2014; Winstein et al., 2016) The guidelines strongly encourage future research to explore the broader application and effectiveness of assisted gait training to benefit cardiovascular and pulmonary systems after stroke.

### **Why aerobic walking exercise?**

In this review, we are unable to fully evaluate the potential of aerobic walking exercise on cardiopulmonary and bone health in non-ambulatory stroke survivors, due to the limited number of clinical studies reported in the literature. In the following, we present information revealed from our literature review on several important aspects in which indirect evidence

strongly imply the potential benefits of aerobic walking exercise for cardiopulmonary and bone health in non-ambulatory stroke survivors, even though direct evidence from clinical trials in the targeted population are lacking.

Aerobic walking exercise may improve cardiovascular health in non-ambulatory stroke survivors through its optimal effect on elevating heart rate during exercise, when compared to other forms of physical exercises. Previous study reported that walking exercise prevented diabetes in stroke survivors.(Ivey, Ryan, Hafer-Macko, Goldberg, & Macko, 2007) Non-ambulatory stroke survivors may develop deep vein thrombosis during the first few months after stroke onset.(Dennis, Mordi, Graham, & Sandercock, 2011; Dennis et al., 2015) Ivey et al.(Ivey et al., 2003) observed that a single session of low intensity aerobic walking exercise immediately enhances endogenous fibrinolysis in chronic stroke patients. Increased fibrinolysis can reduce the risk of deep vein thrombosis because it breaks down fibrin in blood clots. Exercise in an upright position (i.e. walking) is an optimal form of exercise to increase heart rate during the exercise, which is essential for beneficial outcomes of aerobic exercise.(Gordon et al., 2004) When compared to lying down and sitting, standing up can significantly elevate heart rate because the decreased venous return due to gravitational force leads to elevated heart rate in order to overcome reduced venous return and maintain cardiac output.(Jones et al., 2003) During stroke rehabilitation program, a positive correlation between time spent in target heart rate zone that induced aerobic effects and time spent in standing position has been reported, in contrast to a negative correlation between time spent in target heart rate zone and time spent in sitting position.(M. J. MacKay-Lyons & Makrides, 2002a) Increased heart rate raises blood pressure and



the shear stress against the vessel walls, which enhances the vessels health and vasodilation function.(Young et al., 2016)

Aerobic walking exercise may improve cardiopulmonary fitness level in non-ambulatory stroke survivors through activation of lower limb muscles. Exercise targeting lower limb muscles, such as walking, leads to more gains in fitness level compared to exercise of upper body muscles because leg muscles are larger and more powerful in helping venous muscle pump function (Bakkum et al., 2015; Billinger et al., 2012). Past studies reported improvement in cardiopulmonary fitness level in stroke survivors through an aerobic walking exercise (Delussu et al., 2014; M. Mackay-Lyons, McDonald, Matheson, Eskes, & Klus, 2013). Passive walking using robot-assisted treadmill training increased the oxygen uptake due to contraction of large leg muscles, mostly in the unaffected side (Stoller et al., 2014). During assisted walking, muscles in the affected lower limb are activated due to central pattern generators (CPGs) in spinal cord which is stimulated by loading on hip joint and guided from afferent inputs from lower limbs sensory receptors (Maguire, Sieben, & de Bie, 2017). The maximum oxygen uptake in stroke survivors is 50% lower when compared to healthy and sedentary peers with similar ages, and increasing oxygen uptake is crucial for stroke survivors in performing their daily living activities (Billinger et al., 2012; Chang et al., 2012; Lloyd et al., 2018; Stoller et al., 2015).

In fact, past studies in healthy people and individuals with other health conditions have reported that aerobic walking exercise can stress the cardiovascular and cardiopulmonary systems more effectively than exercise in sitting position. In maximal cardiopulmonary test controlled at 85% of the age-predicted maximum heart rate,

healthy adults showed significantly higher heart rate, blood pressure, and oxygen consumption when tested on treadmill walking compared to arm ergometry exercise (Coplan, Gleim, Scandura, & Nicholas, 1987). In individuals with heart failure, the maximal cardiopulmonary test resulted in higher heart rate reserve and peak oxygen consumption when walking on a treadmill compared to exercise on cycloergometer (Goldraich et al., 2017). In an incremental test, patients with incomplete spinal cord injury showed a higher maximum oxygen consumption when tested using a robot-assisted treadmill exercise compared to arm ergometry exercise (Jack, Purcell, Allan, & Hunt, 2010). Walking exercise may be better exercise modality than sitting exercise to stress the cardiovascular and cardiopulmonary systems because walking exercise may increase the myocardium oxygen demand, (Coplan et al., 1987) and activate larger muscles in the trunk and lower limbs (Jack et al., 2010).

Aerobic walking exercise may help to maintain normal physiology of muscles in trunk and lower limbs in people after stroke. Non-ambulatory stroke survivors are usually physically inactive (Wang, Wang, Fan, Lu, et al., 2014) that leads to decrease in muscle oxidative capacity (Ivey et al., 2008; Katz-Leurer, Shochina, Carmeli, & Friedlander, 2003) and transformation of muscle fibers to type II that are easily fatigable and resist insulin uptake (Billinger et al., 2012; Ivey et al., 2008; Katz-Leurer et al., 2003). Aerobic walking exercise can provide the needed loading to prevent lower limb muscles atrophy, (Booth, Roberts, & Laye, 2012) and improve trunk muscle function and balance control (Katz-Leurer et al., 2003; Winter, MacKinnon, Ruder, & Wieman, 1993).

Aerobic walking exercise may stimulate sensory and motor neurons in the central nervous system through afferent inputs to induce neuroplasticity in the brain and enhance CPGs in spinal cord, which may result in improvement in capability for locomotion and daily living function in stroke survivors.(Arya & Pandian, 2014; Belda-Lois et al., 2011; Chieffo et al., 2016; Katz-Leurer et al., 2003; Luft et al., 2008; Maguire et al., 2017; Veerbeek, Koolstra, Ket, van Wegen, & Kwakkel, 2011) Aerobic walking exercise using treadmill increased the neural activities in premotor cortex in healthy subjects and in affected and unaffected hemispheres in stroke survivors.(Arya & Pandian, 2014; Belda-Lois et al., 2011) In addition, basic walking is partially regulated by CPGs located in the spinal cord, which is intact in stroke survivors.(Arya & Pandian, 2014; Maguire et al., 2017) Inputs into CPGs from both supraspinal centers and proprioceptive sensors located in muscles and joints of lower limbs are important to produce a walking pattern with high quality.(Arya & Pandian, 2014; Maguire et al., 2017) For instance, loading on hip joints and extensor muscles of lower limbs facilitated walking in healthy adults and people with spinal cord injury because increased loading enhanced activities of CPGs.(Maguire et al., 2017) Walking velocity and endurance were increased after walking exercise using treadmill in ambulatory stroke survivors (Mehrholz, Pohl, & Elsner, 2014). Some of non-ambulatory stroke survivors may regain walking ability after a walking exercise program (Chieffo et al., 2016). For instance, some of non-ambulatory stroke survivors regained walking ability after 4 weeks of treadmill walking using body-weight support system during the early stage of stroke onset (Franceschini et al., 2009).

Furthermore, aerobic walking exercise may improve bone health in non-ambulatory stroke survivors. Loading exercise such as walking is

effective in preventing bone loss.(Booth et al., 2012) Loading on bones during walking helps maintain bone density by stimulating biological factors of bone formation.(Booth et al., 2012; Huo et al., 2016) In a study of ambulatory stroke survivors, those who received 19 weeks of aerobic walking and weight bearing exercises improved their bone health compared to participants in a control group who received upper limb exercise while in a seated position.(Pang, Ashe, Eng, McKay, & Dawson, 2006; Pang, Eng, Dawson, McKay, & Harris, 2005) Through a comparison of measured bone density between runners and cyclists, past studies demonstrated the role of loading in maintaining bone quality.(Rector, Rogers, Ruebel, & Hinton, 2008; Rector, Rogers, Ruebel, Widzer, & Hinton, 2009) In people with paraplegic spinal cord injury, the group who received 12 weeks (3 sessions/week) of walking training gained a significant improvement in biomarkers of bone formation and bone density of femur and lumbar spine bones when compared to the group who received regular exercises (Mobarake, Banitalebi, Ebrahimi, & Ghafari, 2017). Furthermore, in people with quadriplegic spinal cord injury, the group who received 6 months (2 sessions/week) of treadmill walking exercise showed a significant increase in biomarkers of bone formation and decrease in biomarkers of bone resorption when compared to the group who received sitting exercise.(Carvalho et al., 2006) To the best of our knowledge, no study has so far investigated the effect of walking exercise on bone health in non-ambulatory stroke survivors, and therefore future studies on the issue are needed.

In addition, past studies in the last two decades have demonstrated that even periodic standing from breaks in prolonged sitting time can bring health benefits in cardiovascular system. American College of Sports Medicine

recommends that people with sedentary lifestyle break up their prolonged sitting time with periodic standing to reduce the risk of metabolic disorders.(Garber et al., 2011) Standing decreased the risk of obesity(Gupta et al., 2016) and plasma glucose level(Thorp et al., 2014) in healthy office workers. Standing up requires continuous contraction of trunk and lower limb muscles leading to improvement in blood glucose levels and lipid profiles.(Healy et al., 2008; Owen, Healy, Matthews, & Dunstan, 2010; Thorp et al., 2014) In overweight or obese adults with sedentary lifestyle, interrupting the prolonged sitting time by a low intensity walking exercise decreased their systolic and diastolic blood pressure significantly.(Dempsey et al., 2016)

Last, aerobic walking exercise can improve mood in people who present with prolonged sitting in their jobs or in their lifestyle, which may also help to improve the mood of non-ambulatory stroke survivors. In healthy office workers, breaking sitting time by using the sit-stand desk for four weeks improved their mood status.(Pronk, Katz, Lowry, & Payfer, 2012) In chronic stroke survivors, mood status was correlated with time spent on feet meaning that the higher depression led to less time spent standing on feet (Alzahrani, Dean, Ada, Dorsch, & Canning, 2012). In addition, 12 sessions of walking exercise decreased the depression in chronic stroke survivors.(Smith & Thompson, 2008) A 12-week (3 times/week) of walking exercise improved mood status in women who had breast cancer and received chemotherapy when compared to women who had breast cancer and received chemotherapy but not participated in the walking exercise program (Yang, Tsai, Huang, & Lin, 2011). Since mood disturbance is one of the common symptoms affecting stroke survivors, (Mitchell et al., 2017) and more common in stroke survivors who had moderate to severe motor

disabilities,(Srivastava, Taly, Gupta, & Murali, 2010) we believe that non-ambulatory stroke survivors would improve the mood status after a walking exercise program that may lead to the improvement in their interaction with other people and in performing their daily activities (Jeong et al., 2014; Smith & Thompson, 2008).

### **Current development in technology making it feasible**

Recent development in new technology, especially in body-weight support and robot-assisted gait training, have made the walking exercise feasible for non-ambulatory stroke survivors.(Chang et al., 2012; Morone et al., 2011; Stoller et al., 2015; Tong et al., 2006) For instance, a past study trained non-ambulatory subacute stroke survivors using a robot-assisted treadmill for four weeks.(Stoller et al., 2015) In a different study, the investigators recruited subacute stroke survivors and trained them using robot-assisted gait training for four weeks (Morone et al., 2011). In a recent systematic review and meta-analysis (Lloyd et al., 2018), eleven studies used 4 different assistive walking devices during walking training for non-ambulatory stroke survivors. Treadmill gait training with some types of assistive devices have had no report of any adverse event. Although walking exercise is feasible for non-ambulatory stroke survivors, they might not receive the walking exercise probably due to a lack of assistive devices especially in the community settings because the robotic-assistive devices are expensive and require professional therapist to operate them.(Lloyd et al., 2018) Thus, we believe it is important to provide non-ambulatory stroke survivors with an access to walking assistive devices and body-weight support systems for walking exercise by developing affordable training devices through future research and development.



## Limitations

This narrative review has several important limitations that should be considered when interpreting the findings. First, the inclusion of studies was not guided by a systematic, comprehensive search strategy, but rather by the authors' knowledge of the existing literature and subjective selection of relevant articles. This approach introduces the potential for bias in the coverage and representation of the available evidence.

Second, the narrative format of this review inherently involves a degree of subjectivity in the synthesis and interpretation of the literature. The conclusions drawn are shaped by the authors' perspectives and may not fully capture the nuances and complexities present in the underlying studies.

Third, the review encompasses studies published over several decades, during which time the theoretical conceptualizations, research methodologies, and clinical practices in this field have likely evolved. The lack of a defined timeframe limits the ability to contextualize the findings within the appropriate historical and technological context.

Finally, the review did not systematically assess the methodological quality or risk of bias in the primary studies, which could have implications for the reliability and validity of the synthesized evidence. Despite these limitations, this narrative

review offers a comprehensive overview of the existing literature on the benefits of aerobic walking exercise on cardiopulmonary and bone health in non-ambulatory stroke survivors.

## Conclusion

Past rehabilitation interventions for stroke survivors have not focused on controlling risks of cardiovascular and cardiopulmonary diseases, especially in strokes survivors who could not walk independently. Up to date, there has been very limited number of clinical trials that attempted to examine the effects of aerobic walking exercise on risks of cardiovascular disease, pulmonary function, and bone health in non-ambulatory stroke survivors. However, many indirect supporting evidence in past studies strongly indicated the great potential of walking exercise for non-ambulatory stroke survivors, as mentioned in this narrative review. Thus, future studies should focus on feasibility, efficacy, and revision of guidelines of aerobic walking exercise and its effects on cardiopulmonary and bone health in non-ambulatory stroke survivors.

## Disclosure of interest

The authors report no conflict of interest.

## Acknowledgement

This review was a part of a thesis submitted to fulfill the requirements for the doctorate's degree of Rehabilitation Sciences.

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