Energy Expenditure and Cost during Walking after Stroke: A Systematic Review

Title: Energy expenditure and cost during walking after stroke: A systematic review

ABSTRACT:

Objective: To systematically review the evidence to determine energy expenditure (EE) and energy cost (EC) during walking post-stroke and how it compares to healthy controls.

Data Sources: CENTRAL, Medline, EMBASE, CINAHL were searched on 9 October 2014 using search terms related to stroke and energy expenditure. Additionally we screened reference lists of eligible studies.

Study Selection: Two independent reviewers conducted the initial screening of title and abstract of 2115 identified references. After screening the full text of 144 potentially eligible studies, we included, 29 studies (n = 501 stroke survivors, n = 132 healthy controls) that met the following criteria: studies including participants with confirmed stroke and studies including healthy controls, measure of volume of oxygen uptake (VO_2) during walking using breath-by-breath analysis.

Data Extraction: Two reviewers independently extracted data using a standard template which included patient characteristics, outcome data and study methods.

Data Synthesis: Mean age of the included stroke survivors in 29 studies was 57 years (range 40 to 67). In 23 studies the time since stroke was >6 months. Post-stroke EE during walking was not pooled due to heterogeneity between studies. At matched speeds, EE during steady-state overground walking was significantly higher in stroke survivors compared to healthy controls (MD 4.06 VO_2 ml/kg/min; 95% CI 2.21-5.91; 1 study, n=26); there was no significant group difference at self-selected speeds. EC during steady-state overground walking was higher in stroke survivors at both self-selected (MD 0.47 VO_2 ml/kg/m; 95% CI 0.29-0.66; 2 studies, n=38) and matched speeds compared to healthy controls (MD 0.27 VO_2 ml/kg/m; 95% CI 0.03-0.51; 1 study, n=26).

Conclusions: Stroke survivors expend more energy during walking than healthy controls. Low intensity exercise as described in guidelines might be at a moderate intensity level for stroke survivors; this should be taken into account when prescribing exercise programs post-stroke.

Key Words: Systematic review, meta-analysis, stroke, energy expenditure, energy cost, oxygen uptake, walking

List of abbreviations

CI = confidence interval

Kg = bodyweight in kilograms

EE = energy expenditure

EC = energy cost

MD = mean difference

ml/kg/m = millilitres per kilogram per meter

ml/kg/min = millilitres per kilogram per minute

n = number

VO_2 = volume of oxygen uptake

Stroke is one of the leading causes of disability and death in the world.[1] Stroke survivors are often reliant on rehabilitation programs to improve their physical functioning. Exercise is increasingly recognised as an important component of post-stroke rehabilitation programs. Exercise is defined as a physical activity that is performed with the intention to improve physical fitness.[2] Outside of direct therapy time however, physical activity levels are very low early after stroke, with stroke survivors spending most of the day lying or sitting[3, 4] It is well established that inactivity and low physical activity levels post-stroke are associated with low cardiorespiratory fitness and low muscle strength and power.[5, 6] Meta-analyses and systematic reviews have shown that increased therapy- and exercise-time post-stroke leads to better functional outcomes, including functional independence, walking ability and ability to perform activities of daily living.[7, 8]

Cardiorespiratory exercise programs improve fitness after stroke, but the optimum dose and intensity of post-stroke fitness training is unclear.[9] A commonly used resource to determine dose-intensity is the American College of Sports Medicine (ACSM) guidelines for exercise testing and prescription.[10] The described thresholds and parameters in these guidelines are based on heart rate, maximum oxygen uptake and metabolic equivalents (METs). METs are derived from the average oxygen use that is needed for different activities and are based on healthy adults. However, post-stroke impairments such as spasticity, abnormal muscle activation patterns and reduced oxygen uptake capacity of hemiparetic skeletal muscles have been associated with higher energy demands compared to a healthy population.[11-13] Higher energy demands potentially limit a stroke survivor's ability to be physically active and engage in rehabilitation programs. A comprehensive review of relevant studies could lead to a better understanding of the energy demands post-stroke and help inform the development of stroke specific exercise prescription guidelines.

Energy demand is an estimate of the 'cost' of physical activity, and can be expressed as volume of oxygen uptake (VO_2) in millilitres (ml) standardised to bodyweight in kilograms (kg). Oxygen uptake during walking is commonly measured in VO_2 ml/kg/minute (min), which we will refer to as energy expenditure (EE), or in VO_2 ml/kg/metre (m), which we will refer to as energy cost (EC). Furthermore, EE and EC can be measured during steady-state conditions or during the total walking time (which includes both steady-state and pre-steady-state conditions). At the start of a walking activity, the increase in muscle activity leads to an increase in oxygen demand. After a short period of walking, a balance between the energy required by working muscles and the oxygen rate and delivery is reached, which is called steady-state. In this review we were interested in EE and EC during both steady-state and total walking time.

Several studies have examined energy demands during walking of stroke survivors, but we are not aware of any systematic reviews that attempted to summarise the available evidence of EE and EC in stroke survivors. Our aim was to systematically examine relevant literature of post-stroke EE and EC during walking and we hypothesized that EE and EC are higher in stroke survivors compared to healthy controls.

Methods

Search strategy

CENTRAL, Medline, EMBASE, CINAHL were searched from inception to the 9th of October 2014 (by SK) using search terms for stroke and energy expenditure including: exp cerebrovascular disorders/, cerebrovascular$.tw., energy expenditure.tw., oxygen rate$.tw., oxygen cost$.tw. The full search strategy is available online. Additionally we screened the reference lists of the included studies for any potentially relevant studies.

Selection

The title and abstract of the references identified by the database search were screened for eligibility by two independent researchers (SK and EH). The full text publication of the potentially eligible studies were retrieved and screened by two independent reviewers (SK and LJ). Any discrepancies were resolved by consensus and a third independent reviewer was consulted (TC) if consensus could not be reached.

The inclusion criteria were: (1) clinical studies (including cohort, observational, randomised and clinical controlled studies); (2) full text published in English, German or Dutch; (3) VO_2 uptake measured using breath-by-breath analysis during overground or treadmill walking; (4) studies including participants that were clinically diagnosed with stroke. Studies including a sample with mixed diagnoses were included if data for the stroke survivors were reported separately or if over 75% of the included participants were diagnosed with stroke. Studies in which VO_2 uptake was only measured at rest, case studies, case reports, case series and studies only published as an abstract were excluded. Studies were included if EE and EC of walking was measured at comfortable self-selected walking speeds, since it represents typical day-to-day walking. We also included studies in which participants walked at a percentage of their comfortable walking speed to allow stroke survivors to reach steady-state conditions. EE and EC data that as collected during maximal or slow walking speeds were not included in this review, since we did not classify this as a normal walking activity. Data pertaining to AFO use were only included if the participants typically wore an AFO~~In studies in which the effect of an ankle foot orthosis (AFO), we included the data of the walking tests that were performed with the use of an AFO in cases where participants were used to wearing an AFO~~. If participants ~~were not used to~~did not typically wear~~ing~~ an AFO, only data of walking tests that were performed without the use of an AFO were included.

Outcomes

Our main outcomes were a) post-stroke EE and ~~post-stroke~~ EC during overground and treadmill walking under steady-state conditions and over total walking time; and b) the differences ~~in EE and EC~~ between stroke survivors and healthy controls in EE and EC during overground walking under steady-state conditions and over total walking time.

Our secondary outcomes were c) the difference in EE and EC between stroke survivors and healthy controls during treadmill walking under steady state conditions and over total walking time; and d) all other EE and EC outcomes.

Data extraction

Two reviewers (SK and LJ) independently extracted data from the included studies using a purposefully developed form to collect the following information: type of design, sample size, type of population, age, outcome measures and test protocols. Additionally, we extracted data on the walking ability of stroke participants reported as functional ambulation category (FAC) scores[14], use of walking aids and ankle foot orthoses (AFO). For the studies that did not report FAC scores, we assessed the score retrospectively based on the reported inclusion and exclusion criteria. If there was insufficient data available, we assessed the FAC score as unclear. We scored the FAC on a 0-5 scale: 0 = non-functional, 1 = requires constant manual contact for body weight support, balance and coordination, 2 = requires intermittent or continuous manual contact, for balance and coordination, 3 = requires supervision, 4 = independent on a level surface and 5 = independent on all surfaces. All relevant EE and EC data during walking at self-selected comfortable walking speed and achieved walking distance during the walking test were extracted for stroke survivors and healthy controls. We only extracted the baseline data of studies that tested an intervention to ensure we excluded any intervention effects. In studies in which a walking test was performed twice, we only extracted the data of the first test to exclude any training effects.

Any discrepancies were resolved by consensus. If consensus could not be reached, a third independent reviewer (TC) was consulted.

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Risk of bias

We assessed the ~~R~~risk of bias in the included studies ~~was assessed and~~using a criteria were ~~based on~~ commonly used ~~criteria in different~~as a critical appraisal tool~~s for~~ in cross-sectional non-controlled studies.[15, 16] We included the following criteria: 1) explicit detailed eligibility criteria, 2) reporting of confounders (age, time since stroke and walking ability should ~~at least~~ be explicitly reported at a minimum), 3) definition of outcome (~~clearly defined outcome i.e.~~ EE and/or EC~~-~~, average or steady-state, what period of walking was selected to represent steady-state conditions) and 4) number and reasons reported of drop outs and missing data. Additionally, for the studies that included a healthy control group, we assessed if 1) the selection of the control group was from the same source as the stroke survivors (e.g. same geographical area) and if 2) they were age and sex matched. Each criterion was assessed as high (+), low (-) or unclear (?).

We categorised the studies as having a~~in~~ high, low or unclear overall risk of bias using the following rules. We assessed overall risk of bias of studies that did include a control group as: "high" if the majority of items (at least 3/5) were assessed as high, and as "low" and "unclear" if the majority were assessed as low or unclear respectively. For the studies that did not include a healthy control group, overall risk of bias was assessed as: "high" if at least two out of four criteria were assessed as high risk of bias,~~;~~ "low" if at least three out of four were assessed as low risk of bias, and "unclear" if at least two were assessed as unclear and no more than one was assessed as high risk.

Individual criteria and overall study risk of bias was assessed by two independent reviewers (SK and LJ). Any discrepancies were resolved by consensus or a third independent reviewer (TC) was consulted.

Data analysis

Descriptive statistics were used to report the characteristics of the included studies. We summarised and reported data for all stroke survivors and for comparisons between stroke survivors and healthy controls separately. Where possible, all data were converted to VO_2 ml/kg/min or ml/kg/m. Data that were reported as VO_2 in ml/min or in ml/m were standardised to body weight by dividing the estimate by the average body weight if this was provided in the original study.

To summarise and calculate mean post-stroke EE and EC, we used the generic inverse variance meta-analysis. Mean differences were calculated to summarise the differences in EE and EC between stroke and healthy controls using the inverse variance meta-analysis.[17] For both post-stroke and stroke versus healthy controls analyses we used the random effects model, assuming that there is a normally distributed variation in EE and EC between studies.[17] For each outcome we included the following subgroups in the analyses: >6 months post-stroke, 1-6 months post-stroke and <1 month post-stroke.

Heterogeneity

The I^2-statistic was calculated to estimate the percentage of between-study variation due to heterogeneity. We used the Cochrane classification of heterogeneity which is as follows: 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity.[17] If heterogeneity was substantial or considerable and we were not able to explain heterogeneity by subgroup analyses, we did not perform a meta-analysis.

We used Review Manager 5.3 software (http://tech.cochrane.org/revman) to create forest plots and to perform meta-analyses.

Results

The initial literature search yielded 2,156 references. We excluded 2,012 record that did not meet our eligibility criteria on the bases of the title and abstract. The full text publications of 144 references were screened. We have included 29 studies, including 501 stroke survivors and 132 healthy controls of which eleven studies provided data for quantitative analyses (fig 1). VO_2 uptake was assessed during overground walking in 14 studies,[13, 18-30] treadmill walking in 13 studies[31-43] and during both overground and treadmill walking in two studies.[44, 45] Of the 29 studies, nine compared VO_2 uptake during walking in stroke versus healthy controls; four examined overground walking (stroke n=54; healthy controls n=77)[13, 18, 20, 23] and five which examined treadmill walking (stroke n=73; healthy controls n=55).[33, 35, 37, 38, 42]

Fig 1 Flow diagram of study screening process.

Participants

Characteristics of the participants in 20 included studies reporting post-stroke EE and EC are reported in table 1 and characteristics of the nine studies that compared post-stroke EE and EC to healthy controls are reported in table 2. In three of the studies, a population with mixed diagnoses was included,[21, 25, 31] we were unable to extract stroke data for one study and therefore we reported the data based on the total group including eight stroke and two participants with traumatic brain injury (TBI).[31] The other two studies with a mixed population did report data for stroke survivors separately.[21, 25] The average age of stroke survivors included in the studies was 57 years, ranging from a mean of 40 to 67 years. The average age of the healthy controls was 46, ranging from 23 to 63. The number of stroke survivors included in the studies ranged from four to 53 and the number of healthy controls in nine studies ranged from 16 to 59.

The time since stroke onset was >6 months in over 75% (23 studies) of the included studies and there were no studies that included stroke survivors at <1month post-stroke.

Walking ability

In 23/29 studies, only stroke survivors who were able to walk independently (FAC ≥4) were included. Three studies included participants who were able to walk with supervision (FAC score 3) and independently (FAC score ≥4) [28, 33, 43] and in two studies only participants that required constant manual contact or supervision while walking (FAC 2 and 3 respectively) were included. [23, 30] In one study the included participants had a FAC score ranging from 1-5 which indicates that participants had a broad range of walking abilities; this includes participants who need continuous manual support, supervision and also participants who can walk independently.[20]

Walking speed

Stroke survivors in three studies were asked to walk at slower than usual walking speeds to enable participants to reach steady-state, the participants walked at 70% to 75% percent of their comfortable walking speed.[36, 39, 41] Walking speed was not reported in one study.[33]

Outcomes

VO_2 uptake during walking was measured under steady-state conditions in 15 studies,[13, 18, 19, 23, 30, 33-39, 41, 43, 44] and over the total walking time in 6 studies.[20, 22, 24, 25, 27, 28] In two studies VO_2 uptake was measured during a single overground walking test over 20 [26]and 30 meters [29] and in six studies NET VO_2 uptake (VO_2 uptake during walking – resting VO_2 uptake) during steady-state conditions was reported. The results of the studies that measured VO_2 uptake during a single bout of walking over a short distance (i.e. 20 and 30 meters) and the studies that reported NET VO_2 uptake are discussed under "Other outcome".

Risk of bias

The eligibility criteria for stroke survivors were not clearly described in five studies.[18, 22, 24, 31, 32] In one out of the nine studies that included healthy controls, it was unclear how and where the healthy controls were recruited from or if they were matched to stroke survivors,[18] and four studies were assessed to be at high risk of selection bias since the healthy controls were not age- and gender-matched to the stroke survivors.[20, 35, 37, 42] In 11 studies the confounders age, time since stroke and walking ability/impairment were not explicitly reported.[18, 20, 26, 32, 34, 36-40, 42] In 12 studies the outcome definitions were not clearly described.[18, 19, 21, 29, 32, 36, 38-41, 43, 44] The authors of 11 studies specified the exact minutes during which the data were acquired for steady-state data-analysis,[13, 19, 21, 23, 30, 33-36, 38, 45] and the authors of only one study reported a definition of steady-state and defined it as *a period of at least 3 minutes, during which the variability of heart rate was less than 4 beats/minute*.[37] Regarding missing data, one study was assessed as being at high risk of attrition bias since 15 of the 30 survivors that were recruited could not be tested as intended, and the reasons for exclusion were not explicitly stated,[18] and one study did not report any details about the selection process and was therefore assessed as unclear risk of attrition bias. Overall risk of bias was low in 13/20 studies that did not include a healthy control group and in 8/9 studies that included a healthy control group.

Table 1 Characteristics of included studies measuring post-stroke EE and EC (n=20)

Table 2 Characteristics of included studies comparing EE and EC in stroke survivors and healthy controls (n=9)

Main outcomes

Post-stroke EE

All post-stroke EE data for each outcome group reported in the included studies are shown in a forest plot (fig 2). Data of two studies could be pooled, the two studies included participants at 1-6 months post-stroke (low risk of bias, 18 participants); the result showed a mean post-stroke EE during overground walking under steady-state conditions of 11.29 VO_2 ml/kg/min; 95% CI 9.70 to 12.87 (not shown in forest plot fig 2). [13, 23] None of the other EE data could be pooled due to substantial heterogeneity (I^2 >70). No studies were identified that examined EE at <1 month post-stroke, and none of the included studies measured post-stroke EE during treadmill walking over total walking time.

Fig 2 Post-stroke energy expenditure during overground and treadmill walking: steady-state and total walking time, 1-6 months and >6 months post-stroke.

Post-stroke EC

All data for each post-stroke EC outcome group are shown in fig 3. Post-stroke EC during overground walking under steady-state conditions was reported in 3 studies.[13, 18, 23] Pooled data of two studies (low risk of bias, 19 participants)[13, 23] showed a mean EC post-stroke of 0.64 VO_2 ml/kg/m; 95% CI 0.44 to 0.85). Data from one study (high risk of bias, 30 participants) (0.21 VO_2 ml/kg/m; 95% CI 0.17 to 0.25), could not be included since the authors did not report the time since stroke.[18]

In five studies post-stroke EC during overground walking over total walking time was reported. Pooled data from two studies (low risk of bias, 29 participants) that included participants at 1-6 months post-stroke[20, 22] showed a mean EC of 0.29 VO_2 ml/kg/m; 95% 0.16 to 0.42. Pooled data from three studies (low risk of bias, 58 participants) that included participants at >6 months post-stroke,[24, 25, 27] showed a mean EC of 0.63 VO_2 ml/kg/m; 95% 0.53 to 0.72.

Post-stroke EC during treadmill walking was reported in five studies; one study (low risk of bias, 6 participants) included participants between 1-6 months post-stroke[23] and four studies (low risk of bias, 93 participants) included participants at >6 months post-stroke (fig 3).[34, 35, [37, 43] No studies were identified that reported post-stroke EC of overground walking over total walking time.

Fig 3 Post-stroke energy cost during overground and treadmill walking: steady-state and total walking time, 1-6 months and >6 months post-stroke.

Stroke survivors versus healthy controls EE during overground walking

The pooled data of two studies showed that there was no significant difference in EE during steady-state overground walking between stroke and healthy controls (low risk of bias, 38 participants).[13, 23] In one of these studies (26 participants) the healthy controls walked at speeds matched to the stroke survivors and EE was higher in stroke survivors compared to healthy controls (fig 4).[13]

Fig 4 Higher EE during overground steady-state walking in stroke survivors compared to healthy controls at matched but not at self-selected speed.

In one study ta none significant difference was found between stroke survivors and healthy controls in EE of overground walking over total walking time was assessed at 1-6 months post-stroke (low risk of bias, 59 participants) (MD 0.57 VO_2 ml/kg/min; 95% CI -0.54 to 1.68).[20]

Point estimates for both EE and EC outcomes for each study are reported in table 3.

Table 3 Stroke survivors versus healthy controls energy expenditure and energy cost during overground walking (n=5)

Stroke survivors versus healthy controls EC during overground walking

Pooled data of two studies (low risk of bias, 38 participants) showed a higher EC under steady-state conditions in stroke survivors at 1-6 months post-stroke compared to healthy controls walking at self-selected speed.[13, 23] EC was higher in stroke survivors when healthy controls were walking at matched speeds (26 participants)[13] (fig 5).

Fig 5 Higher EC during overground steady-state walking in stroke survivors compared to healthy controls.

In one study (high risk of bias, 30 participants) EC under steady-state conditions was higher in stroke survivors compared to healthy controls at matched speeds, but the time since stroke was unclear and therefore the results were not included in the forest plot (table 3).[18]

In one study (low risk of bias, 59 participants) the difference in EC was measured over total walking time in stroke survivors at 1-6 months post-stroke (table 3).[20]

Stroke survivors versus healthy controls EE during treadmill walking

The data of three studies comparing EE during treadmill walking at self-selected speed under steady-state conditions between stroke survivors and healthy controls (low risk of bias, 70 participants) could not be pooled due to heterogeneity (I^2=76%)(table 4). [33, 35, 38] No studies were identified that compared EE between stroke survivors and healthy controls during treadmill walking averaged over total walking time.

Table 4 Stroke survivors versus healthy controls EE and EC during treadmill walking: steady-state (n=4)

Stroke versus healthy controls EC during treadmill walking

Pooled data from two studies (low risk of bias, 63 participants)[35, 37] showed that EC during treadmill walking under steady-state conditions was higher in stroke survivors compared to healthy controls at self-selected speeds (MD 0.20 VO_2 ml/kg/m; 95% CI 0.12 to 0.27). The point estimates in each study are reported in table 4.

No studies were identified that compared EC between stroke survivors and healthy controls during treadmill walking averaged over total walking time.

Other

Six studies reported VO_2 uptake as NET VO_2 and in all studies the outcome was measured during steady-state conditions (table 5). ~~In one study (low risk of bias, 10 participants) NET EE during treadmill walking was reported.[31, 32] Five studies reported NET EC of which one study (unclear risk of bias, 4 participants) reported NET EC during overground,[21] two studies (high risk of bias=1[32] and low risk of bias=1,[40] 12 participants) during treadmill walking[32, 40] and one (low risk of bias, 24 participants) during both overground and treadmill walking.[45]~~ One study measured NET EC for both overground and treadmill walking reported results for walkers who were dependent on a walking aid and those who were not (time since stroke was 1-6 months). The results of this study indicate that NET EC during overground and treadmill walking was higher in the group that was dependent on a walking aid (12 participants) compared to the independent walkers (11 participants).[45] Only one of the studies compared oxygen uptake of stroke survivors to healthy controls. In this study NET EC of treadmill walking under steady-state conditions was higher in stroke survivors when healthy controls walked at speeds matched to stroke survivors (1 study, low risk of bias, 31 participants).[42]

Two studies measured post-stroke VO_2 uptake during a short overground walking test at > 6 months post-stroke.[26, 29] Measured over a single 20 meter walk, mean EE was 6.20 VO_2 ml/kg/min; 95% CI 5.65 to 6.75 and EC was 0.30 VO_2 ml/kg/m; 95% CI 0.24 to 0.36 (low risk of bias, 37 participants).[26] When measured over a single 30 meter walk, the average EE was 8.70 VO_2 ml/kg/min; 95% CI 7.58 to 9.82 (low risk of bias, 15 participants).[29]

Table 5 Other outcomes, NET EE and EC (n=6)

Discussion

This is the first comprehensive review that has examined EE and EC of walking post-stroke. We have shown that stroke survivors expend more energy (EE) compared to healthy controls, when controls walk at the same speed as the comfortable walking speeds of stroke survivors. Similarly, EC is higher in stroke survivors compared to healthy controls at both matched and non-matched walking speeds.

We included 29 studies, but there was great variability in methods between studies. For example, studies measured oxygen uptake during overground walking or during treadmill walking; or measured it during steady-state conditions or over total walking time. As a consequence, we were restricted in our ability to pool the results of the included studies, limiting the degree to which we could explore associations between EE and EC and walking ability, age, and time since stroke. Our results do indicate that walking speed is related to oxygen uptake during walking which confirms similar findings from other studies in healthy older adults[46, 47] and in stroke survivors.[48]

Our findings indicate that we cannot just rely on commonly used guidelines to prescribe exercise post-stroke, since these guidelines are based on healthy adults and do not take higher energy demands in people with disabilities into account. For example, walking slowly around the home is categorised as light physical activity and equates to approximately 2 METs, according to the ACMR guidelines. One MET is equivalent to 3.5 VO_2 ml/kg/min. In this review we found that the average EE of walking at a comfortable pace in stroke survivors is approximately 10 VO_2 ml/kg/min and would be closer to 3 METs, indicating that exercise such as walking, can be moderate intensity exercise in stroke survivors as opposed to low intensity for none disabled people.

As expected there was great variability in energy demands in the stroke survivors across the studies. The number of stroke survivors that used a walking aid and ankle foot orthoses was not consistently recorded across the studies. The inclusion criteria regarding walking ability however, were very similar across the studies. All but six studies included stroke survivors that were able to walk independently with or without a walking aid on a level surface. Comparing the results in these studies to the results of the studies that also included dependent did not show consistently higher EE or EC.[20, 23, 28, 30, 33, 43] We did not identify any studies that directly compared the energy demands of walking in stroke survivors who were able to walk independently to stroke survivors who needed physical assistance to be able to walk. A review that examined the effect of AFOs on energy expenditure during walking after stroke suggests that using an AFO can reduce the EC of walking.[49] Furthermore, there is a signal from one of the studies included in our review that stroke survivors who are able to walk independently without a walking aid have lower EE and EC compared to stroke survivors who are dependent on a walking aid.[45] It should be noted however, that these studies are small (n=22-32). There is a clear gap in the literature of evidence in more disabled stroke survivors, which is needed to guide exercise prescription.

A common consequence of stroke is hemiparesis. Hemiperetic muscle mass can decrease dramatically and the proportion of fast twitch muscle fibres increases after stroke.[50, 51] These muscle fibres are prone to fatigue and lead to higher energy expenditure and cost of walking. Stroke can also lead to changes in the autonomic control of cardiac function such as blood flow and cardiac regulation, which may lead to impaired exercise capacity.[52] The degree to which stroke survivors are impaired by hemiparesis and changes in autonomic cardiac control is highly variable and not only dependent on the stroke itself but also on pre-existing disability or fitness levels. This makes research in this area challenging and supports the need for larger studies with well-defined samples to provide more precise estimates.

In the majority of studies, EE and EC were measured during steady-state conditions. None provided a clear definition of steady-state, with the exception of Fredrickson et al (2007) who defined steady-state as "*a period of at least 3 minutes, during which the variability of heart rate was less than 4 beats/minute*".[37] This definition however, is based on a study of a healthy aged population[53] and might not be appropriate in a stroke survivors. The lack of detailed information about the definition of steady-state is indicative of a broader issue, which is the absence of consensus in defining steady-state condition during activity in stroke survivors. The authors of several studies rationalised that steady-state would be reached after a few minutes of walking and thus selected data after several minutes of walking to determine VO_2 uptake during steady-state walking. The time period selected for steady-state data acquisition varied between studies and may be a contributing factor to the marked heterogeneity we found in EE and EC between studies. There is an obvious need for a clear definition of steady-state, and consistent methods of identifying the steady-state condition, during walking post-stroke.

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The inclusion of both steady-state as well as the transition from rest to steady-state activity might also explain some of the heterogeneity we found in the studies that examined overground walking. During the transition period, the body needs to quickly adjust VO_2 uptake to meet the increased energy demands of the activity. The mechanisms to provide oxygen to the skeletal muscles that have been activated are delayed and follow a specific pattern, which is called VO_2 on-kinetics. The VO_2 on-kinetics patterns vary across individuals; it is slower in deconditioned individuals, older adults and in people with cardiac or respiratory diseases compared to healthy persons.[54] These confounding factors (i.e. older age, sedentary lifestyle, and comorbidities) are not uncommon in stroke survivors, but were not consistently reported in the included studies. Their prevalence might have been unevenly distributed across the different studies and potentially could explain some of the heterogeneity in EE and EC between studies.

Generalizability of the results

This review included data from 29 studies that assessed energy demands whilst walking in stroke survivors and in 11 of these studies EE was compared to healthy, age-matched controls. The results of this review suggest that EE and EC are higher in stroke survivors. These findings are based on a small number of studies, including a relatively small number of participants. The incidence of stroke is higher in people >65 years,[55] yet in this review, the average age of the stroke survivors in the included studies was 57 ranging from 40 to 77 years. We also found most of the studies in this review (22/28) included participants at >6 months post-stroke. Our understanding of EE and EC in the first months after stroke the time period in which most rehabilitation is occurring is very limited.

Study limitations

We excluded three studies that were published in a language other than English, German or Dutch. This could potentially lead to a high risk of publication bias, though it is unlikely that the results in these studies would have made a significant difference in the findings of this systematic review. We searched three different electronic data-bases using a simple search strategy. To limit the risk of not identifying potentially relevant studies through the electronic search, we screened the reference lists of the included studies. In this review we focussed on walking impairment as a factor that might be related to energy demands of walking post-stroke. Other post-stroke impairments such as cognitive functioning, balance impairments or spasticity might also be related to energy demands of walking after stroke, but these were not consistently reported in the included studies.

Conclusion

The common assumption that stroke survivors expend more energy during walking than people without a stroke was supported by the results of this review. Understanding the energy expenditure and energy cost of walking after stroke is important when prescribing exercise. What is described as low intensity exercise in ACSM guidelines[10] and current stroke guidelines[56] might be at a moderate intensity level for stroke survivors. Future studies with larger sample sizes should increase confidence in our finding and are needed to inform the development of stroke specific exercise guidelines. These studies should include a broad range of stroke survivors, with different levels of disability, including older stroke survivors (>60 years) and across different stages of recovery after stroke including the early stages after stroke.

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Figure legend

Fig 1 Flow diagram of study screening process.

Fig 2 Post-stroke energy expenditure during overground and treadmill walking, steady-state and total walking time, 1-6 months and >6 months post-stroke.

Fig 3 Post-stroke energy cost during overground and treadmill walking, steady-state and total walking time, 1-6 months and >6 months post-stroke.

Fig 4 Higher EE during overground steady-state walking in stroke survivors compared to healthy controls at matched, but not at self-selected, speed.

Fig 5 Higher EC during overground steady-state walking in stroke survivors compared to healthy controls.