Physical activity in secondary stroke prevention

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Summary

After having a stroke the main challenges are reducing the risk of recurrent stroke, improving impaired brain function, quality of life, independence in activities of daily living and reintegration into the community. [1] Lesion-induced impairment of brain function also has, besides its effects on e.g. motor, sensory, visual and speech function, an influence on e.g. cognition and mood, all of which are determinants of post-stroke physical activity.

The evidence for a benefit of physical activity in secondary stroke prevention is increasing and treatment strategies aimed at factors which are limiting physical activity are more and more
Zusammenfassung


Résumé

Après un accident vasculaire cérébral (abr. AVC) les plus grands défis sont la réduction de risque d'un nouveaux AVC, des conséquences d'AVC, l'amélioration des fonctions perdues, de la qualité de vie, de l'indépendance dans les activités journalières et de la réintégration sociale. [1] L'AVC peut affecter autant la fonction moteur, sensible, visuelle et la langue que la cognition et l'humeur. Ces fonctions représentent des facteurs limitants pour l’activité physique après l'AVC. L'évidence pour un effet bénéfique de l'activité physique après l’AVC devient de plus en plus consistante et des stratégies pour améliorer les facteurs limitants pour l’activité physique sont de plus en plus reconnu comme efficace.

Case report

A 65-year old female patient suffered an acute ischaemic stroke with acute right sided hemineglect, global aphasia and right sided hemiplegia, corresponding to a NIHSS score of 15 points. The head MR-arteriography showed an acute ischaemic lesion as depicted in Figure 1. Successful bridging- therapy was performed. Head MR-arteriography 24 hours after thrombectomy showed open vessels and no new ischaemic lesion. So, the patient was mobilized to the edge of the bed on day 1. In cardiac rhythm monitoring, an episode of atrial fibrillation of 90 seconds duration occurred. Rivaroxaban 20 mg daily was initiated, as was a high-dose statin (LDL-cholesterol levels of 4.8 mmol/L) and an ACE-inhibitor because of newly diagnosed arterial hypertension.

At discharge, a mild non-fluent aphasia and a moderate right sided hemiparesis persisted, corresponding to a NIHSS score of 4 points. The patient got transferred to a rehabilitation clinic, were a supervised 3-weeks physical therapy programme was started.

After leaving the rehabilitation clinic, a spastic gait pattern with circumduction of the right leg persisted, which allowed for a 6-Minutes Walk Test distance of 177 meters. An ambulatory
rehabilitation group-programme consisting of walking and stationary cycle ergometry followed, with 3x sessions/week of 30 minutes, at an intensity of 40-70% of age adjusted maximal heart rate. At three months a light residual gait impairment persisted, lightly affecting the activities of daily living. The 6-meter walk distance improved to 360 meters.

Introduction
A recurrent stroke is potentially disabling, impairing activities of daily living, of mental health, decreasing quality of life and causing death. The risk of recurrent stroke but also of other vascular events after a first ever stroke is considerable. [2,3,4,5] It can be lowered by timely identification of stroke aetiology and consecutive initiation of secondary prevention measures. [1,6]
However, although widely available, up to 60% of patients in Europe have been shown not to have access to basic interventions such as to cardiac monitoring, statins, blood-pressure control at follow-up, carotid endarterectomy, face-to-face follow-up in hospital, direct oral anticoagulants and to lifestyle management programmes. [3]
Also, there has been demonstrated to be impaired awareness and control of risk factors, including physical activity, after stroke. [3,7] An Austrian observational cohort study (n=1,730) including 20.1% (n=348) participants with recurrent ischaemic stroke or transient ischaemic attack (abr. TIA) showed significantly poorer risk factor control, including lifestyle modification, compared with those with a first ever event. [7] A Danish observational study (n=121) found awareness of risk factors to be present at discharge from a stroke unit. 12 months after stroke there was an increase of proportion of inactive patients from 36 to 59% (p<0.0001). Also, poor control of arterial hypertension, of cholesterol levels and unchanged
cigarette smoking frequency, but less excessive alcohol consumption was found. [8]
Because of lesion-induced disruption of brain function, patients after stroke are showing a
different behavior of physical activity. For example, there might be a reduced ability of the
body to be physically active because of motor and sensory deprivation, impaired balance, falls
and a decreased cardiorespiratory fitness. [9] Secondary depression, anxiety, pain, cognitive
disturbances and fatigue are also affecting physical activity, as is impaired self-efficacy, which
is the belief of being able to successfully complete a task. [10]

Physical activity after stroke
A case-control study (n=13,249, 39,747 controls) demonstrated that stroke survivors are less
likely to reach 150 min/week of physical activity compared to controls. [11]
A prospective study (n=40) investigated physical activity in stroke survivors with
accelerometers (which are measuring mobility, step number and calculating calories). Despite
the ability to walk, some patients did not reach the daily recommended level of physical
activity. Latter was defined as
30 minutes of exercise a day with an intensity of more than 142 kcal/day (1,000 kcal/week)
reaching 215-285 kcal/day (1,500-2,000 kcal/week). [12]
What are the factors that negatively affect physical activity after stroke?
A recent meta-analysis of cohort and prospective cross-sectional studies (n=26, 1,349 stroke
survivors) investigated factors associated with physical activity after stroke. It found higher
age, female sex, impaired physical function (quantified with 6-Meter Walking Test distance,
comfortable gait speed, Berg-Balance-Scale and cardiorespiratory fitness), fatigue, depression,
falls, impaired self-efficacy, balance and impaired health-related quality of life to be
significantly associated with physical activity, whereas analyses for neglect, infarct side,
cognition and time delay since stroke were inconclusive. Cognition measured with MoCA
(Montreal cognitive assessment) – not with Mini Mental Test – showed significant association
with physical activity. Moreover, physical function accounted for only half of the variance in
post-stroke physical activity levels (defined as the quantity of the physical activity performed).
[9]

Self-efficacy
Confidence is a measure of self-efficacy. Improving it, is one of 10 main priorities related to life
after stroke, established by a consensus as agreed by stroke survivors, caregivers and health
professionals. [13,14]
A systematic review, which included 17 studies showed a positive association between self-
efficacy and mobility, activities of daily living, depression and health-related quality of life.
[10]
Different self-efficacy enhancing strategies have been proposed [12] and studied prospectively
in 4 randomized clinical trials (abr. RCTs) (n=630 participants). They have shown a trend to be
effective for e.g. functional independency, walking and anxiety. [10]
Fatigue

Fatigue has a negative effect on physical activity on its own and by its contribution on health-related quality of life. [9,15]

Fatigue in stroke patients is defined as a feeling of early exhaustion developing during mental activity, with weariness, lack of energy and aversion to effort. [16] More than one type of fatigue in stroke patients has been proposed: chronic fatigue, which may be classified into primary (i.e. absence of any causes besides the stroke) or into secondary (i.e. caused by co-morbidities or use of certain medications) and activity-dependent fatigability or exertional fatigue, which is an activity-induced decrement in performance. [1,17,18]

Fatigue is prevalent after stroke. A survey-study in stroke survivors (n=4,023, follow-up 2 years) concluded that 10% of patients always and 29% often were affected. [19]

Chen et al. studied the correlation between post-stroke fatigue and health-related quality of life (n=218 patients) at 3 months after ischaemic stroke and concluded that severity of fatigue was a significant contributor to stroke-specific quality of life, accounting for 39% of the variance. [15]

RCTs specifically studying the effect of physical activity alone on post-stroke fatigue are lacking. However, one RCT (n=83 stroke patients) compared the effect of cognitive therapy combined with physical activity training on fatigue over 12 weeks. It showed that both treatment options had a significant benefit on fatigue, with the group of combined treatment having more gains on outcome scales (measuring fatigue, anxiety, depression, sickness, pain, sleep and walking). [20]

A systematic review identified three cross-sectional studies (n=444 patients), which found no significant association of fatigue with physical activity. [17] However, one of those studies found an association of severe fatigue with low self-efficacy, causing less engagement in physical activity. The American Heart Association/American Stroke Association (AHA/ASA) Guidelines from 2014 recommend physical activity as a non-pharmacologic therapy for fatigue after stroke. [1]

An aggravating factor for fatigue is sleep-disordered breathing, which is prevalent after stroke. A systematic review (n=37 studies, n=3,242 participants with cerebrovascular disease) demonstrated that obstructive sleep apnea, defined as an apnoe-hypopnoe index (AHI) >10 per hour in this study, was present in 61.9% of stroke survivors, mostly diagnosed 7-28 days after index-event. Identification and treatment of sleep apnea potentially has a beneficial effect on fatigue and possibly on physical activity behavior. [21]

Another factor associated with fatigue in stroke survivors is post-stroke pain. Choi-Kwon et al. (n=364 patients, 1 year after ischaemic stroke) found that 135 (37.1%) patients had pain, of which 78 (21.4%) was musculoskeletal, 22 (6%) central post-stroke type, 16 (4.4%) combined and 19 (5.2%) other pain. Pain was significantly associated with fatigue (p=0.026) and mRS (p=0.004). [22] The causality between pain and fatigue is unclear and may be bilateral. Identifying pain and treating it may have a positive effect on physical activity. Data regarding the direct effect of physical activity on post-stroke pain are lacking.
Depression

Depression is highly prevalent in stroke survivors and negatively associated with physical activity after stroke. [9]
After analyzing the data available from 51 publications (n=25,671 patients), Hackett et al. found depression among stroke survivors in 33% (95%CI 29-36%). [23]
A retrospective cohort-study showed that post-stroke depression significantly increases disability. Effectiveness of rehabilitative treatment, activities of daily living and mobility was worse in patients with post-stroke depression, besides their longer length of hospital stay. Post-stroke depression added 15% to the disability in stroke survivors. [24]
A meta-analysis (n=1,022, 13 studies, data up to 2014 included) showed a significant reduction of depressive symptoms after resistance training, functional training, aerobic physical activity, treadmill physical activity, Bobath physical activity, individualized physical activity with education and community based rehabilitation services (p=0.03). Physical activity had a positive effect on depressive symptoms across both the subacute (≤6 months post-stroke) and chronic stage of recovery (>6 months). Furthermore, there was a significant effect of physical activity on depressive symptoms when higher intensity studies were pooled. [25]

Cognitive impairment

Cognitive impairment is common after stroke and cognitively impaired individuals are less likely to engage in physical activity. [26]
After a 5-year follow-up of 2,914 stroke survivors, aged over 65 years of age, 64% had cognitive impairment and patients with cognitive impairment were 6 times more likely to suffer a recurrent stroke than patients with normal cognition. Incident stroke was associated with transition from cognitive impairment no dementia to dementia. Cognitive impairment may be an independent risk factor for stroke through worse adherence to treatment and altered attitude of physicians towards control of risk factors. [27]
There is evidence for a reverse causality between physical activity and cognition in stroke survivors. A systematic review (9 studies, up to 2011, n=716 participants) showed a significant benefit of physical activity on cognition (p=0.015). [28]

Falls

Falls occur regularly in stroke survivors. Falls cause low self-efficacy, which is negatively associated with physical activity. [9]
In one study, between 14-65% of people with stroke fell at least once during hospitalization and between 37-73% during the first 6 months. [29]
A RCT studied the effects of body-weight supported treadmill rehabilitation after stroke over 12-16 weeks in 408 stroke survivors (one group started the therapy 2 months after stroke, the 2nd group after 6 months) compared with a 3rd group (supervised home-exercise programme consisting of enhancing flexibility, range of motion in joints, strength of arms and legs, coordination and static and dynamic balance). No significant difference of falls was noted.
between the three groups. However, in the subgroup with severe walking impairment, early therapy showed more falls than late therapy (52% vs. 36%, p=0.05) or than the home group (52% vs. 30.3%, p=0.009). The balance however, showed a clinically relevant improvement. [30] Another RCT (n=61 stroke patients, aged >65 years) assigned patients to two exercise programmes: an agility programme consisting of standing in various postures and walking with various challenges and a stretching/weight-shifting exercise programme focused on slow and low impact movements. The participants in the agility programme had significantly fewer falls than the stretching/weight-shifting programme. Functional balance was significantly improved with both interventions. [31]

Miscellaneous factors

The kinetic gait pattern in health controls is different from stroke survivors. Latter use other kinetic strategies to achieve an efficient walking. When applied to persons with stroke, movement patterns of healthy individuals do not translate into better results and trying to teach stroke patients to walk as healthy individuals do, may be counterproductive. [32] A systematic review (n=764, 29 studies) concluded that stroke survivors use more energy for comfortable walking speed than their healthy peers. [33] Physical activity preference changes after stroke were examined in another survey study (n=23 adult stroke survivors, n=41 controls). The study identified stroke survivors to prefer physical activity to be demonstrated to them and to be performed in a facility. [34] However, not all stroke patients have access to instructors and facilities.

Logistical difficulties are another factor negatively influencing the physical activity after stroke. Marzolini et al. (n=61) studied the main factors related to poor attendance to an ambulatory stroke rehabilitation programme. Weather, transportation problems, health problems (e.g. hospital readmissions, influenza/colds, diabetes mellitus, cardiac complications and musculoskeletal issues), traveling long distances and language barrier were the main factors identified to negatively affect the attendance to ambulatory rehabilitation. [35]

Reduced cardiorespiratory fitness is another factor limiting physical activity after stroke. Cardiorespiratory fitness is the capacity of the heart, lungs, vessels and muscles to deliver oxygen and to remove metabolic products during physical activity. It reflects vascular health. [36] Mackay-Lyon et al. measured VO2max maximal oxygen consumption, reflects the overall cardiorespiratory fitness) in stroke survivors (n=29) with unilateral deficits after 26+/−8.8 days and found that it corresponded to 60+/−16% of that of normative values for healthy sedentary individuals. [37] Physiological factors contributing to reduced cardiorespiratory fitness are: change of paretic-muscle structure, increased intramuscular fat and shift to fast-twitching fibers which are more insulin resistant and fatigue prone, increased muscle TNA-alfa, which is involved in muscle atrophy and insulin resistance, increased systemic pro-inflammatory cytokines (TNF-alfa, VCAM-1 and IL-6), altered glucose metabolism, impaired autonomic
control of the vascular system not related to medication (e.g. beta-blockers) and impaired breathing mechanics because of muscle weakness. [36]

A meta-analysis (17 studies, n=4,571 mostly ischaemic stroke survivors) showed a significant increase of cardiorespiratory fitness (measured in VO2max) and significantly better results in 6-Meter Walking Test with high intensity training (defined as achieving >60% of heart rate reserve/VO2max or >70% HRmax), compared to mild-to-moderate intensity training without increasing the rate of adverse events. [38]

Effects of physical activity on risk factors and stroke risk in secondary stroke prevention

The question arises whether performing physical activity is having a positive effect on risk factors and lowering stroke and vascular recurrence rate. There is increasing evidence.

After analyzing 12 meta-analyses (n= 210,926 patients, 106 studies) on secondary stroke prevention (11 meta-analyses) and mixed secondary/high risk primary prevention (1 meta-analysis) Hackam et al. concluded that 5 treatment interventions consisting of lifestyle modification, aspirin, a statin and an antihypertensive agent are sufficient to reduce the risk of a major vascular event (i.e. nonfatal stroke, nonfatal myocardial infarction, and vascular death) by 80%, which would translate in a number needed to treat of 5 and in a residual 5-year risk of 5%. [6] 11 trials included in the 12 meta-analyses studied physical activity (n=2,285) with a relative risk reduction of a major vascular event (i.e. nonfatal stroke, nonfatal myocardial infarction, and vascular death) of 28% (relative risk 0.72, 95%CI 0.54-0.95).

Putting it into perspective, Aspirin (n=18,270) had a relative risk reduction of 22% (relative risk 0.78, 95%CI 0.71-0.85), statins (n=90,056) of 21% (relative risk 0.79, 95%CI 0.77-0.81) and antihypertensives (n=15,527) of 21% (relative risk 0.79, 95%CI 0.66-0.95).

A negative association of cardiorespiratory fitness and incident stroke, atrial fibrillation and all-cause mortality in primary stroke prevention is well established. [39] However, the role of physical activity and cardiorespiratory fitness in secondary stroke prevention is less clear. A comprehensive meta-analysis (n=58 intervention trials, data included up to 2014, n=2,797 participants) investigated the effect of physical activity on vascular mortality after stroke. Only 13 of 2,797 participants died before the end of the intervention and 9 of 1,256 until the end of the follow-up (months). The included participants were at lower risk of death compared with the wider stroke population. However, the inclusion of stroke patients in intervention trials may be biased because of self-selection of physically active participants. [40]

A recent meta-analysis (22 RCTs, data included up to 2015, n=2,574 patients after ischaemic stroke/TIA) studied the effects of lifestyle intervention trials, including cardiorespiratory fitness (n=1,800) and combined programmes (n=222) on overall vascular mortality in secondary stroke prevention. A significant reduction in systolic blood pressure (mean difference -3.6 mm Hg) was achieved in the subgroup where the intervention lasted longer than 4 months and where more than 3 behavioral change techniques were applied. No effect of lifestyle interventions on vascular event rate, mortality, diastolic blood pressure or total cholesterol levels was found, likely because of the small study sample and the short follow-up.
time of a mean duration of 5.5 months. [41]
An intervention trial on patients with mild stroke/TIA (initially n=110 participants, n=80 completed the intervention, mean intervention-interval 33 weeks) analyzed the effect of a comprehensive rehabilitation programme consisting of physical activity (2x/week administered by bachelor kinesiologists or 4x/week following patient’s choice, supervised by phone), besides an educational programme and diet change on modifiable risk factors. The use of medication was not significantly changed throughout the intervention. The investigators found a significant improvement of cardiorespiratory fitness, total/HDL-cholesterol levels and waist circumference and importantly a highly significant shift (p<0.001) from low Duke-Treadmill-Score (abr. DTS) to higher ones. [42] The DTS was used as an expression of risk of vascular mortality. High DTS scores are associated with lower mortality. The score is calculated taking the duration of physical activity, ECG changes and angina pectoris during the exercise into account.
A meta-analysis of intervention trials (18 RCTs up to 12/2016, n=930 participants) showed physical activity as an effective way of reducing resting systolic blood pressure (p=0.01), fasting glucose (p<0.0001) and fasting insulin (p=0.03), and increasing HDL-cholesterol levels (p=0.008). [43]
The SAMMPRIS trial studied best medical treatment, including a supervised physical activity programme with/without percutaneous angioplasty and stenting of symptomatic intracranial stenosis. [44] The lifestyle modification programme called INTERVENT, previously shown to be effective reducing vascular event rates, took physical activity besides nutrition, stress management and smoking cessation into account. [45] Physical activity was quantified using the Physician-based Assessment and Counseling for Physical Activity (PACE) Self-Report Questionnaire with 3 points corresponding to vigorous or moderate physical activity but not being physically active regularly, 4 points corresponding to moderate physical activity <5x/week or vigorous physical activity <3x/week and 6 points corresponding to at least 30 minutes of moderate physical activity a day for at least 5 days a week for the past 6 months or more. [46,47] Physical activity within the target (defined as ≥4 points) had a significant protective effect against myocardial infarction, stroke and vascular death at 3 years (OR 0.5, 95%CI 0.4-0.7, p<0.05). Other modifiable risk factors such as LDL-/non-HDL-cholesterol levels and systolic blood pressure within the target, also protected against vascular events.

What about physical activity recommended in stroke survivors in the acute and in the rehabilitation phase?
Physical activity after stroke has the goal of preventing recurrent vascular events and possible post-stroke complications and of improving impaired body functions. The type and quantity of physical activity has to be adapted to individual co-morbidities and to specific residual deficits (e.g. to impaired gait pattern).
The current statement of the AHA/ASA from 2014 recommends specific strategies of physical activity according to different goals after stroke: [1]
In the acute phase, evidence is in favour of early mobilization (with few exceptions which we
consider at our Bernese Stroke Centre such as e.g. haemodynamic ischaemic stroke, large artery occlusion and persistent penumbra). The goal of mobilization in this phase is to prevent deconditioning, orthostatic intolerance, pneumonia and depression. The intensity of physical activity should be light, with an increase of the HR of 10-20 bpm whilst exercising.

A graded exercise testing under ECG monitoring helps to assess the response of the vascular system and to adequately identify tolerance of physical activity (including optimal intensity and quantity) and thus to adjusted recommended intensity and levels of physical activity after stroke. There are no trials that answer the question of how soon after stroke a graded exercise testing can be safely performed (not done earlier than few weeks after stroke at our Bernese Stroke Centre).

During graded exercise testing, heart rate >120 bpm or >70% of the age-predicted maximal heart rate, systolic blood pressure >250 mmHg or diastolic blood pressure or >120 mmHg are criteria recommended for terminating the testing. Clinically relevant ECG abnormalities during testing are ST-segment depression, angina pectoris, ventricular arrhythmia, ventricular tachycardia or bundle branch-block. Although these ECG abnormalities are present in few stroke patients, the frequency of serious adverse events is very low. This may be due to the fact, that stroke residual defects may not allow maximal effort levels.

In the rehabilitation phase a supervised exercise programme is recommended as follows: Aerobic activity such as walking, stationary cycle ergometry, arm ergometry and seated exercises with an intensity of 40-70% HRmax, 3-5 days/week, 20-60 min sessions (or multiple 10 min sessions) may be performed. The goals of aerobic exercise are to increase walking speed and efficiency, to improve exercise tolerance, to increase independence in activities of daily living (abr. ADL), to improve cognition and to reduce risk factors of stroke. Muscular strength and indurance exercise helps increasing muscle strength, facilitating to perform leisure time and occupational activities and decreasing the maximal voluntary contraction that a given activity demands. It is suggested to perform 1-3 sets of 10-15 repetitions of 8-10 exercises involving the major muscle groups at 50-80% of maximum repetition strength, 2-3x/week. Flexibility exercises such as stretching may prevent contractures, increase the range of movement, improve ADLs and decrease the risk of injury. Static stretches for 10-30 seconds before or after aerobic or strength exercise, 2-3x/week are recommended. Balance and coordination activities, Tai chi, Yoga, recreational activities using paddles/sport balls to ameliorate hand-eye coordination are said to improve balance, quality of life and mobility and to decrease fear of falling and to increase safety during ADLs. These activities should be used as a complement to aerobic and muscular strength exercises 2-3x/week.

Conclusions

Besides improving independence and quality of life, physical activity in stroke survivors improves risk factors such as arterial hypertension, impaired glucose tolerance, overweight, depression, impaired cognitive function, lipid profile and cardiorespiratory fitness. Interestingly, the limiting factors for physical activity after stroke such as impaired balance, falls, fatigue, reduced self-efficacy, depression, reduced cardiorespiratory fitness and impaired
cognitive function can be improved through performing individually tailored exercise. Some of these limiting factors such as reduced cardiorespiratory fitness, impaired cognitive function and depression are also independent risk factors for stroke. Implementing efficient secondary prevention measures, including physical activity is challenging, mainly because of reduced awareness or access. However, ambulatory post-stroke programmes including education, addressing risk factors, healthy lifestyle and stroke residual deficits are efficient in reducing risk of recurrent stroke and other vascular events. A supervised exercise programme should be implemented in the rehabilitation phase. Physical activity after stroke appears to be generally safe.

Key messages

- There are various limiting factors for physical activity after stroke, largely due to post-stroke residual and secondary symptoms, which can be treated by performing physical activity.
- Physical activity is a generally safe and effective intervention in secondary stroke prevention.
- The awareness of the beneficial effect of physical activity after stroke is generally low.
- The current statement of the AHA/ASA from 2014 recommends specific strategies of physical activity according to different goals after stroke.

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