Physical Functioning, Body Composition and Exercise in Elderly Community-living Individuals with Stroke

BIRGIT VAHLBERG
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Abstract

A comprehensive view of physical function, body composition and exercise post-stroke that is based on clinical examination is lacking. The effects of a progressive resistance and balance (PRB) exercise program have not been fully evaluated in community-living individuals after stroke.

The overall aim of this thesis was to explore and describe physical function, physical activity, body composition, nutritional status and psychological factors. Another aim was to evaluate both the short-term and long-term effects of a PRB exercise program.

Physical function, physical activity, body composition, nutritional status and psychological factors were assessed in community-living individuals (65-85 years) approximately 1 year after stroke. Paper I-II (n=195, n=134) had a cross-sectional design and the main outcome was mobility and physical activity. In paper III-IV, (n=67, n=43) individuals were randomly assigned to either a PRB exercise program group or a control group. The main outcomes were balance, mobility, fat-free mass (FFM) and fat-mass (FM).

In paper I, mobility was reduced and physical activity level was low compared to age-matched healthy controls. Factors explaining the variance in mobility were age, physical activity, fall-related self-efficacy and EQ-5D. In paper II, >20% had a BMI ≥30 kg/m² and had an altered body composition that was mainly characterised by a high fat-mass index (FMI). Neither fat-free nor FM were associated with mobility in this cohort. The factors associated with low mobility were low physical activity Odds ratio (OR) (CI 95%) 8.2 (2.8-24.2), risk for malnutrition, OR 5.8 (1.6-21.1), and each 10-year period, OR 2.8 (1.24-6.24). Individuals participating in the PRB exercise program (paper III, n=67) revealed significantly higher balance, walking capacity and comfortable walking speed compared to the control group at 3 months. The faster walking speed persisted at 6 and 15 months. In paper IV (n=43), at 3 months, the PRB exercise group had a significant reduction in FM percentage and a decrease in IGF-1 compared with the control group. Further, changes in FMI were associated with improved walking capacity.

Many individuals perceived partly modifiable disabilities 1 year after stroke. Exercising in groups for 3 months improved physical function and decreased fat-mass percentage and IGF-1.

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List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACoSM</td>
<td>American College of Sports Medicine</td>
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<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>Apo A1</td>
<td>Apolipoprotein A1</td>
</tr>
<tr>
<td>Apo B</td>
<td>Apolipoprotein B</td>
</tr>
<tr>
<td>BIA</td>
<td>Bioimpedance analysis</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CI</td>
<td>Cerebral infarction</td>
</tr>
<tr>
<td>CCI</td>
<td>Charlson Comorbidity Index</td>
</tr>
<tr>
<td>CCT</td>
<td>Circuit Class Training</td>
</tr>
<tr>
<td>CG</td>
<td>Control group</td>
</tr>
<tr>
<td>CRS</td>
<td>Cardiovascular disease risk score</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>EuroQol-5D</td>
</tr>
<tr>
<td>EQ-5D-VAS</td>
<td>EuroQol-5D Visual Analog Scale</td>
</tr>
<tr>
<td>FES(-S)</td>
<td>Falls Efficacy Scale-Swedish version</td>
</tr>
<tr>
<td>FFM</td>
<td>Fat free mass</td>
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<tr>
<td>FFMI</td>
<td>Fat free mass index</td>
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<tr>
<td>FM</td>
<td>Fat mass</td>
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<tr>
<td>FMI</td>
<td>Fat mass index</td>
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<tr>
<td>FM%</td>
<td>Fat mass percentage</td>
</tr>
<tr>
<td>FoF</td>
<td>Fear of falling</td>
</tr>
<tr>
<td>GDS-20</td>
<td>Geriatric Depression Scale</td>
</tr>
<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
</tr>
<tr>
<td>HRQoL</td>
<td>Health Related Quality of Life</td>
</tr>
<tr>
<td>IG</td>
<td>Intervention group</td>
</tr>
<tr>
<td>IGF-1</td>
<td>Insulin-like Growth factor-1</td>
</tr>
<tr>
<td>ICH</td>
<td>Intracerebral hemorrhage</td>
</tr>
<tr>
<td>ICF</td>
<td>International Classification of Functioning Disability and Health</td>
</tr>
<tr>
<td>LDL</td>
<td>Low density lipoprotein</td>
</tr>
<tr>
<td>M-MAS UAS-99</td>
<td>Modified Motor Assessment Scale Uppsala University Hospital-99</td>
</tr>
<tr>
<td>PASE</td>
<td>Physical Activity Scale for the Elderly</td>
</tr>
<tr>
<td>PRB</td>
<td>Progressive Resistance and Balance</td>
</tr>
<tr>
<td>RS</td>
<td>Riksstroke</td>
</tr>
<tr>
<td>SPMSQ</td>
<td>Short Portable Mental Status Questionnaire</td>
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The International Classification of Functioning, Disability and Health (ICF) can be divided into two different parts: functioning, where functioning mirrors the positive aspects between a person and the surroundings, and disability, where disability (an umbrella term for impairments, activity limitations and participant restrictions) describes the negative aspects, i.e., loss of function (1). Further, the ICF comprises the following components: 1) body functions, anatomic structures and their related impairment; 2) activities and activity limitations; and 3) participation and participating restrictions as well as environmental and personal factors (Figure 1). The ICF can be used in different ways for rehabilitation and research and in mapping function and disability. The aim of ICF is to provide a unified and standardised language and framework to describe health and related states (1). In the present thesis, ICF is used to visualise the targeted areas.

**Figure 1.** The International Classification of Functioning, Disability and Health (ICF)
Preface

The experiences I have working as a physiotherapist with post-stroke individuals at the Geriatric Clinic at The Uppsala University Hospital are the basis for this thesis. These clinical experiences made me wonder how the patients continued with rehabilitation and their ordinary lives henceforth. Over the years, I also had the opportunity to spend some summers working in a 4-week stroke program at Sätra Brunn, an old health spa located near Uppsala. This program included both individual treatments as well as group sessions. Rehabilitation was carried out in a beautiful environment with numerous social possibilities. I realised that participation in these stroke programs, several years after the stroke, enabled the individuals to improve their functional and psychological status. Meeting other individuals who had suffered strokes previously seemed crucial for their well-being.

The long-term effects of a stroke may differ between individuals, despite a similar location and stroke magnitude, as the effects are influenced by personal and environmental factors. This is crucial for planning an individualised rehabilitation. I realised that I wanted to find out in more detail how the individuals with stroke perceived their lives from a long-term perspective and what type of disabilities and functional losses were most common. This provided the basis for the two first cross-sectional studies in this thesis. I also wanted to evaluate group-exercising with respect to the individual’s functioning, muscular prerequisites, nutritional status and cardiometabolic risk factors; the latter were new areas for me.

This thesis is dedicated to all the individuals with stroke that shared their experiences with me and thereby made it possible to compare my former clinical knowledge with new scientific knowledge.

I wish to thank all the participating individuals for making this thesis possible and my wish is that this research can add some missing pieces and contribute to a better everyday life for individuals post-stroke.
INTRODUCTION

Stroke

In Sweden, approximately 30,000 people have a stroke each year, and approximately 23,000 of those people suffer from their first stroke according to Riksstroke (the Swedish stroke register, RS) (2). The mean age for stroke in Sweden is 74 years for men and 79 years for women (3). Approximately 80% are more than 65 years old at the time of the stroke. The definition of stroke according to the World Health Organization (WHO) is “rapidly developing clinical symptoms and/or focal signs, and at times global loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin” (4). Stroke is one manifestation of cardiovascular disease (CVD) and can be divided into different types: cerebral infarction or ischemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage (3). Stroke and transient ischemic attack (TIA) have similar pathophysiological backgrounds and TIA is a strong predictor of stroke, especially in the first 90 days after the TIA (2). The incidences of TIA are 8000 – 12000 cases annually in Sweden according to RS. Further, the total cost for stroke in Sweden is calculated to be 18.3 billion Swedish kronor per year according to RS (2).

In the RS individualised data within health-care production concerning hospital care, rehabilitation and secondary prevention are registered. All hospitals admitting patients with acute stroke are included in the register, which covers > 80% of all stroke events in Sweden (2). At 3 and 12 months follow-ups, additional data are gathered by a postal questionnaire sent to the individual and then are further registered in RS. In this thesis, some data are collected from RS at the time of the stroke and after 1 year. In 2013, approximately 41% of the individuals with stroke displayed unmet needs of rehabilitation after 1 year, according to RS 1-year follow-up (5). Based on earlier reports, that was the origin of the present thesis. Among the older individuals (> 75 years), self-perceived unmet rehabilitation needs are even higher. In the Uppsala University Hospital, only cases of acute stroke are reported to the RS register.

Long-term survival after stroke continues to improve, and because the elderly population is growing, this results in an increased number of individuals in Sweden who previously have had a stroke (5). Stroke is more common in men > 65 years old and in women ≥ 85 years (6). The preva-
The prevalence of stroke is approximately 30% higher in men, but women have a higher rate of cardio-embolic stroke and experience a worse outcome because of the typical greater age at stroke onset. Women also tend to suffer from post-stroke depression and low quality of life more frequently compared to men (7).

If the strong decline in stroke mortality seen in the past decades continues, this may not result in a change in the absolute number of stroke deaths, because of the aging population (8). The morbidity burden after stroke is likely to become more important than the mortality burden because of better survival rates. Preventive strategies and rehabilitation methods must be improved to reduce stroke-related disability, enhance physical fitness and prevent future cardiovascular events (8, 9).

Risk factors for stroke

The population-based Framingham Heart Study has played an important role since 1949 in establishing the now widely accepted knowledge regarding cardiovascular diseases (CVD) (10). The study is still ongoing and has recently enrolled a third generation of participants. The Framingham Heart Study has been able to identify important risk factors for CVD and, in fact, coined the term “risk factors” (10). Stroke is a heterogenic disease, and there can be differences in risk factors between the types of stroke and gender (7). Lifestyle related diseases, including cardiometabolic diseases (i.e., CVD, obesity, metabolic syndrome and type II diabetes), can, to a high degree, be prevented by a healthy lifestyle. Hypertension, abdominal obesity, smoking, diabetes, alcohol, physical inactivity, depression and an unhealthy diet are examples of modifiable risk factors that are important both for prevention of the primary event and for recovery after a stroke (11).

Hypertension and hypercholesterolemia

Hypertension is the greatest risk factor for stroke and is also the most modifiable factor (12, 13). Hypertension can be defined as a systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic BP ≥ 90 mm Hg. Lifestyle modifications, as a component of antihypertensive therapy, are associated with a reduction in blood pressure and include dietary modifications and regular physical activity (13).

Hypercholesterolemia is another risk-factor for atherosclerotic CVD and mortality, especially a high concentration of low-density lipoprotein (LDL) (13). A low concentration of high density lipoprotein (HDL) is also a risk factor for atherosclerosis. The HDL is primarily affected by regular physical activity, whereas high LDL can be modified through nutritional changes and lipid-lowering medications, e.g., statins. If necessary, lipid-lowering medica-
tion should be prescribed following a stroke according to current guidelines (13). However, statins also have some side effects that are primarily associated with muscle symptoms (e.g., myopathy) (14). Individuals with stroke have an increased prevalence of hypertension, diabetes and hypercholesterolemia (metabolic syndrome) (13). Additionally, individuals with diabetes also have an increased risk for death following stroke as well as an increased risk for having another stroke or a myocardial infarction (15).

Lipid disorders can also be measured with the ratio between apolipoprotein B (apoB) and apolipoprotein A1 (apo-A-1) (16, 17). Apolipoproteins are found to predict cardiac risk in individuals above the age of 70(18).

Physical inactivity
Physical activity is defined as any bodily movement produced by skeletal muscles resulting in energy expenditure (19). Reasons for a sedentary lifestyle can include an increased dependence on cars because work and home are separate units, an increased number of automatic procedures, increased television and computer usage and a feeling of insecurity about moving around in society (20). Physical inactivity and a sedentary lifestyle together increase the likelihood for inflammatory processes and hence increase the risk for CVDs (21). A high level of physical activity has a beneficial effect on most stroke risk factors. Moreover, it has been proven that individuals with high levels of physical activity have a 67% lower prevalence of metabolic syndrome compared to individuals reporting a sedentary lifestyle (22). There is a lack of evidence on the effect from non-pharmacological studies, i.e., well-designed exercise studies, on cardiovascular risk-markers and body composition after stroke (9). Knowledge about the effects of sedentary behaviour and ways to optimise physical activity after stroke are important issues in physiotherapy.

Nutritional risk and prevention
Hankey (23) concluded that the two main threats to global health and risk of stroke are over-consumption of salt and calories. Salt reduction can lower blood pressure and reduce stroke mortality, whereas obesity and over-nutrition can lead to diabetes mellitus, hypertension and hypercholesterolemia. A diet rich in fruits, vegetables, dietary fibre and fish in conjunction with a limited intake of saturated fat, trans-fatty acids and cholesterol helps to protect against stroke (13, 24). The INTERSTROKE study highlighted that increased consumption of fish and fruit reduces the risk for stroke (11). Over-nutrition can increase the risk for stroke; the development of obesity, hypertension, hypercholesterolemia and diabetes as a result of a high caloric intake might be the cause of this increased stroke risk (23). There is a profile of cardiometabolic and inflammatory markers that be-
comes apparent when one’s Body Mass Index (BMI) increases from a normal weight to obesity. Individuals with a BMI of \( \geq 30 \text{ kg/m}^2 \) have a doubled risk of ischemic and haemorrhagic stroke compared to individuals with a BMI of \( < 23 \text{ kg/m}^2 \) (24). Among both men and women, obesity is most common in the elderly. Interestingly, and in contrast, recent studies have reported lower mortality, improved functional outcomes and a lower risk for re-admission from recurrent stroke in obese patients compared with lean patients (25, 26).

Many individuals with stroke are undernourished at hospital admission, and their nutritional status is known to deteriorate further during their hospital stay (24). Both under-weight and overweight/obesity are important states to consider in individuals after stroke. Nutritional status can affect C-reactive protein (CRP), plasma albumin and serum insulin-like growth factor-I (IGF-I). Furthermore, it is suggested that inflammatory markers, such as CRP, are a triggering factor for stroke, because increased concentrations have been associated with metabolic syndrome and FM (27). CRP-levels are influenced by weight changes, i.e., increased body fat is positively related to CRP, while increased intake of dietary fibre is related to lower CRP (28). Albumin is a marker of malnutrition and deficiency in caloric and protein intake and is an indicator of mortality and morbidity (24). Albumin levels have been proven to be neuro-protective because there is an association between high serum albumin and protein supplementation and better functional outcomes, as well as lower mortality rates in sub-acute stroke patients (29). Except for nutritional intake, the IGF-1 level can vary with different ages, gender, oestrogen status, exercise status, stress levels and BMI (30). Higher levels of physical activity, optimal protein intake and younger age predisposes for higher IGF-1 levels. In addition, both normal high and low levels of IGF-1 are associated with insulin sensitivity (31).

Post-stroke conditions

Stroke causes disabilities of various degrees; the localisation of the stroke and the severity of the brain injury determine the impact of stroke. A typical sign of stroke and TIA is sudden weakness/numbness of the face, arm or leg occurring mostly on one side of the body. Motor function can be lost; the major part of motor recovery occurs within the first 6 months (32). Confusion and difficulties in speaking or understanding, walking and balance difficulties are also common symptoms. Other consequences that are not immediately apparent could be of a cognitive and perceptual (e.g., sensory and visual impairments) nature. In the latest report and 1-year follow-up from RS (2013), it was found that 88% were independent in daily activities at the time of the stroke (5). After 1 year this was 75%, which can depend on another stroke or fall incidences. Another cause for the loss of independence might
be that rehabilitation stops after approximately 3 months. Moreover, most individuals < 75 years are independent in moving inside and outside their homes, but this is in contrast to being > 75 years. In women > 75 years, about half need help in walking and transferring (5).

Long-term changes in physical function, psychological factors, nutrition and body composition after stroke can include affected mobility (33), motor impairments (34), inactivity (35, 36), reduced health-related quality of life (37), depression (38), low fall-related self-efficacy (39), falls and fear of falling related to balance disturbances (40), problems with walking in the community (40), altered body composition with less muscle mass, or increased fat mass and malnutrition (24, 41, 42). Further, white matter changes or leukoaraiosis are also issues in the elderly, as well as in stroke subjects, and result in cognitive decline, balance disturbances and increased depression (43).

Physical function and physical activity
In this thesis, physical function is an umbrella term for measurements that include mobility, walking, motor function and balance. Different definitions of mobility can be obtained from different perspectives (44). Mobility is not stabilised after post-stroke inpatient rehabilitation and it is reported that 12-43% of post-stroke individuals show further deterioration of mobility during the next one to three years (45-47). Gait speed, balance and lower extremity function, as measured by the Short Physical Performance Battery (SPPB), provides a good estimate of the future risk for hospitalisation, health deterioration and mortality in initially nondisabled, older adults (48). However, the value of using the SPPB in assessment of functional progression after stroke needs to be further explored (49).

Self-selected gait-speed below 1 m/s can identify older persons at risk for health-related outcomes (50, 51), and a gait-speed of more than 1.2 m/s is needed to cross a street safely (52). This is in line with a meta-analysis proposing that a faster gait-speed, i.e., > 1.0 m/s in older people, suggests a better life-expectancy while a slower gait-speed, < 0.6 m/s, is indicative of poor physical function and health (53). Small or substantially meaningful changes for the Six Minute Walk test (6MWT) are 20 or 25 to 50 meters, respectively, compared to 0.05 m/s to 0.1 m/s for the walking speed in comparable groups (54, 55). The above knowledge can be used in clinical assessments of gait and in designing preventive interventions.

Individuals who have impaired balance at least six months after stroke are at risk for falls and are shown to have low activity and participation scores (56). This highlights the importance of focusing on factors such as falls and balance self-efficacy during rehabilitation. Another study on post-stroke individuals confirms this finding because fallers are more likely to report a reduced fall-related self-efficacy compared with non-fallers (40). Within 12
months post-stroke, there is a two-fold increase in hip and femur fractures caused by falling (57). Increased risk for falls is also connected to sarcopenia and associated disabilities (27, 58).

Community-living individuals without stroke have a higher level of physical activity compared to individuals of the same age with stroke, measured by the Physical Activity Scale for the Elderly (PASE) (35). The mean PASE score was 161 in the healthy control group and 119 in the stroke group. Interestingly, but not unexpectedly, motor function was not crucial for the level of physical activity. A low level of physical activity after stroke can depend on the consequences from the stroke as well as a sedentary lifestyle before, due to the effects of age and comorbid diseases (21). Cardiorespiratory fitness in stroke victims is found to be approximately 50% of the expected value in an age- and gender matched reference group (59). Activity limitations, such as in walking and chair-rising, are associated with low cardiorespiratory fitness level as well as low muscle strength (59, 60). It is important to assess how physical function can interact with physical activity to identify possible actions to support and assess the level of physical activity after stroke.

Body composition

Skeletal muscle can be considered the main organ for disabilities after stroke, but it receives little attention despite structural, functional and metabolic changes. Beginning at age 50, there is a normal loss of muscle mass ranging from 1 to 2% per year that also affects muscle strength and muscle quality (41, 42, 51, 61, 62). Muscle strength in the legs is associated with physical function, such as being able to climb stairs, walk at different speeds and maintain mobility, which are all common difficulties after a stroke (63). Stroke can further be linked to skeletal muscle changes as a result of abnormalities, denervation, remodelling and spasticity causing atrophy, especially in more severe cases (64). A stroke-induced sarcopenia in hemiplegic stroke was recently introduced that partly differs from age-dependent sarcopenia (64).

Impaired glucose metabolism is found in more than 80% of stroke survivors (65). Changes in muscle and fat mass in aging and after stroke, together with inactivity, can lead to impaired glucose metabolism and progression to diabetes, which increases the risk for another stroke or myocardial infarction. There is evidence that post-stroke individuals have significantly less muscle mass in the paretic limbs compared to their non-paretic side (41). Muscle mass loss after 1 year is also different in those who regain walking capacity 2 months after stroke compared to non-walking individuals, which is not surprising because weight-loading is important in preventing or slowing muscle loss (66). Considering the role muscles play in glucose metabo-
lism and in slowing bone mineral loss, changes in muscle mass may be even more important.

For this thesis, sarcopenia was defined as a “fat free mass index (FFMI, kg/m²) below the 25th percentile of a reference population together with usual gait speed < 1.0 m/s” according to the International Working Group on Sarcopenia (51, 67). Currently, no definition of sarcopenia is fully accepted, and sarcopenia is not included in the classifications of diseases. Sarcopenia can predict loss of mobility and independence and may be a consequence of physical inactivity, age, nutritional deficits and hormonal changes (62). Unfortunately, limited data are available on muscle pathology after stroke and the state is not considered in current guidelines. There are also few studies that describe body composition, i.e., muscle mass and FM and sarcopenia after stroke, as well as few studies that measure changes in body composition over time or that reports effects from intervention studies after stroke (41).

An increasing prevalence of obesity in older individuals causes an increased burden on health care systems in developed countries as a result of sarcopenic obesity, i.e., obesity and sarcopenia occurring together (27, 68). Sarcopenic obesity in this thesis was defined as a FFMI below the 25th percentile and a fat mass index (FMI) above the 50th percentile of a reference population, as earlier described (69). Baumgartner showed that individuals older than 60 years with sarcopenic obesity have a much higher risk for reduced balance, gait and falls in the previous year, but not much is known about sarcopenic obesity in individuals post-stroke (41, 42, 70). Obese, elderly individuals have a higher muscle mass but poor muscle quality compared to the non-obese and frail elderly due to the anabolic effect induced by their body weight (71). This may contribute to the obesity paradox, recently reported after stroke (26). Lower mortality, improved functional outcomes and a lower risk for re-admission has recently been reported in obese individuals with stroke, in contrast to previous findings (25). It can be assumed that low physical activity level and reduced cardio-respiratory fitness may be greater health threats than obesity itself (72).

Nutritional changes

Malnutrition, i.e., weight loss after stroke, is common (24, 73). Different neurological deficits may occur as a result of decreased function, and motor functions that allow for the necessary arm-movements for eating, chewing and swallowing can be lost due to hemiparesis. Perceptual deficits, visual-field defects and oral or motor apraxia are conditions that can also affect nutritional status. A number of stroke patients are malnourished upon hospital admission and continue to deteriorate further after being hospitalised (24).
Jönsson et al. (73) also showed an increased prevalence of overweight in individuals approximately one year after stroke, rising from 52% immediately after the stroke to 61%, 1 year after the stroke. A reduction of five to ten percent of one’s bodyweight can improve lipid profiles and insulin sensitivity in overweight and obese individuals (74).

Inflammatory activity, as measured by CRP, is often elevated in individuals with stroke and upon discharge from the hospital, and also associated to further vascular events and deaths together with aging (75, 76). Further, CRP levels can be used to stratify post-stroke individuals into high risk and low risk groups, with CRP levels ≥ 1.5 g/L having a poorer diagnosis. Albumin levels have been found to associate mortality with cardiovascular disease, cancer and other causes (77). Furthermore, low levels of albumin in ischemic stroke are reported to be significantly associated with a higher score (> 3 on the modified Rankin scale) and poor outcome, together with high recurrence of stroke and death in different stroke subtypes (24, 78). In conclusion, relatively high serum albumin levels in acute stroke have a positive effect on functional outcome. After ischemic stroke, the IGF-1 levels are revealed to be both neuroprotective, regenerative and correlated with better functional outcomes (79). Low levels of IGF-1 have been observed after stroke and might reflect malnutrition and low levels of physical activity (80).

Psychological factors

Post-stroke individuals have a broad range of symptoms, but few studies have comprehensively assessed these physical and psychological factors (81). Major psychological consequences after stroke include decreased cognitive function (82), depression (38), low health-related quality of life (HRQoL) (37), decreased fall-related self-efficacy (83) and fear of falling (FoF) (40). After a stroke, individuals may have impaired cognitive functions, such as problems with memory, language, calculation and executive functions, indicating problems in daily living (82).

Depression has a great impact on life satisfaction 1 year after stroke; active rehabilitation can affect life satisfaction and thus lead to decreased depression (38). Anti-depression treatment is another option in more severe cases. It is important to detect and manage depression several years after stroke to improve life satisfaction and reduce the risk for another stroke (11). However, it is unclear what type, intensity and duration of exercise might improve depression as well as HRQoL; additional controlled studies are therefore warranted (84).

In Sweden, health-related quality of life (HRQoL) using EQ-5D is known to vary between socio-economic groups and diseases (85). Moreover, the frequency of moderate and severe problems increases with age. Individuals with both myocardial infarction and stroke have lower HRQoL compared with patients with other diagnoses and those with stroke revealed the lowest
HRQoL, which was even lower when combined with myocardial infarction (37).

Self-efficacy can be defined as the degree of confidence a person perceives that is connected to their ability to perform specific behaviours (83). Individuals with high self-efficacy tend to cope better with challenging tasks, put forth more effort, and persist longer with particular tasks in the face of aversive stimuli. Fall-related self-efficacy is a psychological issue that might influence functional decline and limit individual functions beyond that of physical function. The activities in daily life over 10 months after a stroke can be predicted by fall-related self-efficacy (39). Low fall-related self-efficacy is also significantly associated with impaired physical function in individuals after stroke (40). Impaired vision, low cognition or a wrong idea about one’s own physical abilities in any direction are characteristics that may influence fall-related self-efficacy (40). Knowledge pertaining to how self-efficacy influences behaviour is important in the planning of effective interventions and in identifying individuals with low self-efficacy.

Physical function and previous falls are associated with fear of falling in individuals with stroke (40, 86). A FoF can be defined as an ongoing concern about falling that might restrict the performance of daily activities (87). An increased risk for falling, hip fractures and FoF are common after stroke and the reported incidences vary between 40% to 70% (88).

Exercise and recommendations among individuals with stroke

Exercise and training are used synonymously in this thesis and are classified as a subcategory of physical activity; the definition of exercise is a physical activity that is planned, structured and repetitive for the purpose of conditioning any part of the body (19). Furthermore, physical fitness is defined as a set of physiological attributes including cardiorespiratory fitness, muscle strength, body composition and flexibility and relates to the ability to perform physical activities for an extended period (19). Due to physical inactivity or immobilisation, physical fitness can deteriorate 12-14% in 10 days but aging also reduces fitness level. The American College of Sports Medicine (ACoSM) and the American Heart Association (AHA) guidelines on secondary prevention after stroke recommend that those capable of participating in physical activity and with stroke or TIA receive at least 30 minutes of moderate-intensity exercise, 1-3 times a week (13). Moderate intensity can be defined as vigorous activity sufficient to break a sweat or noticeably elevate the heart rate. Supervision from a healthcare professional is needed for individuals with disabilities. An expert in physical therapy or in cardiac rehabilitation can provide supervision, or at a minimum, an exercise regimen (13).
Progressive resistance training after cardiovascular disease including stroke

Muscle strength and power are closely related to muscle function and are essential for standing up from a sitting position or when walking (89). A small decline in muscle function has a greater impact on weaker individuals with disabilities and can consequently lead to difficulties in daily activities. Progressive resistance training (PRT) is carried out to improve muscle strength and endurance or muscle power output by making repeated muscle contractions resisted by body weight, elastic devices, free weights or specialised machines in a progressive manner (84). Currently, there is insufficient data to report effects on physical fitness, mobility (i.e., walking speed and walking capacity) and further physical function after participating in PRT after stroke, according to a recent systematic review (84). There is also a lack of well-designed randomised controlled trials reporting on the effects of PRT on psychological factors such as health-related quality of life and mood/depression after stroke (84).

The training dose is important and includes duration (minutes of sessions), frequency (days/weeks) and intensity (amount of effort) (90). The recommendation for PRT to be effective is that it should be performed 2-3 times/week, with 8-10 different exercises that target all major muscle groups (90, 91). Duration in different exercise interventions are usually 8-12 weeks in older adults (92). The ACoSM also recommends 1-2 minutes of resting between lower intensity exercises.

Percentage of maximum load, i.e., a repetition maximum (RM), can be used to describe the intensity of a strength exercise (93). The definition of 1-RM is the maximum weight that can be lifted one time. Another way to describe the intensity of strength training is by the maximum amount of weight being lifted. Furthermore, for individuals with CVD, the resistance should be reduced with an increasing number of repetitions (reps) (90). Using weight loads permitting > 15 reps enhances endurance and is considered to be performed with low intensity. Using weight loads with 8-15 reps is performed with a moderate intensity and improves muscular strength and endurance (90).

Effects of training can also be influenced by whether the training is task-specific and whether progression is being made (94, 95). Progression in this thesis refers to gradually adjusting the load for the exercise improvement of the individual (91, 96). The ACoSM recommends that balance training should include dynamic movements affecting the centre of gravity, progres-
sively more challenging postures that reduce the base of support, stressing postural muscles and reducing sensory input (97).

According to the AHA, the early stages of PRT should allow for musculoskeletal adaptation and good techniques at a moderate level to follow the recommendations on repetition range (90). This is of particular importance for individuals with cardiovascular disease such as stroke, because many are sedentary and have comorbidities. Absolute contraindications are e.g., unstable coronary heart disease, uncontrolled hypertension (> 180/110 mm Hg) and uncontrolled arrhythmias (90).

Aerobic training and regular cardiac rehabilitation together with lifestyle counselling have shown some effects on cardiovascular risk-markers in chronic stroke patients (9, 98). Circuit Class Training (CCT) is when individuals use workstations to practice intensively in groups with a focus on repetition of functional exercises and continual progression (99). Gym training, performed as CCT for 12 weeks, has shown some positive effects on gait speed and walking capacity after stroke compared to the typical physiotherapy (99). Changes in gait speed in that study persisted at follow-up after 24 weeks. Further, CCT favours group dynamics while including peer support and social interaction and are considered to be effective in individuals with mild to moderate disability after stroke (100). Social interaction is known to provide psychological benefits such as improved mood and higher self-efficacy (101).

Rationale

Suffering a stroke can turn life up-side-down and might lead to lifelong disabilities and fears. Thus, to meet the perceived unmet rehabilitation needs 1 year after stroke there was a need to explore physical function and physical activity, nutritional status, body-composition and psychological factors in older individuals with chronic stroke. Further, obtaining a comprehensive objective view of their everyday life situation post-stroke was essential. The intended meaning was to further develop and evaluate exercising to reduce the effect of the stroke and in many cases, a sedentary lifestyle. This knowledge may be used in the future planning of rehabilitation.
AIMS

The overall aim of this thesis was to explore and describe physical function, physical activity, body composition, nutritional status (including cardiometabolic risk markers) and psychological factors in elderly community-living individuals, approximately 1 year after stroke. Furthermore, another aim was to evaluate the short-term and long-term effects of a progressive resistance and balance exercise program.

The specific aims in this thesis were:

1. To explore and describe mobility and physical activity and investigate the association with psychological determinants and demographic characteristics (Paper I).

2. To explore and describe body composition, physical function and lifestyle factors, such as physical activity and nutritional status, and their impact on mobility. In addition, in the same cohort, another aim was to evaluate inflammatory, nutritional and cardiometabolic biomarkers (Paper II).

3. To evaluate the effects of a 3 month progressive resistance and balance exercise program on short-term and long-term physical and psychological functioning and physical activity level (Paper III).

4. To: (1) investigate the effect of a progressive resistance and balance exercise program on body composition, cardiometabolic risk markers and indicators of growth and nutrition; (2) evaluate possible associations between changes in physical function and body composition (Paper IV).
METHODS

Design
The thesis comprises paper I-II with a cross-sectional design and papers III-IV as a randomised controlled trial (Table 1). Written informed consent was provided by all subjects. The studies have been approved by the Regional Ethical Review Board, Uppsala (Dnr 200:067/2). The intervention trial was registered at ClinicalTrial.gov (Unique identifier: NCT1161329).

Recruitment and participants
All of the papers were based on the same sample presented in paper I. All eligible subjects in the geographic area of Uppsala County were identified, treated previously and registered to RS at the Uppsala University Hospital. After the stroke, rehabilitation and after-care were delivered in different settings throughout Uppsala County. Recruitment was carried out between October 2009 and April 2011.

In paper I, community-dwelling individuals between 65 and 85 years of age with a first or recurrent stroke 1-3 years before inclusion were included. Excluded were individuals with severe cognitive dysfunction, dementia or other communication problems (revealed from medical records or during examination). In total, 279 individuals were found to be eligible for paper I, and a total of 195 individuals, i.e., 70%, provided their full consent for participating. Three individuals were further excluded at the time of examination, due to difficulties understanding questions and instructions. If the individual declined to fully participate, they were asked whether they wanted to participate by answering the EQ-5D by telephone (102). From the 279 eligible individuals, 81 of the 82 individuals who did not want to participate fully were willing to answer questions on the EQ-5D and the EQ-5D-Visual Analog Scale (VAS) (102).

In Paper II, data from 134 of the individuals presented in paper I is included. Individuals not being able to perform BIA for any reason were further excluded (Figure 2).
For the randomised controlled trial (RCT), paper III comprised data from 67 of the 195 individuals found eligible in study I (76% male, mean age: 73 years). A median of 13 months had passed since the stroke. Individuals were included if they had the ability to walk a minimum of 10 m and had at least one of the following: lack of outdoor walking for at least 5 days per week (derived from the Physical Activity Scale for the Elderly) (103), a low fall-related self-efficacy (Falls Efficacy Scale-Swedish version < 115 points) (39), balance difficulties (Berg Balance Scale ≤ 52 points) (104), or repeated falls within the last year. Individuals with cognitive deficits (Short Portable Mental Status Questionnaire < 7 points)(105), or a systolic blood pressure >180 mmHg were excluded. Those matching the inclusion criteria who were willing to participate were randomised to an intervention group (n=34) or a control group (n=33). Of the 67 individuals included at baseline, 24% (n=8) and 6% (n=2) were lost to follow-up at 3 months in the intervention group (IG) and control group (CG), respectively. The attrition rate increased to 29% at 15 months in the intervention group (Figure 3).
In paper IV, 43 of the 67 individuals in paper III were evaluated. Individuals with pacemakers and those lacking BIA were further excluded. Eligible individuals participated in the same PRB exercise program as described in paper III (IG, n=20) or a control group (CG, n=23). Data from 24 individuals were excluded because of the following reasons: reduced static balance and standing capacity (n=17), pacemaker (n=4) and technical error (n=3) (Figure 4).
Procedure in the paper I-II (Cross-sectional design)

In paper I and II, potential participants received written information by mail about the study. The participants were also contacted by phone, and if they provided oral consent, a meeting at the hospital was scheduled. Self-reported questionnaires including physical activity level (PASE) the prior week (103, 106), psychological factors such as depression (GDS-20) (107), fall-related self-efficacy (FES(S)) (108) and HRQoL (102), were sent to the eligible individuals ahead of the clinical assessment meeting. These self-reported questionnaires were rechecked at the time of the assessment. At the hospital, after signing the written consent for participation, non-fasting venous blood samples were obtained. The samples were stored frozen (at -70°C) in a biobank until forthcoming analysis.

Approximately 7% were examined in their own home or at other smaller hospitals in the region around Uppsala. Performance-based data were collected at one time in the hospital by one person (BV): motor function (M-MAS UAS-99) (109); mobility (SPPB) (110); balance (BBS) (104) and the 10-m walking test (111, 112) at a self-selected pace were recorded. Age and comorbidity were collected via patient records and questionnaires. Level of cognition (SPMSQ) (113) and self-reported data such as FoF and number of falls within the last year were also obtained at the time of the assessment. The cognition test was performed as a face-to-face interview.
In addition, data were recorded at the clinical examination for further use in paper II and paper IV: body composition (BIA), nutritional status (MNA-SF) (106) and current prescribed drugs. Data were also obtained from RS register at the time of the stroke, including risk factors such as diabetes mellitus, atrial fibrillation, hypertension, smoking, and previous stroke or TIA. At the 1 year follow-up, the participants’ need for social support and information on whether they were living alone were gathered from the RS register.

Procedure in paper III and IV (Randomised controlled trial)

All individuals were informed about the study and had provided written informed consent before entering the study. Sixty-seven individuals from study I were randomised to an intervention group (IG, n=34; progressive resistance and balance (PRB) exercise program twice weekly for 3 months) or a control group (CG, n=33) in paper III. An experienced physiotherapist, blinded to group allocation, performed all the assessments at study start, and after 3, 6 and 15 months, respectively.

In Paper III, the **Primary outcomes** were: Balance (Berg Balance Scale) (104) and mobility (Short Physical Performance Battery) (114) at 3 months. The **Secondary outcomes** were: walking capacity (The 6-MWT) (115), 10-m comfortable walking speed (111), physical activity levels (The PASE) (103), health-related quality of life (EuroQol-5D (EQ-5D) (102), depression (The Geriatric Depression Scale (GDS-20) (107), and fall-related self-efficacy (the Swedish version of the Falls Efficacy Scale FES(S) (39).

Approximately 1 year after stroke, 43 of the 67 selected individuals presented in paper III (n=67) were further analysed in paper IV. They were part of the same intervention group as previously described in paper III (IG, n=20; progressive resistance and balance exercise program twice weekly for 3 months) or a control group (CG, n=23).

**Primary outcomes** were: FFMI, kg/m², FMI, kg/m² and how potential changes in body composition related to improved physical function including walking capacity, balance and mobility. **Secondary outcomes** were: cardiometabolic risk markers and bio-chemical indicators of growth and nutrition.
Assessments (paper I-IV)

An overview of the different measurements in the papers is given in table 1.

**Table 1. Assessments used in paper I-IV**

<table>
<thead>
<tr>
<th>Design Assessments</th>
<th>Cross-sectional</th>
<th></th>
<th>RCT</th>
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<tbody>
<tr>
<td></td>
<td>Paper I n=195</td>
<td>Paper II n=134</td>
<td>Paper III n=67</td>
</tr>
<tr>
<td><em>Body structure and function</em></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Body composition, BIA</td>
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<td>x</td>
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<tr>
<td>Body Mass Index, BMI</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression, GDS-20</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Cognition, SPMSQ</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Inflammatory, nutritional and cardiometabolic biomarkers</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Body function and activity</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor function, M-MAS</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Nutritional status, MNA-SF</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><em>Activity</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bergs Balance Scale, BBS</td>
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<td></td>
<td>x</td>
</tr>
<tr>
<td>Mobility, SPPB</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>10 MWT</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>6-MWT</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><em>Participation</em></td>
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<tr>
<td>HRQoL, EQ-5D</td>
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<td></td>
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<tr>
<td>Physical activity scale for the elderly, PASE</td>
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<td>x</td>
<td>x</td>
</tr>
<tr>
<td><em>Personal factors</em></td>
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<td></td>
<td></td>
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<tr>
<td>Fear of falling, FOF</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Fall-related self-efficacy, FES(S)</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Falls, yes/no</td>
<td></td>
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</tbody>
</table>

**Abbreviations**: RCT. Randomized Controlled Trial; 6MWT, the 6-Minute Walk Test; 10mWT, the 10 meter walk test.

Demography and morbidity

Demographic data, including age, gender and comorbidity, were collected via patient records and questionnaires. The Charlson Comorbidity Index (CCI) was used to classify comorbid conditions (116). Leukoaraiosis was identified by roughly screening brain imaging answers at the time of the stroke. Blood pressure was measured manually with the subject in the supine position after resting for 10 minutes. Values were recorded once to the nearest even figure.

The following assessments are ordered according to the International Classification of Functioning, Disability and Health (ICF) (1).
Body structure and function:

**Body composition measurements**

Body composition as measured by BIA was performed with Tanita total innerscan BC-545, Tanita Inc., Tokyo, Japan, with age, gender, weight, height and exercise specificity. Measurements were performed while the individual was standing and while weighing the individual barefoot with light indoor clothing. BIA actually determines resistance to the flow of an electric current through body tissues for estimation of total body water and calculation of FFM in absolute kg and FM as a percentage of total mass.

Definition of FFM depletion: FM (kg) was calculated using FM% multiplied with body weight divided with 100. The FMI, (kg/m²) was calculated as the FM (kg) divided by the height (m) squared. The FFMI was calculated as FMI subtracted from BMI, i.e., skeletal muscle, bone and organ weight was considered.

Definition of FMI: Fat mass was measured in kg and was normalised to the subject’s height (m) squared into an FMI.

Definition of obesity: Obesity was defined by a FM% and FMI above the 90th percentile of a reference population. Reference values for FM% are 20-30% for women and 12-20% for men. Further, BMI values ≥ 30 kg/m² also indicated obesity.

**Body Mass Index**

BMI (kg/m²) was calculated from the individual’s weight (kilogram) and height in meters square, kg/m², in accordance with the World Health Organization (WHO) standards. Values < 18.5 kg/m² were considered underweight, values between 18.5-24.9 kg/m² were considered normal, values from 25 to 29.9 kg/m² were considered overweight and values ≥ 30 kg/m² indicated obesity.

**The Geriatric Depression Scale**

Depression symptoms were assessed using the Geriatric Depression Scale (GDS-20) (107). The original version has been tested for reliability and validity in subjects who have experienced a stroke (120, 121). The GDS has 20 items (0-20 points) and includes insomnia, anxiety, panic, pain, and hypochondria (107). Greater than or equal to 6 points was used as the cut-off for possible depression.

**Short Portable Mental Status Questionnaire**

The Short Portable Mental Status Questionnaire was used to evaluate cognition (113). It consists of 10 questions, such as, “Who is the present prime minister?” Ten correct answers give a maximum score of 10. The scale has been tested for reliability and validity when administered by telephone (105).
**Inflammatory, nutritional and cardiometabolic biomarkers**

Non-fasting venous blood samples were drawn, and the samples were frozen at -70°C. The biochemical variables were as follows: apoB/apoA1-ratio, total cholesterol, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), plasma albumin, serum IGF-1 and CRP. The biochemical analyses were performed and analysed in agreement with the Department of Clinical Chemistry at the Uppsala University Hospital, Sweden. Apolipoprotein A1 and B, total cholesterol, LDL, HDL, albumin and CRP were analysed on an Abbott Architect ci8200 Analyzer (Abbott Laboratories, Abbott Park, IL, USA) using reagents obtained from Abbott. IGF-1 was analysed on a Siemens Immulite 2000 XPi with reagents obtained from Siemens (Siemens AG, Erlangen, Germany).

**Body function and activity**

**Modified Motor Assessment Scale UAS-99**

The Modified Motor Assessment Scale UAS-99 (M-MAS UAS-99) was used to assess motor impairments (109), which includes eight areas of motor function, e.g., transfers, arm and hand function, and one item related to sitting balance. The maximum score is 55, indicating a good overall performance (109). The original M-MAS has been used in stroke-affected individuals and has well-established reliability and sensitivity (122).

**Nutritional status**

A Mini Nutritional Assessment scale-Short Form (MNA-SF) (123) was used to identify nutritional status. The MNA-SF consists of six questions and anthropometric measures that cover the past three months and address food intake and weight loss, mobility, acute diseases or psychological stress and neuropsychological problems (123). The scale is scored from 0 to 14. Normal nutritional status without risk for malnutrition is indicated by a score of 12 or more. Risk for malnutrition is indicated by a score of 7 to 11; current malnutrition is indicated by a score of less than 7 points (123). Malnutrition was also estimated according to BMI < 22 kg/m², which implies a risk for malnutrition in individuals’ ≥ 65 years old and in individuals who have experienced a stroke. MNA-SF is found to be reliable and valid among an older population (106, 124).

**Activity**

**The Berg Balance Scale**

Functional balance was assessed using the Berg Balance Scale (104). It consists of 14 balance items, mainly in standing positions, and is scored from 0 to 56 points. Each item is scored 0 to 4 points. A higher score indicates bet-
ter balance. A cut-off of 45 points has been used to predict which individuals are not likely to fall (112). The scale is valid and reliable and is frequently used in individuals with stroke (104, 125).

**Short Physical Performance Battery**

Mobility was assessed by the SPPB (110), which includes an assessment of balance, gait speed, and chair rising. The performance is scored from 0 to 4, providing a sum score of 12 points, where a higher score reflects better mobility. The SPPB is valid and reliable in older persons (54, 114, 126). By converting the 10 mWT (m/s) into 5 subgroups based on the walking speed, we were able to give 0 to 4 points for walking speed on the SPPB. 0 points (p) = not able to walk, 1p = ≤ 0.43 m/s, 2 p = 0.44-0.60 m/s, 3 p = 0.61-0.77 m/s, 4p = ≥ 0.78 m/s. Classification of limitations based on Short Physical Performance Score: 0-3 severe limitations; 4-6 moderate limitations; 7-9 mild limitations; 10-12 minimal limitations (127).

**10-meter walking test (10mWT)**

The 10-mWT (self-selected pace) (111, 112) was used to measure gait-speed. The time taken to walk was measured with a stop watch while the observer stood behind the participant. Definition of slow walking speed: a cut-off of > 1.0 m/s was used for normal walking speed. The test has acceptable psychometric properties in individuals who experienced a stroke (111).

**The Six-Minute Walk Test (6-MWT)**

This test was developed to assess cardiopulmonary function and was used in this thesis to evaluate walking capacity (128). The maximal distance at a usual pace over a 30 m course during 6 minutes was recorded (129). The test was standardised according to the American Thoracic Society and feedback was given each minute (129). Heart rate and perceived exertion were recorded before starting and after the test. The test is used in individuals with cardiopulmonary problems and stroke (84, 130) but reliability and validity has not been established for stroke patients.

**Participation**

**Health-related quality of life**

EuroQol-5D (EQ-5D) was used to assess health related quality of life, either by assessing 5 items (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each with three levels, or by using EQ-VAS as a rating scale from 0 to 100 (102). A weighted index value between 0 and 1 was calculated, where 1 indicated the highest quality of life. Any value from the index scale below 0 was calculated as a score of 0. EQ-5D is valid and reliable in individuals who have experienced a stroke (131, 132).
Physical Activity Scale for the Elderly
The PASE assesses level of physical activity in elderly individuals (103). The calculation of the PASE score was performed by taking the average number of hours spent on an activity per day in the prior week multiplied by an activity coefficient. The item categories are walking outside the home, light sports, moderate sports, strenuous sports, muscle strength, light housework, heavy housework, home repairs, lawn work or yard care, outdoor gardening, caring for another person and work for pay or as a volunteer. The PASE score may range from 0 to more than 400. The original scale has an acceptable reliability and has been used in subjects that have experienced a stroke. In addition, the scale is valid in elderly persons with disabilities and stroke (103, 133-135).

Personal factors
Fear of falling
One single-item question was used to assess fear of falling: “Are you afraid of falling?” Answers of “yes” or “no” were used to dichotomise the items. The question was constructed for this study.

The Swedish version of the Falls Efficacy Scale
Fall-related self-efficacy was assessed using the Swedish version of the Falls Efficacy Scale FES(S). This questionnaire consists of 13 activities, including both personal and instrumental activities of daily living (108). The confidence when performing the different activities was rated using a visual analog scale ranging from 0 (not confident at all) to 10 (completely confident). FES(S) has a maximum score of 130 and has an acceptable test-retest reliability and validity for assessing subjects who have experienced a stroke (108, 136).

Falls
One single-item question was used to assess falls: “Have you fallen in the last year?” Answers of “yes” or “no” were used to dichotomise the items. The question was constructed for this study.

Exercise intervention (Paper III-IV)
Individuals assigned to the exercise intervention, i.e., the progressive resistance and balance (PRB) exercise program, received a graded circuit class training program twice a week for 3 months. The training consisted of dif-
different work stations with functional exercises involving the major muscle groups, particularly the lower extremity function (Table 2) (137).

Table 2. Descriptions of the progressive resistance and balance exercise program and the group discussion.

<table>
<thead>
<tr>
<th>Warming up: Stationary cycling or walking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive resistance and balance exercises:</td>
</tr>
<tr>
<td>Squat in a parallel or walking stance</td>
</tr>
<tr>
<td>Body weight transfer in a parallel or walking stance</td>
</tr>
<tr>
<td>Standing up from sitting in parallel or walking stance</td>
</tr>
<tr>
<td>Side and forward lunge</td>
</tr>
<tr>
<td>Step-up</td>
</tr>
<tr>
<td>Walking forward in tandem gait</td>
</tr>
<tr>
<td>Walking in various directions</td>
</tr>
<tr>
<td>Walking with turns</td>
</tr>
<tr>
<td>Walking over obstacles</td>
</tr>
<tr>
<td>Step onto and over boxes</td>
</tr>
<tr>
<td>Walking on a soft surface</td>
</tr>
</tbody>
</table>

Questions concerning physical activity:
“What is a physical activity to you?”
“What are the barriers and facilitators for you to be physically active?”
“What reasons do you perceive for increasing your physical activity level in your daily life?”
“How ready are you to make changes to your physical activity level in the near future?”
“What pro and cons do you perceive with being physically active?”
“How much time do you spend sitting each day?”
“What are your future plans to be physically active?”

A: static (fixed base of support) and dynamic (changing base of support) balance exercises in combination with strength exercises
B: dynamic balance exercises while walking

The intervention included three stages: 1) warming up (10 minutes; stationary cycling or walking), 2) circuit training (approximately 45 minutes) and 3) motivational session consisting of discussions related to physical activity (20 minutes). A short rest of 5-10 minutes was also provided after the first seven exercises. The exercises were retrieved from the high intensity functional exercise program (HIFE) (137).

The exercises applied in the RCT were performed at a low to moderate intensity and were intended to improve strength and muscular endurance. At least 10 repetitions were performed for each exercise in accordance with statements from the ACoSM/AHA (90, 138). Any medical reason for drop out was recorded together with exercise fidelity (e.g., attendance and weight progression). The Borg scale of perceived exertion was used to regulate the intensity throughout the study (139). During training, all individuals wore a belt around their waist that could be loaded with individual weights ranging from 1–12 kg. The program consisted of 14 exercises. The first 7 exercises
in the circuit training were combined balance and lower-limb strength exercises. The next 7 were balance exercises performed while walking. The individuals worked in intervals at their own highest possible intensity for 2 minutes, followed by 1 minute to rest and change to the next exercise. The exercise progression included increasing the weights according to the perceived exertion or adjusting the exercise performance to increase the balance demands (137).

One physiotherapist and one assistant conducted the PRB exercise program, and the number of participants ranged from 2 to 7. An individually tailored home-exercise was added to support the in-house PRB exercise program. During the group discussion, physical activity behaviour and risk factor modifications were discussed for 20 minutes. One or two questions were discussed at each session from an individualised perspective. Follow-ups of the home-exercises were also included.

Serious adverse advents were defined as any fall or other adverse advents, such as heart problems, occurring during training. Level of exercise and physical activity were only recorded during the assessments at 3, 6 and 15 months.

Individuals allocated to the control group were not encouraged to make any changes in their daily lives; however, they were not restricted from being physically active.

Statistics

Analyses used in paper I-IV are presented in table 3. All statistical analyses were performed by BV with some supervision from Uppsala Clinical Research Center.

**Table 3. Statistical analyses used in paper I-IV**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Cross-sectional</th>
<th>Randomized controlled trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paper I</td>
<td>Paper II</td>
</tr>
<tr>
<td><strong>Descriptive analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median and interquartile range</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Numbers and frequencies</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mean and standard deviations</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Distribution of data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shapiro-Wilk W test</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Histogram</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Differences between groups:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chi-squared test</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fishers exact test</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
### Student’s two sample $t$-test

- X

### Mann-Whitney U-test

- X

### Wilcoxon’s sign-rank test

- X

### Paired sample $t$-test

- X

### Area under the receiver operating characteristics curve

- X

### Wilcoxon’s sign-rank test

- X

### Cohen’s $d$ test

- X

### Associations between variables:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Paper I</th>
<th>Paper II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson’s correlations coefficient</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Spearman’s rank correlation</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Linear regression</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Binary logistic regression</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

---

### Descriptive statistics

Descriptive statistics were used for demographic data in all studies. Continuous variables were presented as the mean and standard deviation (SD). Given ordinal data, the median and the inter-quartile range (IQR) were presented. For nominal data, absolute or relative numbers (%) or both were described.

### Statistics: Paper I-II

The statistical analyses included both descriptive univariate and multivariate models. Two separate multiple linear regression models were used to explore factors associated with mobility (SPPB) or physical activity (PASE).

Before explanatory variables were included in the multivariate regression models, unadjusted (i.e., univariate) analyses were conducted. The correlation between the dependent variables SPPB and PASE, together with potential independent variables, were analysed using the Spearman’s rank correlation. Further, all significant independent variables were included in the multivariate analysis. Both mobility and physical activity scores were treated as quantitative and continuous variables in the analyses. Ordinal explanatory variables were dichotomised due to median values or a known cut-off. The SPPB was used as the independent variable when the PASE was the dependent variable and vice versa. All regression analyses were controlled for age, sex and comorbidity. The variance inflation factors (VIF) were calculated and found acceptable. The residuals were normally distributed and no standardised residuals $>3$ were found. A variance explained by an adjusted R square $0-0.25$ was considered little to poor, $0.25-0.50$ fair, $0.50-0.75$ moderate and $\geq 0.75$ very good to excellent (140). When data were missing for one item (chair-stand, SPPB, n=24), it was replaced with information from a
similar subscale (sit to stand, M-MAS). A total of 195 individuals were included and the amount of missing data did not exceed 3% in any scale, but totalled 9% all together. Imputation by group mean or median values was performed in cases of missing values.

In paper II, the data were categorised into two different age classes: 65-74 years and 75-85 years. The results are reported separately for men and women. The amount of missing data in the present study was low, and the imputation technique originated from paper I. The correlation between the SPPB and potential independent variables were analysed using the Spearman’s rank correlation. Logistic regression models were used to predict binary outcomes in the presence of several explanatory variables after testing for multi-collinearity. Odds ratios and 95% CIs for low versus high mobility, with SPPB as a dependent variable, were calculated to determine independent covariates. Univariate binary logistic analysis was used to analyse the associations with mobility (SPPB). Body composition was not significantly associated with the SPPB and was therefore excluded from further analyses. Nutritional status (MNA-SF), physical activity (PASE), age and gender were used as independent variables. Identified independent variables with a P-value <0.05 were further included in the multiple logistic regression models. All estimates were adjusted for age (65-74 and 75-85 years) and gender.

To estimate the prevalence of sarcopenia and sarcopenic obesity, different percentiles of a gender- and age-matched reference population were used to define the conditions (67). For details, see paper II.

Statistics: Paper III-IV

The RCT presented in paper III was designed to have 80% power to detect a 2-point difference on the Berg Balance Scale between the exercise and control group with a standard deviation of 8 points and with the statistical significance level set at 0.05 (two-tailed) for all analyses. This calculation was based on effects from a pilot study performed prior to the PRB exercise group. However, this exercise study was completed with fewer participants than had been calculated for as a result of statistically significant improvement on the BBS (primary outcome) and slow recruitment.

The intention-to-treat principle was applied in the analyses using all available data according to the individuals’ original group assignment. A multiple imputation was performed for missing values according to the hot deck method (141). This technique sorts available respondents in certain subsets; in this study, gender and comorbidity. Values selected randomly from matching subjects were used to replace missing data. If no matching subject was detected, data were randomly selected from the entire dataset. In addition, a complete case analysis was also performed.
An attendance rate was calculated for each participant as the number of attended exercise sessions divided by the total sessions. Because the distribution of data was unknown and included some outliers, the Mann-Whitney U-test was used for all between-group analyses at 3, 6 and 15 months. The median differences in changes were calculated as Hodges-Lehmann estimates. The difference between the individuals’ pre- and post-treatment data was used to calculate the effect size by using the area under the receiver operating characteristics curve (AUC). The null hypothesis was that the true area = 0.5 indicated no differences in effect between the groups. A complete case analysis was also applied and was performed in a similar manner as the intention to treat analysis.

Paper IV was considered to be exploratory. All statistical analyses are based on complete case analysis. An attendance rate was calculated for each participant as the number of attended exercise sessions divided by the total sessions. The results are reported separately for men and women. Cardiovascular disease risk scores (CRS) was calculated using a prediction algorithm based on age, resting blood pressure, smoking status at the time of stroke, diabetic status, total cholesterol and HDL (142). Smoking status and diabetes were considered unchanged at 3 months. Student’s two-sample t-test was used to compare changes between the exercise and control groups during the intervention period, given normally-distributed and continuous data. Given ordinal or not normally distributed data, the Mann-Whitney U-test was used for between-group analysis at 3 months. Within-group effects for continuous variables were analysed by paired sample t-test, comparing outcome measures at baseline and after 3 months, respectively. Given not normally distributed or ordinal data, the Wilcoxon sign-rank test was used to analyse within-group changes from baseline to 3 months. The association between changes in FFMI or FMI and changes in the 6MWT at 3 months was evaluated either using Spearman’s rank correlation or Pearson’s correlation coefficient.

All statistical analyses were performed with SPSS 19.0 (IBM, Armonk, NY, USA) and were considered statistically significant if \( P > 0.05 \).
RESULTS

Associations with mobility and physical activity in elderly community-living individuals (paper I-II).

In paper I, 195 individuals were included. Eighty-one individuals declined full participation but answered questions on the EQ-5D (56% women). The mean age at study start was 74±5 years. A median of 13 months had passed since stroke onset. The proportion of men was 71%. The distribution of 1 or more comorbidities according to the Charlson Comorbidity Index was 41%. Mobility was reduced with a SPPB score of less than 10 points in 50% of the individuals, walking speed was slower (1.10 ± 0.86 m/s), and level of physical activity was lower (mean PASE 97 ± 66 points) in older individuals following stroke compared to age-matched healthy controls (35). The median value of motor function according to M-MAS UAS-99 was 55 points and 59% reached the highest possible score, indicating ceiling-effects and high motor function. Possible depression and FoF were reported in more than one-third of individuals post-stroke. The proportion of more than one fall in the most recent year was reported to be 46%. The EQ-5D was slightly reduced compared to an age- and gender matched reference population (143). Furthermore, the EQ-5D scores were 0.63 and 0.73 in the not fully participating and the full participants, respectively ($P= 0.006$). Additionally, corresponding EQ-5D VAS mean scores were 0.54 and 0.71, respectively ($P= <0.001$).

Factors explaining the variance in mobility were age, physical activity, fall-related self-efficacy and health-related quality of life, which described 42% of the variance in mobility (SPPB) for older individuals after stroke (Table 4).
Table 4: Multiple regression analyses with performance-based mobility (SPPB) as the dependent outcome variable and age, sex, comorbidity, fall-related self-efficacy, cognitive impairment, physical activity, depression, HRQoL, fear of falling and falls as the independent variables in individuals 1-3 years after stroke (n=195).

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>P</td>
</tr>
<tr>
<td>Age, y</td>
<td>-.26</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>-.06</td>
<td>.38</td>
</tr>
<tr>
<td>CCI</td>
<td>-.11</td>
<td>-.12</td>
</tr>
<tr>
<td>Falls-related self-efficacy, FES(S), &lt;124 points</td>
<td>-.51</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cognitive impairment, SPMSQ, 10 points</td>
<td>-.26</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physical activity, PASE ≥ 0 points</td>
<td>.52</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depression, GDS, ≥ 6 points</td>
<td>-.26</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HRQoL, EQ-5D, 0-1</td>
<td>.48</td>
<td>&lt;.001</td>
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<tr>
<td>Fear of falling, yes</td>
<td>-.23</td>
<td>.001</td>
</tr>
<tr>
<td>Falls, yes</td>
<td>-.21</td>
<td>.003</td>
</tr>
</tbody>
</table>

Total adjusted $R^2$ = 0.42

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; Euro-QoL, EQ-5D; FES(S), Fall-related Self-efficacy Scale (Swedish version); Swedish version of the Geriatric Depression Scale; HRQoL, health-related quality of life; PASE, Physical Activity Scale for the Elderly; SPMSQ, Short Portable Mental Status Questionnaire; SPPB, Short Physical Performance Battery. $P < 0.05$. 

Table 5. Multiple regression analyses with self-reported physical activity (PASE) as the dependent outcome variable and age, sex, comorbidity, mobility, fall-related self-efficacy, cognitive impairment, depression, HRQoL and fear of falling as the independent variables in individuals 1-3 years after stroke (n=195).

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th></th>
<th>Multivariate analysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>P</td>
<td>95% CI</td>
<td>Beta</td>
</tr>
<tr>
<td>Age, y</td>
<td>-.11</td>
<td>.13</td>
<td>-3.2 to 0.4</td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>-.05</td>
<td>.49</td>
<td>-27.6 to 13.3</td>
<td></td>
</tr>
<tr>
<td>CCI</td>
<td>-.13</td>
<td>.17</td>
<td>-17.8 to 3.2</td>
<td></td>
</tr>
<tr>
<td>Mobility, SPPB,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 9 points</td>
<td>.5</td>
<td>&lt;.001</td>
<td>-81.8 to -49.5</td>
<td>-.33</td>
</tr>
<tr>
<td>Falls-related</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>self-efficacy,</td>
<td>-.43</td>
<td>&lt;.001</td>
<td>-73.5 to -40.0</td>
<td>-.18</td>
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<tr>
<td>FES(S), &lt;124</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>impairment,</td>
<td>-.20</td>
<td>.005</td>
<td>3.6 to 20.5</td>
<td></td>
</tr>
<tr>
<td>SPMSQ, 10 points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression, GDS,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 6 points</td>
<td>-.28</td>
<td>&lt;.001</td>
<td>-56.1 to -19.3</td>
<td></td>
</tr>
<tr>
<td>HRQoL, EQ-5D,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index 0-1</td>
<td>-.43</td>
<td>&lt;.001</td>
<td>78.9 to 144.4</td>
<td>.19</td>
</tr>
<tr>
<td>Fear of falling,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>-.4</td>
<td>.051</td>
<td>-38.0 to .93</td>
<td></td>
</tr>
<tr>
<td>Total adjusted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.31</td>
<td></td>
<td></td>
<td></td>
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</table>

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; Euro-QoL, EQ-5D; FES(S), Fall-related Self-efficacy Scale (Swedish version); Swedish version of the Geriatric Depression Scale; HRQoL, health-related quality of life; PASE, Physical Activity Scale for the Elderly; SPMSQ, Short Portable Mental Status Questionnaire; SPPB, Short Physical Performance Battery. $P < 0.05$. 

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One additional multiple regression analyses model was further performed; mobility, HRQoL and fall-related self-efficacy were related to physical activity (PASE) and described 31% of the variance (Table 5). Both analyses were controlled for sex, age and comorbidity.

Paper II was complemented by measurements of body composition, BMI, cardiometabolic risk markers and nutritional status; 134 individuals of the 195 individuals in paper I were analysed. The mean age was 74 ± 4 years and the proportion of men was 69%. The BMI values indicated that 71% of the individuals studied were overweight or obese (BMI > 30 kg/m² in 22%). Total percent fat mass (FM%) was > 20 in 86% of the men, whereas 90% of the women had an FM% above 30% of the reference population. Fourteen percent were considered at-risk for malnutrition according to MNA-SF. Walking speed was slow (1.08 ± 0.25 m/s), and the level of physical activity was low (mean PASE 108 ± 65 points) in the study population. Further, mobility was affected (median SPPB of 10 points) and SPPB cores ≤ 9 in 40% indicated increased risk for disability. Sarcopenia, i.e., reduced FFMI and a gait speed < 1 m/s, was noticed in 3% while 7% displayed sarcopenic obesity defined as increased FMI together with reduced FFMI. Further, a significant association between chair-stand, one item in the SPPB, and physical activity (r= -0.35, P>0.001), nutritional status (r= -0.21, P=0.015) and FMI (r= 0.21, P= 0.017) were revealed.

Neither FFMI nor FMI was associated with mobility, as measured by the SPPB, in this cohort. The logistic regression analysis revealed that the factors associated with low mobility was low physical activity, Odds Ratio; OR (CI 95%) 8.2 (2.8-24.2), risk for malnutrition, OR 5.8 (1.6-21.1) and each 10-year period, OR 2.8 (1.2-6.2) (Figure 3).
Figure 5. The odds ratio of low mobility (SPPB) based on the Physical Activity Scale for the Elderly (PASE; medium vs. high and low vs. high) and the Mini Nutritional Assessment-Short Form (MNA-SF). Analyses were adjusted for gender and age (per 10-year increment).

Furthermore, 10% percent of the individuals had plasma cholesterol concentrations ≥ 6 mmol/l and LDL values ≥ 3.5 mmol/l. Women had significantly higher total cholesterol and HDL levels compared to men.

The short-term and long-term effects of a progressive resistance and balance exercise program in elderly community-living individuals after stroke (paper III-IV).

Of 67 individuals randomly assigned to the PRB exercise program (intervention group, IG, n=34) in paper III, 57 individuals completed the whole intervention period (85%). At 3 months, in the short-term, the attrition rate was 24% in the PRB exercise group, increasing to 29% at 15 months. Thirty-
three individuals were included in the control group (CG) and the attrition was 6%. The proportion of males was 76% (mean age: 74±5 years). According to the GDS, approximately 42% scored > 6 points at baseline, indicating possible depression. Sixteen percent of the participants scored < 45 points on the BBS and 63% scored < 10 points on the SPPB at baseline measurements. Motor function was considered to be high at baseline. Age and gender did not differ between PRB exercise completers and drop-outs, but differences were noted in the BBS and motor function M-MAS UAS-99, with the drop-outs having significantly less scores. Attendance rate in the exercise group was 91% (median). In addition, no adverse events were noted during exercise.

The Intention-to treat analysis revealed that the PRB exercise group was associated with significantly higher scores in terms of balance (2.5 vs. 0 points, ES; 0.72 (SE 0.062); P=0.001), walking capacity (30 vs. 0 m, ES; 0.64 (SE) 0.07); P=0.05) and comfortable walking speed (0.04 vs.-0.05 m/s, ES; 0.68 (SE 0.067); P=0.012) compared to the control group at 3 months (Table 6). There were no other significant differences between the groups for any other outcomes at any time point. The complete case analysis confirmed this result (data not shown).

In paper IV, 20 individuals were analysed from the PRB exercise group described in paper III and 23 individuals from the control group, due to available BIA measurements. The mean age was 73±5 years (73% men). In both groups (at study start), BMI indicated that the individuals were overweight or obese and had an average supine blood pressure values above recommended levels, e.g., 58%. No significant between or within-group changes in BMI or blood pressure were seen after 3 months of exercising. Cardiovascular disease risk score revealed a 10 year increased risk of a future cardiovascular disease event > 20% at baseline, with no between-group changes present at 3 months.

At 3 months, a complete case analyses revealed a significant reduction in the PRB exercise group in terms of FM% (-1.5 vs. 0.13%; effect size, ES, 0.62, standard error (SE), 0.80; P=0.39) and a decrease in serum IGF-1 (-12 vs. 4 μg/l, ES; 0.62, P=0.026) compared with the control group, whereas levels of CRP and albumin were stable (Table 7).

A significant within-group reduction in the FM% (-1.50, ES; 0.56, P=0.023) and fat mass (FM, kg) (-1.47, ES; 0.57 P=0.021) of the IG, but not in the CG (-0.19 kg, ns), were also revealed. Changes in FMI were associated with improved walking capacity (6MWT, 25 vs. -10 m) at 3 months, in favour of the IG (r=0.47, P= 0.04).
Table 6. Physical Function, Physical Activity and Psychological Factors after 12 weeks of PRB exercise or Control Group revealed by the Intention-To-Treat analysis

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Assessment</th>
<th>PRB exercise (n=34)</th>
<th>Control Group (n=33)</th>
<th>Median Difference in Change (95%CI)</th>
<th>Effect size (ES)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline level and Absolute Change Median(IQR)</td>
<td>Baseline level and Absolute Change Median(IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BBS (0-56 points)</td>
<td>Baseline</td>
<td>49(6)</td>
<td>51(7)</td>
<td></td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>2.5(5)</td>
<td>0(2)</td>
<td>-2.5(-4 to -1)</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>1(4)</td>
<td>0(3)</td>
<td>-1(-3 to 1)</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>1(3)</td>
<td>0(3)</td>
<td>-2(-4 to 0)</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>SPPB (0-12 points)</td>
<td>Baseline</td>
<td>9(4)</td>
<td>9(3)</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>1(2)</td>
<td>0(1)</td>
<td>-1(-1 to 0)</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>0(2)</td>
<td>0(1)</td>
<td>0(-1 to 1)</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>1(3)</td>
<td>0(2)</td>
<td>0(-2 to 0)</td>
<td></td>
<td>0.3</td>
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<tr>
<td>6-MWT, meters</td>
<td>Baseline</td>
<td>365(198)</td>
<td>345(198)</td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>30(72)</td>
<td>0(40)</td>
<td>-25(-50 to 0)</td>
<td></td>
<td>0.46</td>
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<tr>
<td></td>
<td>6 mo</td>
<td>25(97)</td>
<td>25(70)</td>
<td>-10(-45 to 20)</td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>-7(71)</td>
<td>0(47)</td>
<td>5(-20 to 30)</td>
<td></td>
<td>0.77</td>
</tr>
<tr>
<td>10mWT,(m/s)</td>
<td>Baseline</td>
<td>1.0(0.59)</td>
<td>1.11(0.52)</td>
<td></td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>0.04(0.24)</td>
<td>-0.05(0.21)</td>
<td>-0.11(-0.19 to -0.03)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>0.09(0.22)</td>
<td>-0.007(0.24)</td>
<td>-0.15(-0.24 to -0.06)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>0.90(0.24)</td>
<td>-0.07(0.26)</td>
<td>-0.11(-0.21 to 0.007)</td>
<td></td>
<td>0.034</td>
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<tr>
<td>PASE (≥0 points)</td>
<td>Baseline</td>
<td>79(80)</td>
<td>59(95)</td>
<td></td>
<td></td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>10(77)</td>
<td>2(71)</td>
<td>-0.5(-26 to 26)</td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>-3(59)</td>
<td>10(64)</td>
<td>-21(-3 to 49)</td>
<td></td>
<td>0.074</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>1(60)</td>
<td>-2(60)</td>
<td>4(-18 to 34)</td>
<td></td>
<td>0.74</td>
</tr>
<tr>
<td>EQ 5D, (0-1)</td>
<td>Baseline</td>
<td>0.725(0.23)</td>
<td>0.725(0.23)</td>
<td></td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>0(0.22)</td>
<td>0(0.16)</td>
<td>0(-0.12 to 0.05)</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>0(0.33)</td>
<td>0(0.17)</td>
<td>0.047(0 to 0.16)</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>0(0.30)</td>
<td>0(0.22)</td>
<td>0.016(-0.09 to 0.12)</td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
<td>3 mo</td>
<td>6 mo</td>
<td>15 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
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<td></td>
</tr>
<tr>
<td><strong>GDS-20</strong> (0-20 points)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3(9)</td>
<td>-1(5)</td>
<td>0(2)</td>
<td>0(-2 to 1)</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>-1(4)</td>
<td>-1(3)</td>
<td>0(-1 to 2)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>-1(5)</td>
<td>-1(2)</td>
<td>0(-2 to 1)</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td><strong>FES(S)</strong> (0-130 points)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0(26)</td>
<td>0(26)</td>
<td>0(20)</td>
<td>0(-10 to 7)</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>-2(24)</td>
<td>0(26)</td>
<td>2(-8 to 11)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 mo</td>
<td>0(31)</td>
<td>0(27)</td>
<td>-2(-17 to 6)</td>
<td>0.56</td>
<td></td>
</tr>
</tbody>
</table>

All variables are obtained from non-parametric analyses. Median difference in change is calculated as Hodges Lehmans Estimate.

Abbreviations: BBS, Berg Balance Scale; FES(S), Fall-Related Self-Efficacy Scale; GDS-20, Geriatric Depression Scale; IQR, Interquartile range; PASE, Physical Activity Scale for the Elderly; PRB, Progressive Resistance and Balance; SPPB, Short Physical Performance Test; 6-MWT, 6-Minute Walk Test; 10mWT, 10-meter Walk Test. *P*<0.05.
Table 7. Within-group and Between-group differences of body composition and physical function at the start of intervention and after 3 months.

<table>
<thead>
<tr>
<th>Assessment occasion</th>
<th>Base-line</th>
<th>3-mo follow-up</th>
<th>Absolute Change</th>
<th>P-value</th>
<th>Base-line</th>
<th>3-mo follow-up</th>
<th>Absolute Change</th>
<th>P-value</th>
<th>Mean/Median difference in change (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FFM, kg, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>All individuals</td>
<td>61.30 (11.1)</td>
<td>59.82 (7.6)</td>
<td>-0.80 (9.1)</td>
<td>0.14</td>
<td>56.20 (15.7)</td>
<td>56.5 (8.9)</td>
<td>-0.95 (3.0)</td>
<td>0.18</td>
<td>0.50 (-2.0 to 4.2)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61.30 (11.1)</td>
<td>59.82 (7.6)</td>
<td>-0.80 (9.1)</td>
<td>0.14</td>
<td>56.20 (15.7)</td>
<td>56.5 (8.9)</td>
<td>-0.95 (3.0)</td>
<td>0.18</td>
<td>0.50 (-2.0 to 4.2)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>43.10 (14.2)</td>
<td>42.57 (3.7)</td>
<td>0.75 (6.6)</td>
<td></td>
<td>47.15 (3.8)</td>
<td>43.2 (7.0)</td>
<td>-2.60 (7.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FFMI, kg/m², median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All individuals</td>
<td>0.26 (1.2)</td>
<td>0.53</td>
<td>0.02 (1.3)</td>
<td>0.93</td>
<td>-0.16 (-0.9 to 0.4)</td>
<td>0.53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19.95 (2.6)</td>
<td>20.09 (2.3)</td>
<td>0.13 (1.4)</td>
<td>0.53</td>
<td>20.50 (3.2)</td>
<td>20.75 (2.0)</td>
<td>-0.16 (1.0)</td>
<td>0.93</td>
<td>-0.16 (-0.9 to 0.4)</td>
<td>0.53</td>
</tr>
<tr>
<td>Female</td>
<td>16.83 (1.4)</td>
<td>17.11 (1.1)</td>
<td>0.44 (0.7)</td>
<td></td>
<td>17.8 (3.3)</td>
<td>17.51 (1.8)</td>
<td>0.06 (1.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FM, kg, mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All individuals</td>
<td>-1.47 (2.6)</td>
<td>0.021</td>
<td>-0.019 (2.2)</td>
<td>0.97</td>
<td>1.45 (-0.5 to 2.9)</td>
<td>0.057</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23.96 (6.4)</td>
<td>22.30 (7.4)</td>
<td>-1.66 (2.8)</td>
<td>0.31</td>
<td>24.95 (6.2)</td>
<td>24.95 (6.2)</td>
<td>0.31 (2.2)</td>
<td>0.97</td>
<td>1.45 (-0.5 to 2.9)</td>
<td>0.057</td>
</tr>
<tr>
<td>Female</td>
<td>30.30 (5.7)</td>
<td>27.47 (7.0)</td>
<td>-0.69 (2.0)</td>
<td></td>
<td>33.80 (12.9)</td>
<td>33.21 (13.0)</td>
<td>-0.59 (2.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FM%, mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All individuals</td>
<td>-1.50 (2.7)</td>
<td>0.023</td>
<td>0.13 (2.6)</td>
<td>0.80</td>
<td>1.63 (0.01 to 3.3)</td>
<td>0.048</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27.01 (4.9)</td>
<td>25.51 (5.9)</td>
<td>-1.51 (2.9)</td>
<td>0.41</td>
<td>28.52 (34.8)</td>
<td>28.22 (3.7)</td>
<td>0.41 (2.3)</td>
<td>0.80</td>
<td>1.63 (0.01 to 3.3)</td>
<td>0.048</td>
</tr>
<tr>
<td>Female</td>
<td>39.68 (3.3)</td>
<td>37.57 (5.2)</td>
<td>-1.45 (2.3)</td>
<td></td>
<td>40.78 (8.7)</td>
<td>40.41 (9.0)</td>
<td>-0.38 (3.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### FMI, kg/m², mean (IQR)

<table>
<thead>
<tr>
<th></th>
<th>All individuals</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.40 (0.9)</td>
<td>-0.44 (0.9)</td>
<td>-0.27 (0.8)</td>
</tr>
<tr>
<td></td>
<td>0.053</td>
<td>8.20 (2.2)</td>
<td>12.94 (8.4)</td>
</tr>
<tr>
<td></td>
<td>-0.20 (1.1)</td>
<td>8.07 (1.9)</td>
<td>12.70 (5.2)</td>
</tr>
<tr>
<td></td>
<td>0.38</td>
<td>-0.18 (1.2)</td>
<td>-0.24 (0.9)</td>
</tr>
<tr>
<td></td>
<td>0.20 (-0.4 to 0.8)</td>
<td>0.38</td>
<td>0.51</td>
</tr>
</tbody>
</table>

### BMI, kg/m², mean (SD)

<table>
<thead>
<tr>
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<th>All individuals</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.23 (1.3)</td>
<td>-0.34 (1.4)</td>
<td>0.24 (0.6)</td>
</tr>
<tr>
<td></td>
<td>0.42</td>
<td>29.07 (4.6)</td>
<td>30.6 (6.7)</td>
</tr>
<tr>
<td></td>
<td>-0.23 (1.2)</td>
<td>28.3 (3.1)</td>
<td>30.3 (6.6)</td>
</tr>
<tr>
<td></td>
<td>0.36</td>
<td>28.2 (5.7)</td>
<td>-0.27 (0.6)</td>
</tr>
<tr>
<td></td>
<td>0.007 (-0.8 to 0.8)</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

### PASE (≥0 points), median (SD)

<table>
<thead>
<tr>
<th></th>
<th>100 (72)</th>
<th>110 (85)</th>
<th>16 (74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>51.5 (7)</td>
<td>53.5 (5)</td>
<td>1 (3)</td>
</tr>
<tr>
<td></td>
<td>0.013</td>
<td>52.5 (6)</td>
<td>52.0 (4)</td>
</tr>
<tr>
<td></td>
<td>0.34</td>
<td>1 (1)</td>
<td>-1 (-2 to 0)</td>
</tr>
<tr>
<td></td>
<td>-0.5 (-34.0 to 36.0)</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

### BBS (0-56 points), median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>51.5 (109)</th>
<th>420 (181)</th>
<th>25 (65)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>390 (141)</td>
<td>385 (170)</td>
<td>-10 (45)</td>
</tr>
<tr>
<td></td>
<td>0.29</td>
<td>-25 (-55.0 to 0.0)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

### 6-MWT (meters), median (SD)

<table>
<thead>
<tr>
<th></th>
<th>9 (5)</th>
<th>11 (4)</th>
<th>0 (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>390 (141)</td>
<td>385 (170)</td>
<td>-10 (45)</td>
</tr>
<tr>
<td></td>
<td>0.29</td>
<td>-25 (-55.0 to 0.0)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

### SPPB (0-12 points), median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>9 (5)</th>
<th>11 (4)</th>
<th>0 (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>390 (141)</td>
<td>385 (170)</td>
<td>-10 (45)</td>
</tr>
<tr>
<td></td>
<td>0.29</td>
<td>-25 (-55.0 to 0.0)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

### Chair rise (sec), median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>14.0 (6.1)</th>
<th>13.5 (6.4)</th>
<th>0.5 (4.7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17.0 (8.1)</td>
<td>15.0 (5.2)</td>
<td>0.05 (2.6)</td>
</tr>
<tr>
<td></td>
<td>0.64</td>
<td>-0.3 (-1.9 to 1.9)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Data are presented as the means (SD) or medians (IQR) and 95% CIs based on the complete-case analysis. The Hodges-Lehmann test was used to estimate the median. P-values were obtained using non-parametric analyses for ordinal and not normal distributed data. The significance level was set at P<0.05.

Abbreviations: BBS, Bergs Balance Scale; BMI, Body Mass Index; CIs, confidence intervals; FFMI, fat-free mass index; FMI, fat-mass index; FM, fat mass; FM%, fat mass percent; PASE, Physical Activity Scale for the Elderly; 6-MWT, Six-Minute Walking Test; SPPB, Short Physical Performance Test.
DISCUSSION

Summary of results

Elderly individuals approximately 1 year after stroke had many apparent reversible disabilities such as low mobility and walking capacity, possible depression, and slow gait-speed even if their motor function was considered high. Further, the level of physical activity was considered low. Another important finding of this thesis was that older individuals who have experienced a stroke had a body composition that consists of an increased amount of fat with overweight and obesity, which can lead to further complications. However, only a few individuals revealed low muscle mass. High values of certain cardiometabolic risk factors, e.g., elevated total cholesterol, LDL-cholesterol and hypertension, were depicted despite medication. Many of these disabilities and risk factors can be changed by increasing the level of physical activity and having more healthy eating habits. Participation in a 3 month progressive resistance and balance exercise program improved balance ability, walking capacity and gait speed, but in the long-term these improvements were mainly lost. Further, we showed a significant decrease in IGF-1 in favour of the exercise group at 3 months, which might reflect improved insulin sensitivity. We were also able to detect a slight increase in muscle mass after exercising together with a similar decrease in FM, while BMI showed an overall reduction except for in the women in the exercise group. Changes in walking capacity were positively associated to changes in fat mass percentage.

Given this result, the negative effects of stroke for community-living elderly individuals may be due to modifiable causes, and can be further addressed. A progressive resistance and balance exercise program improves short-term physical function but further efforts are needed for the change to persist over time. Insulin sensitivity and fat mass percentage might as well be lowered by resistance exercising.

Associations to physical function and physical activity

Age, physical activity, fall-related self-efficacy and health-related quality of life were related to mobility, explaining 42% of the variance in SPPB. This is comparable to a study also reporting on mobility 1 year after stroke (45).
Notably, in that prospective cohort study mobility was measured by the Rivermead Mobility Index (RMI), which is a different scale compared to the SPPB. The RMI covers different activities from turning over in bed to running. That regression model explained 48% of the variance in RMI, which was predicted by functional status, sitting balance, time between stroke onset and baseline measurements and age (45). However, different regression models are difficult to compare due to differences in measures used and methodological shortcomings.

The high proportion of fallers described in paper I, approximately 50%, might be an indication of bodily decline and might therefore explain some of the inactivity found in this cohort, further contributing to progress in the reduction of muscle mass and strength and a decline in mobility. This hypothesis might be true because the fall-related self-efficacy also explained part of the variance in both mobility and physical activity. Self-efficacy while performing daily tasks have previously been found to be closely related to motor function, balance, ambulation and activities in daily living, especially in elderly individuals after stroke (108). Individuals with low self-perceived fall-related self-efficacy showed less improvement, indicating that to minimise dependence in daily life it may be important to consider enhancement in fall-related self-efficacy when planning rehabilitation interventions for individuals after stroke. In our study cohort, the median score of BBS in paper I was 53 points. In healthy older individuals living at home (70 to 79 years), the average score on the BBS varies between 52-55 points for women and 52-56 points for men, respectively (112). The BBS, with a well described cut-off of 45 points, is relatively good in predicting which individuals are not likely to fall (112). By applying this cut-off of 45 points, we showed that among the participants in paper I, 88% scored > 45 points on the BBS (112). Despite this, up to 30% of the individuals with scores > 45 points perceived a FoF. This might be one possible reason for sedentary behaviour, i.e., non-exercise seated or lying behaviour, and low levels of physical activity.

Additionally, HRQoL was significantly associated with both mobility and level of physical activity. This result complements previous results from a review showing that disability and post-stroke depression are consistent determinants of HRQoL (144). Among individuals in paper I, more than one-third revealed possible depression, which, except for HRQoL, also affects functional recovery, cognitive function and health-care use. Additionally, mostly women declined participation in study I, which was not surprising, because women usually reveal lower values on the EQ5D and therefore might be less motivated to participate in research (143). This might have affected mobility as well in this study. With more women participating, the mobility could have been even worse, because women are also likely to show a greater reduction in mobility while aging (145). It can be speculated that this might have been the main cause for the minor difference in HRQoL.

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reported in this study when compared to a population survey in Stockholm (143).

Earlier studies on mobility 1 to 3 years after stroke revealed the presence of several ongoing disabilities, many of which were confirmed by this study (45-47). Further, the multivariate model with SPPB as the dependent variable revealed an association with age, which is in line with previous findings (117). The risk for low mobility increased exponentially from reported low physical activity to medium physical activity compared to those with the highest reported level of physical activity as seen in figure 2 (paper II). In paper I, half of the participating individuals exhibited low mobility with a median SPPB score of 10 (IQR: 4). Because low mobility, i.e., the SPPB, is predictive of disability and hospitalisation, it seems reasonable to highlight those elderly individuals with stroke and mobility < 10 points on the SPPB who should be a cause for concern and therefore addressed in clinical practice (146, 147).

Moreover, we were able to show that being at risk for under-nutrition (MNA-SF < 12 points) was associated with an increased risk for low mobility (OR 5.80, CI 1.26-21.1). Previous studies have reported that individuals with a high percentage of body fat and a high BMI (> 30 kg/m²) also had a higher likelihood of functional limitations and diminished mobility capacity in old age (27, 148). Low muscle strength and obesity combined increases the risk for mobility limitations and a decline in walking speed (149). In contrast, results considering the association between mobility disability and FFM or sarcopenic obesity in older individuals are contradictory (27, 149, 150). Except for a significant association between chair-stand (one individual item from the SPPB) and FMI, we were not able to detect any association between any of the body composition measurements and physical function in paper II. Studies investigating sarcopenic obesity in individuals after stroke are not found, but are needed.

Among the independent factors, 31% of the variance in physical activity was explained by the SPPB, EQ-5D and fall-related self-efficacy as measured by FES(S), indicating an association between mobility and level of physical activity in both regression models. Low physical activity is a general health problem, especially in individuals at-risk for stroke and following a stroke (34, 36, 151). Further, individuals living in the community post-stroke are less physically active, despite good motor function, compared to individuals without stroke of the same age (35). A longitudinal study investigating sedentary behaviour in the first year after stroke reported that despite functional ability, individuals were highly sedentary and remained so over the first year after stroke (152). Developing interventions to reduce sedentary behaviour are, therefore, warranted.

A slow walking speed, one item in the SPPB, could be a prerequisite for the low level of physical activity found in paper I and II. Swedish data (RS) show that on a national level at 1 year, most individuals < 75 years can move
both within and outside independently (5). In contrast, women in specific that were > 75 years need more help when moving around. The mean walking speed in the individuals in paper I was found to be 1.10 (0.86) m/s with a significantly lower gait speed for women, which is in line with previous findings (53). Walking speed is associated with survival and well-being and reflects health and functional status among older individuals; individuals with a walking speed < 1.0 m/s should be a cause for concern (53). An increase of the walking speed of 0.1 m/s has shown to increase the chance of 10 year survival, especially among those > 75 years. A slow gait speed might also reflect reduced muscle mass, primarily in the lower extremities, which is likely to occur while aging (62). Furthermore, walking affects organ systems such as the heart, lungs, circulatory and central nervous systems. A slow walking speed may be a result of damaged systems and a high energy cost of walking (53).

Many more factors are known to influence level of physical activity, e.g., depression, fatigue, available facilities for older individuals and the built environment including transit possibilities (153-155). Altogether, a primary goal should be to support physical activity soon after a stroke. Walking speed being part of the SPPB and age and sex can be valuable tools to be used by the clinician as good indicators of health and survival.

Physical activity was associated with HRQoL as measured by EQ-5D. In our study group, we found a slightly higher deterioration in EQ-5D when compared to individuals in a population-based survey from Stockholm county, Sweden (143). The reduction of HRQoL in individuals with stroke and myocardial infarction is greater when compared to other patient categories and might have contributed as well to the low level of physical activity (37). Individuals with a history of either stroke or myocardial infarction or both report significantly higher proportions of problems compared to individuals without these diseases. In general, higher risk factor levels decrease the HRQoL. Thus, as reported in paper II, risk factors such as diabetes, hyperlipidaemia, hypertension and smoking are likely to have negative influences on HRQoL (37). Another reason for the difference in HRQoL might be that non-participants in cohort studies are more likely to have social problems as well as higher morbidity compared to participants, which might explain the HRQoL in the present study (156). In paper I, approximately 38% revealed possible depression on the GDS-20 indicating mental problems, which are known to have the greatest impact for individuals’ overall HRQoL (index) (37, 85).
Body composition, nutritional status and cardiometabolic risk-markers

Unpublished data presented in paper II reveals that 14% were at risk for malnutrition and that more than 20% had a BMI > 30 kg/m², indicating obesity. Further, we found that 87% of the individuals had a FM% above the reference value used, i.e., > 20% in men and > 30% in women, respectively (118). This, together with a high frequency of overweight, might be the result of a sedentary lifestyle as reported in paper I and other studies and is most likely in concordance with a high energy intake (35, 151). The reported prevalence of protein and energy malnutrition in stroke survival varies from 6 to 62% due to different assessment tools, the timing of the assessment and differences in patient characteristics (157). We are the first to assess and define sarcopenic obesity in individuals with chronic stroke; in paper II, we reported a prevalence of 8% in a relatively high functioning population. In a cross-sectional study with 3136 Spanish individuals older than 65 years, the prevalence of sarcopenic obesity ranged from approximately 14 -18%, defined by using muscle mass and FM cut-off (68). Using a different definition based on BMI and hand-grip strength, epidemiological studies give a prevalence of 4-9% in older individuals (mean age: 75 years) (158). Changes in body composition could be highly variable in individuals after stroke and could be influenced by several factors such as physical activity, nutritional status, hormonal and inflammatory factors (42). Individuals post-stroke with persistent walking ability have reported an increase of FM only in the paretic leg (66). It might be speculated that individuals with more disabilities and a more pronounced motor impairment display a higher prevalence of sarcopenic obesity as well as sarcopenia after stroke.

In paper I-II, motor function was high; 59-67% reported the highest possible score on the M-MAS UAS-99, and all were community-living individuals. Moreover, based on the definition of sarcopenia in this study, we found that 3% had low muscle mass in paper II. In an older population, the prevalence of sarcopenia was 1-29% based on the definitions being used (62). The prevalence of low muscle mass in paper II could be a consequence of the many individuals in our study cohort that had high BMI and high FFM together with mobility limitation, because high BMI may induce underestimation of sarcopenia. Recent data including obese subjects reports that higher amounts of muscle mass are linked with less metabolic alterations such as lower inflammatory profiles and better insulin sensitivity (159).

Further, we report IGF-1 and inflammatory values (CRP) within given reference values despite a low level of physical activity and 14% being at risk for malnutrition. Some studies have reported that high serum IGF-1 after stroke is positively correlated to hemiparesis and functional recovery (79). One recent study failed to confirm this relation but found that the IGF-1 level during the acute stroke phase was influenced by the stroke lesion size.
and that the IGF-1 levels found in stroke individuals were low and might be explained by a low level of physical activity and malnutrition (80).

In addition, further analysis of cardiometabolic risk-markers in paper II revealed that 10% had unfavourable cholesterol levels with plasma cholesterol ≥ 6 mmol/L together with LDL values ≥ 3.5 mmol/L; these cholesterol levels might be linked to nutritional intake. Approximately two-thirds were prescribed statins, targeting the LDL cholesterol level, but we were unable to report any further association between prescribed statins and unfavourable high cholesterol levels. One recently published study with observations from the RS-register reported that more patients were on statins at discharge from the hospital in 2010, approximately 61%, compared to earlier years (160). This can be compared to the 70% in paper II that were on statin treatment. The reason for unfavourable cholesterol levels might be low compliance to the prescribed medication. Furthermore, in paper II we showed that women had significantly higher total cholesterol and HDL cholesterol levels in comparison to the males. Both the women and the men had relatively high HDL cholesterol levels despite the reported low level of physical activity.

In our stroke cohort, many individuals were overweight or obese. It can be concluded that individuals after stroke reveal a special need for intensified focus on increasing the level of physical activity, nutrition care management and rehabilitation. Because individuals after stroke can be either underweight or overweight-obese, an individually tailored long-term treatment plan might be effective, preferably performed in the early rehabilitation phase (24 hours until 3 months) after stroke (24, 73, 157).

Effects of a 3-month progressive resistance and balance exercise program

In paper III, we found significantly improved balance (BBS, 2.5 vs. 0 points) at 3 months after participating in the PRB exercise program relative to the exercise group. There are several potential explanations to the improved balance ability reported in paper III that may be interrelated. By exposing themselves to challenging balance exercises, with some supervision during the organised training, the individual’s self-perceived FoF might have decreased. Thus, some individuals might have exposed themselves to more demanding activities in daily life due to the gradually improved balance. Our result is in contrast to a previous randomised controlled trial reporting on post-stroke individuals after participation in the high intensity functional exercise (HIFE) program (161). In that study, improved performance of everyday life activities and improved falls efficacy were reported but improved balance was not reported. However, older people living in residential care who participated in the HIFE program revealed positive long-term effects on
balance, gait and lower-limb strength (162). The interpretation of the result in paper III-IV is that older individuals with balance disturbances due to stroke need a safe and supervised training situation to improve their balance.

The differences in the 6-MWT and 10mWT (paper III) were 30 m and 0.09 m/s, respectively, after the intervention. Considering the calculated effect size (ES: 0.64-0.68) and the minimum clinically important differences for the 6-MWT and walking speed which have been estimated as 20–25 m and 0.05 m/s, respectively, this finding might be considered a small to moderate effect (55, 163). One reason for impaired walking performance can be called critical power, meaning that one chose the speed to endure almost indefinitely below the ventilatory threshold (164). The 6-MWT reflects the ability and capacity to perform daily activities and is a test of sub-maximal aerobic capacity, approximately corresponding to the first ventilatory threshold. Subjects walking at a self-selected speed do not exceed critical power (164).

The characteristics of the present study population described in paper III and IV are, in many cases, similar to the factors that might reduce the 6-MWT (115). In our study cohort, we found a body composition consisting of increased FM and also, to a minor degree, reduced FFM in conjunction with high BMI, which are factors known to negatively affect the distance walked in 6 minutes (115). Further, participating stroke individuals were elderly and many showed comorbidity in addition to their stroke: diabetes type II, previous myocardial infarction or, in some cases, reduced pulmonary function. All these factors are likely to reduce the distance walked in 6 minutes and, as such, affect the results of an intervention study. It can be speculated that improved balance in favour of the exercise group could be the main reason for achieving a longer distance walked in 6 minutes. In contrast, 76% of the individuals were men in the PRB exercise group (paper III) and had an overall preserved cognitive function, which is also indicative of a longer walking distance. All individuals were exercising in their own highest possible intensity, despite weight loading and number of repetitions, which is comparable to low and moderate intensity with more than 10 repetitions per exercise. This might have improved their aerobic capacity as well, reflecting the increased walking distance in this group of individuals with low physical activity.

A total of 43 individuals, 12 women and 31 men, were able to perform the BIA before and after the intervention period and were included in paper IV. To our knowledge, we are the first to report on changes in body composition after exercising in individuals 1 year after stroke. In our study we found a slight non-significant improvement in FFMI and a reduction in FM% in favour of the PRB exercise group, with an overall reduced BMI. Weight loss and a reduction of BMI are in parallel with a decrease in both muscle and fat mass. Our results indicate that we have managed to counteract the loss of muscle mass related to weight loss, because the FFMI was increased after 3
months of progressive resistance and balance group-training. Moreover, the FM% significantly decreased after exercising in comparison with the control group, which is favourable because a high amount of fat may be associated with muscle weakness and reduced insulin sensitivity (148). Age-related body composition changes affected muscle quality (strength/muscle mass), together with obesity, in older inactive individuals after stroke, can consequently lead to the state known as sarcopenic obesity, which was also affected from the PRB exercise program with a slight reduction (27, 68).

Moreover, we showed a significant reduction in IGF-1 at 3 months after the PRB exercise program in relation to the control group. This is somewhat surprising because resistance training usually stimulates IGF-1 production, which is important for muscle anabolism (62). One may speculate that this could reflect a higher insulin sensitivity, because the participating individuals were obese and older (31).

Ectopic fat deposition can change muscle composition and further decline muscle strength and function, which might be one reason for the negatively affected physical functioning in our study (148). Excessive fat deposition within the visceral area, liver, heart and muscles is clearly associated with negative health consequences but may not be similarly related to physical function. Our previous reported improvement in walking capacity (6-MWT) was not related to an increase in muscle mass in this study population. However, muscle function might be improved regardless of similar changes in mass. Factors, such as myofibrillar proteins, inflammation, nutrition and endocrine status, are important for muscle function, i.e., strength and power (62). At 3 months, our exploratory trial revealed a significant association between improvements in 6-MWT and changes in FMI in the exercise group. This effect might be caused by an altered body composition due to the progressive resistance and balance program and a simultaneous weight reduction, especially among males.

Methodological considerations

Individuals included

All the individuals included in the thesis were living at home at the time of entering the study and therefore individuals with more severe stroke were not captured. This was also the focus of the present study. However, approximately 85-90% were living at home 3 months after stroke, according to RS 1 year follow-up in 2013 (5). All individuals who were enrolled in the present study had had a mild to moderate stroke. From these perspectives, the population in this thesis might be considered representative of the community-living stroke population in Sweden. The mean age of the individuals in the different papers were close to the age where women and man have
their first stroke, which further strengthens the external validity and the generalisability to the whole stroke population. In addition, we excluded individuals with severe aphasia and cognitive impairments, because their problems made it hard to follow the study design and manage the self-report of some measurements.

The recruitment to the exercise study described in paper III-IV progressed slowly, and because significant findings on the primary outcome were noted, the intervention was closed before a sufficient sample was obtained. The risk for type II errors was thereby increased. Based on a pilot-study prior to study start, it was estimated that 128 individuals would be enough to detect differences between the PRB exercise program and the control group. However, the study was finalised with 67 individuals included at baseline. The attrition rate was 24% after 3 months and increased to 29% at 15 months follow-up in the PRB exercise group. This might introduce bias. Still, the intention-to-treat analysis was compared to the complete case analyses and revealed about the same results (paper III). Cut-offs for common acceptable attrition-rates in exercise studies are lacking (165).

It was evident that environmental factors, such as the lack of transport possibilities, sometimes influenced the participation in the PRB exercise group. This could be one reason not to participate in exercising, especially for those living outside the centre of Uppsala. Therefore, it seems important and reasonable for healthcare services to pay attention to those individuals and provide them with advice regarding how to be more physically active and which activities and facilities they can participate in. Prescribed physical activity might be helpful to introduce older individuals suffering from stroke to different exercise modalities and possible activities to perform, to increase their daily activity.

Data collection

The process of identifying eligible individuals for inclusion may be biased because some individuals could not be reached as a result of different reasons. In addition, some factors might have affected external validity and a generalisation to all individuals with stroke. An uneven distribution between genders (male, 71%) was present throughout the papers. Furthermore, those who did not want to fully participate (n=81) answered questions from EQ-5D and reported a lower HRQoL compared to those who were enrolled in the study. This can be compared to a Swedish study reporting a significantly lower health-index for women, especially in the high age-groups and, as such, mirroring the low EQ-5D seen in non-participants (143). In total, approximately 21% of the men declined participation and 44% of the women declined. The study group was, however, not comparable in EQ-5D with a Swedish age-matched normal population, revealing a mean of 0.73 for all individuals compared to 0.80 for the individuals in Stockholm county (143).
Many of the participating individuals had possible depression, which is in line with other studies and reports (5, 38).

In paper I, all data were collected using standardised measurements with acceptable psychometric properties and were collected at one time-point. That strengthens the internal validity. Measurements were made by one single person. The self-reported questionnaires were filled out before the individual came to the hospital for examination, but was then re-checked to minimise missing values. Despite this procedure, there were some data missing, but not > 3% for any scale. Imputation by mean or median values in paper I-II when data were missing could slightly have affected the mean of the whole study population. However, the study population was relatively large in relation to the missing values.

A limitation with self-reporting questionnaires when measuring physical activity is the risk for overestimation due to difficulties in obtaining the exact frequency, intensity and duration. Despite this, such questionnaires are inexpensive and suitable for larger trials. PASE is a questionnaire measuring physical activity in older individuals and has previously been used in the stroke population (34-36). Using self-reporting in a stroke population can be difficult because the respondents could have undetected mental impairment. However, the PASE scores have shown significant correlation to a portable accelerometer in those over 70 years old (r = 0.64, P < 0.05) (166). This adds support to the validity of the PASE, measuring level of physical activity in older individuals (166). In addition, to prevent missing data, the rechecking of answers was also essential to minimise misunderstandings. Objective measurements, such as using accelerometer data for registration of physical activity, might have added more accurate data, but may also be uncertain due to reduced compliance with using the device.

In paper II and IV, measurements of BIA only included individuals who were able to stand, which excluded individuals with reduced static balance. Individuals being examined outside the hospital were further excluded from the BIA assessment as well. This restricts the possibility to generalising the results from the present study to more severe damaged individuals with stroke. There might be a validity problem as well involved in the BIA assessment used in this thesis and therefore there are some concerns about the definition criteria for sarcopenia being used (89). Computed tomography (CT scan) and magnetic resonance imaging (MRI) are the gold standard in research for measuring body composition (89) but dual energy X-ray absorptiometry (DXA) and BIA is also used for research purposes. Further, additional examinations included into the study design, i.e., hand grip strength, might have strengthened the results (89). This method is frequently used and the reason for not including grip strength as a measurement was that the SPPB, including chair-stand, could be considered a functional measurement for muscle strength and performance in the lower extremities (51, 110).
The study population in paper III originated from the first 195 individuals examined in paper I. This paper includes most of the recommendations for a clinical trial with methodological quality, e.g., randomised allocation, control group, intention-to-treat analysis and concealed allocation. The drop-out rate in paper III was 24% after 3 months and increased further to 29% after 15 months, which introduced some bias to the results. To minimise this problem, a multiple imputation technique was used, to preserve the allocation to the different groups. The assessor was blinded to the group allocation, but some unmasking might have occurred during follow-up, since the participants had no restrictions in revealing which group they participated in. This increased the risk of bias.

An independent experienced physiotherapist not involved in the randomisation procedure or the PRB exercise group performed all assessments at baseline, 3, 6 and 15 months, increasing the internal validity.

Main conclusions

• Individuals 1-3 years after stroke, without major cognitive decline and severe aphasia, perceived many disabilities that could be modifiable. Low mobility and low physical activity, high possible depression, reduced walking capacity and a slow walking speed were highly present. Frequent falls and a fear of falling were common among participants as well. Fall-related self-efficacy and mobility may promote the level of physical activity.

• Many individuals were overweight or obese with an unfavourable high fat mass and high cholesterol and LDL levels. Factors associated with risk for low mobility were low and medium physical activity, risk for malnutrition, and age per 10 years.

• A progressive resistance and balance program for 3 months can be effective in the short-term to improve physical function, i.e., balance, walking capacity and gait speed. In the long-term, at follow-up after 6 and 15 months, the increase in walking speed persisted.

• A progressive resistance and balance program slightly altered body compositional changes 1 year after stroke. There was a significant association between changes in walking capacity and changes in fat mass index after exercising. Exercising might improve insulin sensitivity as well, according to the decreased IGF-1 level.
Clinical implications

- If the level of physical activity is low, implying an increased risk for future cardiovascular incidents and low mobility, treatments for enhanced physical activity and reduced sedentary time should be addressed quickly after stroke onset.

- The majority of the post-stroke individuals were overweight or obese with a body composition characterised by increased fat mass, meaning that treatments for healthy eating should be incorporated into stroke-rehabilitation.

- A 3 months progressive resistance and balance training program performed as a circuit class with individualised intensity and progression are effective in improving physical function directly after exercising. Therefore, to maintain improved functions in the long-term, additional strategies targeting behaviour changes might be effective.

- Assessments of body composition should be considered after stroke.
Svensk sammanfattning

Stroke är vanligt i högre åldrar och mer än åttio procent av de som insjuknar är över sextiofem år. Många av de riskfaktorer som orsakar stroke och även hjärtinfarkt är beroende av livsstil och går därmed att förändra. Högt blodtryck, bukfetma, rökning, diabetes, alkohol, fysisk inaktivitet, depression och ohälsosam kosthållning är bland de vanligaste riskfaktorerna för stroke.


Det övergripande syftet med denna avhandling var att beskriva fysisk funktion, fysisk aktivitet, kroppssammansättning, nutritions status (inklusive kardiometabola riskmarkörer) samt psykologiska faktorer hos hemmaboende individer 1 år efter stroke. Ytterligare ett syfte var att utvärdera kortsiktiga och långsiktiga effekter av ett 3 månaders progressivt styrke- och balansträningss program.

Delarbete I:

Det första delarbetet kartlägger nivå på fysisk funktion, fysisk aktivitet samt psykologiska faktorer hos 195 hemmaboende individer, 1 till 3 år efter stroke. Vi ville även studera vilka faktorer som kunde förklara mobilitet och fysisk aktivitet. Personer med kognitiv nedsättning eller påtagliga språkliga svårigheter exkluderades. Inkluderade personer fick svara på enkäter med frågor rörande fysisk aktivitet, hälso-relaterad livskvalitet, fall-relaterad selfefficacy och depression. De tillfrågades också om eventuella fall incidenter det senaste året och om de upplevde fallrädsla. Individerna undersöcktes vid ett tillfälle vad gällde balansförmåga, mobilitet (en kombination av gånghastighet, balans och uppresning från stol), gånghastighet och motorisk funktion. Resultatet visade att patienterna hade låg mobilitet, vilket bedöms kunna öka risken för framtida sjukhusinläggning och funktionsnedsättning. Vi-
dare hade individerna en låg gånghastighet och en låg fysisk aktivitetsnivå i jämförelse med äldre utan stroke. Trettioåtta procent hade möjlig depression och 46% hade fallit mer än en gång senaste året. Kvinnorna uppvisade en signifikant högre fallrädsla i jämförelse med männen och totalt sett angav 37% att de var rädda att falla.


Delarbete II:
I vårt andra arbete studerades kroppssammansättning, nutritions status (inklusive kardiometabola riskmarkörer) och fysisk funktion/fysisk aktivitet hos 134 av de 195 individerna som inkluderades i delarbete I. Exklusionskriterierna var detsamma som i delarbete I, men individer med pacemaker och de som inte kunde utföra mätning av kroppssammansättning (bioelektrisk impedans analys, BIA, (Tanita®) av andra skäl exkluderades. Alla personer i studien besvarade frågeformulär angående sin fysiska aktivitetsnivå och sitt nutritions status. Mobilitet och självoljd gånghastighet undersöktes liksom kroppssammansättning. Varje individisk BMI beräknades utifrån vikt och längd. Resultatet visade att > 20% hade en BMI över 30 kg/m², vilket klassificeras som fetma. Fjorton procent bedömdes ha risk för under-nutrition och 3% uppvisade sarkopeni (låg muskelmassa i kombination med en gånghastighet < 1 m/s) medan 8% hade en kombination av låg muskelmassa och hög andel fettsmassa, dvs sarkopen obesity. Av de inkluderade personerna hade 10% kolesterol nivåer över 6 mmol/l samtidigt med LDL-cholesterol värden över 3.5 mmol/L, vilket bedömdes innebära en förhöjd kardiovaskulär risk. Kvinnorna hade signifikant högre total kolesterol och HDL-cholesterol i jämförelse med männen.

Vi analyserade även sambandet mellan låg mobilitet och faktorer som äldre, kön, fysisk aktivitet och nutritionsstatus. I denna grupp var de starkaste sambanden, uttryckt som Odds kvoter (95 % konfidensintervall), låg fysisk aktivitet, OR 8.2 (2.8-24.2), risk för under-nutrition, OR 5.8 (1.6-21.1) och hög ålder OR, 2.78 (1.24-6.24). Slutsatsen blev att fetma och sarkopen obesity var tämligen vanligt förekommande i denna grupp av individer efter
stroke. Interventioner riktade mot förbättrad nutrition och ökad fysisk aktivitet behövs hos individer efter stroke.

Delarbete III

I det tredje delarbetet har effekterna av ett progressivt styrke- och balans (PRB) träningsprogram på fysisk funktion, fysisk aktivitet och psykologiska faktorer undersöks. Uppföljningar ägde rum efter 3, 6 och 15 månader. Studien har genomförts som en randomiserad kontrollerad studie med totalt 67 försökspersoner (76 % män, medelålder 73 år). Primära utfallsmått var balans (Berg Balans Skala, 0-56 poäng) och mobilitet (Short Physical Performance Battery, 0-12 poäng) vid 3 månader. Sekundära utfallsmått var gångkapacitet, 10 meters gång hastighet, fysisk aktivitetsnivå, hälsorelaterad livskvalitet, depression och fall-relaterad self-efficacy. Trettiofyra försökspersoner randomiserades till en träningssgrupp, som utförde ett funktionellt träningsprogram 2 gånger per vecka under 3 månader, med fokus på ökad benstyrka och balans i stående och gående. Alla personer bar ett Viktband under träningen där vikterna gradvis justerades, utifrån varje individs förutsättning. Individerna fick också en individuellt anpassad hemövning att utföra mellan träningstillfällena. Kontrollgruppen bestod av 33 försökspersoner som inte erhöll några specifika behandlingsåtgärder. Efter 3 månader uppvisade individerna i träningssgruppen en signifikant förbättring av balans (Berg balans test), gångkapacitet (6-minuters gångtest) samt den självvalda gånghastigheten (10-meters gångtest) jämfört med kontroll gruppen. Effekten på gånghastigheten kvarstod vid 6 och 15 månaders uppföljning.

Slutsatsen av detta delarbetet var att ett progressivt styrke- och balanstränings program förbättrade balans, gång kapacitet och gånghastighet kortsiktigt i en kronisk fas efter stroke. Sammanfattningsvis, behövs ytterligare åtgärder för att förbättringarna skall kvarstå över tid.

Delarbete IV

I det här delarbetet låg fokus på effekter av tre månaders gruppträning med avseende på förändring av kroppssammansättning (muskelmassa och fettmassa) och nutritionsstatus i relation till förändringar i fysisk funktion. Studien är genomförd som en explorativ/utforsknings randomiserad kontrollerad studie. Vi analyserade 43 (73% män, medelålder 73 år) av de 67 försökspersonerna som deltog i den randomiserade kontrollerade studien som beskrivs i delarbete III. Primärt ville vi nu studera effekten av ett progressivt styrke- och balansträningsprogram på kroppssammansättning, kardiometabola riskmarkörer och nutritionsindikatorer. Fettfri massa (främst muskelmassa) och fettmassa bestämdes med bioelektrisk impedans-analys (Tanita®). Fysisk
funktion bestämdes som gångkapacitet, balans och mobilitet. Tjugo individer deltog aktivt i PRB-träningsprogrammet, medan kontrollgruppen bestod av 23 individer som inte erhöll några särskilda behandlingsåtgärder. Mätningar utfördes före och direkt efter interventionen.

Vi kunde visa att fettmassan (procent) minskade signifikant efter tre månaders PRB träning jämfört med kontrollgruppen. Den fettfria massan, dvs. bl.a. muskelmassa, ökade något i träningsgruppen, men förändringen var inte statistiskt signifikant. BMI hade totalt sett minskat något i båda grupperna. Serum insulin-like growth factor-I (IGF-1) var signifikant lägre efter tre månaders träning i jämförelse med kontrollgruppen. Detta kan möjligvis vara ett tecken på ökad insulinkänslighet. Varken blodtryck eller kardiovaskulära riskpoäng hade förändrats vid tre-månadersmätningen. Vidare såg vi att minskningen av fettmasseindex (kg/m²) uppvisade ett signifikant samband med ökning i gångkapacitet, mätt med 6-minuters gångtest efter tre månader. Det fanns inga statistiska samband mellan förändringar i muskelmassa och förändringar i fysisk funktion efter tre månaders träning.

Sammanfattningsvis sågs en minskning av fettmassan vilket kan vara fördelaktigt ur kardiovaskulär risk synpunkt. Minskningen i fettmassa var också förenat med bättre gångkapacitet. Muskelmassan ökade något eller kvarstod oförändrad trots en generell minskning av BMI. Serum IGF-1 minskade något i träningsgruppen vilket möjligt kan vara ett uttryck för ökad insulinkänslighet. Effekt av progressiv styrketräning på kroppssammansättning och nutritionsfaktorer är viktigt att studera vidare.
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