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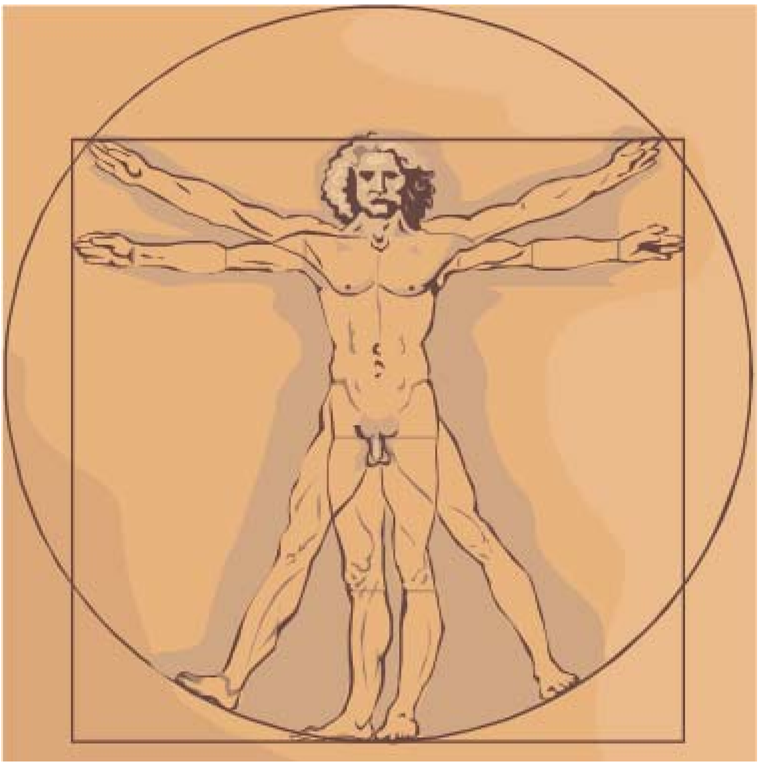
Erja Portegijs

Asymmetrical Lower-Limb Muscle Strength Deficit in Older People



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UNIVERSITY OF JYVÄSKYLÄ

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ABSTRACT

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The aim was to study causes and consequences of asymmetrical strength deficit, i.e. difference in muscle strength between the lower-limbs, and the effects of progressive resistance training in clinical and non-clinical populations of older people.

Data of three larger studies were used. Healthy 63-75-year-old women (n=403-419), 73-96-year-old women 1-13 weeks after hip fracture (n=43), and 60-85-year-old men and women ½-7 years after hip fracture (n=79) were studied. A randomized controlled trial of strength-power training aiming to reduce the lower-limb side-to-side difference was performed (n=46). Leg extension power, isometric knee extension torque, rate of force development, walking and stair climbing speed, balance, lower-limb pain, and lower-limb disease and injury burden were assessed. Injurious falls were followed-up for 1 year.

In healthy women, the side-to-side difference in lower-limb power was on average 15%. After hip fracture, the fractured limb was significantly weaker than the non-fractured limb. A large side-to-side difference in power was associated with mobility and balance limitations in healthy older women and women with a recent hip fracture. In the first 3 months, the improvement in power of the fractured limb correlated with improved mobility function. Years after the fracture, half of the patients had a consistent strength deficit on the fractured side. Pain, and disease and injury burden affecting the non-fractured lower-limb reduced the side-to-side difference, resulting in poor strength in both lower-limbs. The training was feasible and improved muscle strength, especially in the weaker lower-limb. The side-to-side difference, mobility and balance were not clearly affected, but perceived difficulty in outdoor mobility and daily activities decreased.

The study stresses the importance of regaining muscle strength after lower-limb injury such as hip fracture. In addition to poor strength, a considerable side-to-side strength difference compromises mobility and balance in older people. To prevent mobility limitation and falls, multi-component rehabilitation programs including progressive resistance training should be studied.

Key words: muscle force, muscle power, leg, asymmetry, mobility limitation, pain, hip fracture, rehabilitation

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LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following papers, which will be referred to by their Roman numerals. Additionally, some unpublished data are included in the thesis.

I Portegijs E, Sipilä S, Alen M, Kaprio J, Koskenvuo M, Tiainen K, Rantanen T. 2005. Muscle power asymmetry and mobility limitation in healthy older women. Archives of Physical Medicine and Rehabilitation 87, 1838-1842.

II Portegijs E, Sipilä S, Pajala S, Lamb SE, Alen M, Kaprio J, Koskenvuo M, Rantanen T. 2006. Asymmetrical lower extremity power deficit as a risk factor for injurious falls in healthy older women. Journal of the American Geriatrics Society 54, 551-553.

III Portegijs E, Sipilä S, Rantanen T, Lamb SE. 2008. Leg extension power deficit and mobility limitation in women recovering from hip fracture. American Journal of Physical Medicine and Rehabilitation 87, 363-370.

IV Portegijs E, Rantanen T, Kallinen M, Heinonen A, Alen M, Kiviranta I, Sipilä S. 2008. Leg pain and injury burden as determinants of muscle strength deficit after hip fracture. (submitted for publication)

V Portegijs E, Kallinen M, Rantanen T, Heinonen A, Sihvonen S, Alen M, Kiviranta I, Sipilä S. 2008. Effects of resistance training on lower extremity impairments in older people with hip fracture (ISRCTN34271567). Archives of Physical Medicine and Rehabilitation (in press)

ABBREVIATIONS

1RM	One-repetition maximum
95%CI	95 % confidence interval
ACL	Anterior-cruciate ligament
ADL	Activities of Daily Living
ANOVA	Analysis of Variance
cat	Categorized scale
FITSA	Finnish Twin Study on Aging; study of healthy older women
Fract	Fractured limb
Non-fract	Non-fractured limb
HIP-RECOVERY	Study of women 1 and 13 weeks after hip fracture surgery
HIP-ASYMMETRY	Study of men and women ½ - 7 years after hip fracture surgery
IA	Interaction effect
KET	Knee extension torque
LBM	Lean body mass
LEP	Leg extension power
OR	Odds Ratio
n	Number
N	Newton; expression of muscle force
Nm	Newton meter; expression of muscle torque
Nm/s	Newton meter per second; expression of rate of force development
PRT	Progressive resistance training
RCT	Randomized controlled trail
RFD	Rate of force development
RFD_{200}	Rate of force development over the first 200 ms of contraction
ROM	Range of motion
SD	Standard deviation
W	Watt; expression of muscle power
WEAKleg	The weaker lower-limb as defined for the training

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ORIGINAL PAPERS

1 INTRODUCTION

Poor muscle force in the lower-limbs is an acknowledged risk factor for limitations in mobility and balance (Skelton et al. 1994, Rantanen et al. 1994, Rantanen 1998a, Izquierdo et al. 1999, Rantanen et al. 2001, Lauretani et al. 2003), falls (Skelton et al. 2002), and loss of independence (Rantanen et al. 2002,) in older people. Many daily tasks, such as climbing stairs, rising from a chair, and preventing a fall after a trip, require the ability to produce force quickly, and therefore muscle power (the product of force and velocity) may be even more important for mobility function than muscle force alone (Skelton et al. 1994, Izquierdo et al. 1999, Foldvari et al. 2000, Bean et al. 2002, Bean et al. 2003). Muscle strength, or more specifically muscle force and power, decreases with age (Bassey & Short 1990, Skelton et al. 1994, Rantanen et al. 1998b, Frontera et al. 2000, Hughes et al. 2001). The reduction in muscle power is larger since both force and velocity decrease with age (Skelton et al. 1994). Muscle strength is strongly affected by muscle use (Rantanen et al. 1997b, Rantanen et al. 1999b, Hunter et al. 2000). The presence of pain, diseases and injury may also reduce muscle strength (Rantanen et al. 1999b, Lamb et al. 2000, Leveille et al. 2001, Herrick 2004). The effects of pain, certain diseases and injury on muscle strength may, however, be local. For example pain (Wilgen et al. 2003), osteoarthritis (Robertson et al. 1998, Sicard-Rosenbaum et al. 2002, Mizner et al. 2003) or hip fracture (Lamb et al. 1995, Sherrington et al. 1998, Madsen et al. 2000) may affect only one lower-limb and thus reduce lower-limb muscle strength on that side especially, potentially causing a large side-to-side strength difference.

The implications of a large side-to-side strength difference in the lower-limbs have not been studied extensively. A case-control study, comparing relatively healthy women with frequent falls to age-matched non-falling control subjects, showed that the fallers had poorer muscle force and power (Skelton et al. 2002). Additionally, the frequent fallers had a significantly larger side-to-side difference in lower-limb power (Skelton et al. 2002). These results suggest that side-to-side differences in lower-limb power may be among the key risk factors for falls. However, it is unknown to what extent such a side-to-side difference exists in populations of older people and what the consequences of the difference are. Potentially, limitations in mobility and balance may be the result of a large side-to-side strength difference in the lower-limbs.

Hip fracture patients are likely to have poor muscle strength in the lower-limbs, especially on the fractured side (Lamb et al. 1995, Madsen et al. 1995, Madsen et al. 2000). In Finland, a country with 5.3 million people, the annual hip fracture incidence was approximately 400 per 100 000 persons aged 50 or above between the years 1997 and 2004 (Kannus et al. 2006b). The annual number of hip fractures at the end of this period was approximately 7 000. A hip fracture, a fracture of the proximal femur, is a major trauma in older people and 20-30% of the patients die within one year (Keene et al. 1993, Roche et al. 2005, Hawkes et al. 2006). Men have a higher mortality rate than women, but men and women surviving the hip fracture do have a similar rate of recovery in mobility function and activities of daily living (ADL; Hawkes et al. 2006).

Less than half of the hip fracture patients surviving return to their pre-fracture level of functioning within two years (Magaziner et al. 2000). Therefore, hip fracture patients have more ADL and mobility-related disabilities than older people without a hip fracture (Norton et al. 2000, Kirke et al. 2002, Magaziner et al. 2003). Poor muscle strength is likely one of the key factors in the development of mobility limitations and mobility-related disability (Sherrington et al. 1998, Visser et al. 2000). Muscle strength in the fractured limb seems to correlate more strongly with mobility function than muscle strength of the non-fractured lower-limb (Lamb et al. 1995, Madsen et al. 2000). Therefore it is important to take into account the muscle strength of both lower-limbs, which is not done in most studies. It is not known whether the side-to-side difference in the lower-limbs affects mobility function and recovery from hip fracture or whether one strong lower-limb can compensate for the deficit in the fractured limb.

As muscle force and power are determinants of mobility function in older people, increasing muscle strength may help to prevent mobility limitation. Based on current knowledge, the best way to increase muscle strength, is intensive progressive resistance training (Kraemer et al. 2002, Latham et al. 2004). In relatively healthy older people, resistance training has been proven to be effective for increasing muscle force and power (Kraemer et al. 2002, Latham et al. 2004). The effects of resistance training on mobility limitation and disability are, however, less clear (Latham et al. 2004). In more frail people and people with mobility limitation, resistance training seems to have a positive effect on mobility function (Fiatarone et al. 1994, Seynnes et al. 2004). However, the effects of resistance training are less studied in clinical populations, and the training protocols are divers and usually also include other types of exercises. Nevertheless it seems that resistance training is beneficial also in clinical populations (Timonen et al. 2002, Suetta et al. 2004ab). Studies investigating people after hip fracture generally show larger improvements in physical and mobility function after rehabilitation including intensive resistance training compared to standard rehabilitation alone (Mitchell et al. 2001, Hauer et al. 2002, Binder et al. 2004). However, studies often do not take into account the side-to-side difference in the lower-limb strength, which is likely after hip fracture. Progressive resistance training aiming to reduce the side-to-side difference and simultaneously increase muscle force and power of both lower-limbs may therefore be more effective.

This study explores the side-to-side difference in lower-limb muscle strength and its consequences for mobility and balance function in healthy older women and in women with a recent hip fracture. The extent of the strength difference will also be determined in men and women with a history of hip fracture, and the underlying determinants of the difference will be explored. Also the effects of a training program, specifically aiming to reduce the side-to-side strength difference and increase muscle force and power of both lower-limbs, on muscle strength, mobility and balance function will be studied in a population with a history of hip fracture.

2 REVIEW OF THE LITERATURE

2.1 Muscle strength in older people

2.1.1 Muscle strength

A muscle produces force by sliding filaments across each other, which is called a muscle contraction (Enoka et al. 1994). A muscle contraction may be static (involving no movement) or dynamic (involving movement). In static or isometric muscle contraction, the total length of the muscle does not change and the joint angle remains constant. Maximal isometric muscle force is defined as the maximum voluntary contraction performed at a specific joint angle against an unyielding resistance, usually tested with a dynamometer. A dynamic muscle contraction induces movement about a joint. In concentric actions, force production of the muscle is greater than external load and the total muscle length decreases. When the external load is greater than the muscle force produced the muscle lengthens, which is called an eccentric contraction. Maximal voluntary concentric or eccentric force can be assessed with isokinetic testing in a system that controls the speed of movement. The contraction is then performed at a constant velocity over the full range of motion (McArdle et al. 2000). Maximal voluntary concentric force can also be estimated in a one repetition maximum (1RM) test that determines the highest external load one can overcome for one repetition over the full range of motion.

Contractile rate of force development (RFD) is defined as the ability to produce muscle force quickly (Aagaard et al. 2002). RFD is the rate of the rise in force at the onset of contraction, e.g. within the first 100-200 ms of contraction, and is calculated as the slope of the force-time curve. Muscle power is the product of the generated force and the speed of the muscle contraction i.e. the ability of the neuromuscular system to produce the greatest possible force as fast as possible (Enoka et al. 1994). The force-velocity curve shows that at higher force levels, speed decreases, and at higher speed levels, force decreases thus resulting in a lower power output. Muscle power is maximal at approximately one third of the maximal force and one fourth of the maximal velocity.

Muscle strength in this study refers to muscle characteristics such as muscle force, rate of force development and muscle power.

2.1.2 Age-related decrease in muscle strength

Muscle force increases until the age of 20-30 (Lindle et al. 1997, Lynch et al. 1999). Thereafter muscle force either remains constant or starts to decrease, until the decrease in muscle force accelerates after the age of 50 (Lindle et al. 1997, Lynch et al. 1999, Stoll et al. 2000). In cross-sectional studies, muscle force decreases on average about 1–1.5 % each year (Skelton et al. 1994, Lindle et al. 1997, Lynch et al. 1999, Stoll et al. 2000). However, the exact rate of the decline depends on muscle group and testing method (Lindle et al. 1997, Izquierdo et al. 1999, Lynch et al. 1999, Hunter et al. 2000). Hughes et al. 2001 showed that in cross-sectional analyses of people aged 46-78 years isokinetic knee extension force decreased 14% per decade, however, in the longitudinal analyses over 10 years the decline was 60% greater. In other longitudinal studies, the loss in muscle force ranged between 1–3 % per year (Aniansson et al. 1986, Rantanen et al. 1998b, Frontera et al. 2000). In isokinetic knee extension, the decrease in force over 12 years was somewhat greater with higher contraction velocity (240°/s) than with slower contraction velocity (60°/s; Frontera et al. 2000). In addition, the decrease in muscle power is faster than the decrease in muscle force since both muscle force and the velocity of movement decrease with age (Bassey & Short 1990, Skelton et al. 1994, De Vito et al. 1998, Izquierdo et al. 1999, Lamoureux et al. 2001, Macaluso et al. 2003, Dean et al. 2004). Decreases of about 3.5% per year have been reported in cross-sectional studies (Skelton et al. 1994, Bassey & Short 1990).

The decrease in muscle strength is related to muscular and neural changes occurring with age (Lamoureux et al. 2001). Decreases in muscle force are often accompanied by muscle atrophy, which is a decrease in muscle mass (Frontera et al. 2000, Hughes et al. 2001, Lauretani et al. 2003). The decrease in muscle mass is commonly attributed to decreases in the number of muscle fibers (Lexell et al. 1983, Frontera et al. 2000) and the reduction in fiber size (Aniansson et al. 1986, Roos et al. 1997). There is a disproportional loss of the faster type II muscle fibers (Lexell et al. 1983, Aniansson et al. 1986, Roos et al. 1997), which causes slowing of the muscle contraction. The loss of type II muscle fibers is partly due to motor unit remodeling, a process, in which a nerve degenerates and the muscle fibers are reinnervated by another nerve (Lexell et al. 1983, Doherty et al. 1993, Roos et al. 1997). New motor units that are usually of a larger size and of a slower fiber type are formed (Doherty et al. 1993, Roos et al. 1997). Alterations in neural activation occurring with age may affect individual muscles and may lead to poorer coordination of muscle groups. Compared to younger people, older people show larger activity in the antagonist muscles (Hortobagyi et al. 2003) and decreased steadiness of the force production (Hortobagyi et al. 2001, Christou et al. 2002). Additionally, the rate of muscle activation decreases with age (Pijnappels et al. 2005), which likely contributes to the age-related reduction in the rate of force development in the initial phases of a contraction (Häkkinen et al. 1991, Thelen et al. 1996, Christou et al. 2002, Lanza et al. 2003). For example, compared to younger people, older people need longer to develop the same absolute (Häkkinen et al. 1991, Thelen et al. 1996) or relative (Häkkinen et al. 1991) force level. Additionally, older people produced 30-40% less force in the first 200 ms of the contraction (Christou et al. 2002).

Muscle strength is partly determined by genetic factors. For example, Tiainen et al. (2005) showed that in older women isometric knee extension force and leg extension power have a shared genetic component that accounted for 48% and 32% of the inter-individual variation in force and power, respectively. This suggests that partly the same genes regulate muscle function regardless of the type of contraction.

The effects of aging alone on muscle strength are difficult to differentiate from the effects of age-related decreases in levels of physical activity and age-related diseases (Rantanen et al. 1998b, Rantanen et al. 1999b, Hughes et al. 2001). In older people, poorer muscle strength is also associated with factors such as female sex (Lindle et al. 1997, Rantanen et al. 1997b, Hughes et al. 2001, Stoll et al. 2000) and lower body weight (Rantanen et al. 1998b, Hughes et al. 2001).

2.1.3 Decrease in muscle strength related to physical inactivity

With age, the time spent on physical activity and the intensity of the physical activities commonly decrease (Hunter et al. 2000). The reduced physical activity may at least partly contribute to the loss of muscle strength in older age (Rantanen et al. 1997b, Rantanen et al. 1999b, Hunter et al. 2000, Hughes et al. 2001). Many studies with mainly cross-sectional design have shown that muscle strength is lower among people with lower levels of physical activity (sedentary) than among the more physically active people (Sipilä et al. 1991, Rantanen et al. 1997b, Hunter et al. 2000). The effects of decreases in physical activity and muscle strength are mutually reinforcing (Rantanen et al. 1999b). Muscle strength decreases under circumstances of little physical activity. The reduced level of muscle strength may cause discomfort in performing certain tasks and may thereby lead to subsequent avoidance of the task. This again reduces the level of physical activity and a vicious circle of reducing physical activity and muscle strength may be the consequence (Rantanen et al. 1999b). On the other hand, physical exercise increases muscle use, thus increasing muscle force and the vicious circle may potentially be stopped. Increasing muscle strength is possible even in very old people, as will be discussed in the section on progressive resistance training.

Illness, injury and hospitalization may lead to periods of immobilization. Even in younger people, short-term local immobilization (Yasuda et al. 2005, Urso et al. 2006) as well as six weeks of bed-rest (Berg et al. 1997) lead to marked decreases in muscle strength, which may be partly attributed to the decrease in muscle mass and changes in neural factors. Ten days of bed rest in healthy older people led to marked decreases in muscle mass (6%) and isokinetic muscle force (16%), particularly in the lower extremities (Kortebein et al. 2007). Protein synthesis was reduced and the nitrogen balance was negative especially in the last five days. While the effects of aging and immobilization are rather similar, one difference is that during immobilization shortening velocity may increase while it decreases with age (D'Antona et al. 2003).

2.1.4 Decrease in muscle strength related to diseases, injury, and pain

In acute disease or injury, muscle force may reduce quickly. The reduction in muscle force may be due to acute effects of immobilization and inflammation. For example after hip fracture, the inflammatory reaction in response to injury and surgical stress leads to catabolism (Hedström et al. 2006). Injury-induced release of stress hormones and proinflammatory cytokines may sustain a prolonged catabolic state characterized by nitrogen loss and insulin resistance. For example, the level of proinflammatory cytokine Interleukin-6 remains elevated even 12 months after hip fracture and has been associated with poorer recovery (Miller et al. 2006b). An important mediating factor in the poor recovery of muscle tissue is the low level of Insulin-like Growth Factor-1 that was found in hip fracture patients upon hospital admission as well as up to six months later (Ponzer et al. 1999, Hedström et al. 2006). Surgery is often accompanied by a long preoperative period of fasting that will further aggravate the insulin resistance and catabolism induced by the trauma (Hedström et al. 2006). Even in young and healthy volunteers, calorie restriction accelerated the catabolic response to bed rest, leading to loss of lean body mass and protein (Biolo et al. 2007). Additionally, a simulated hormonal stress response typically caused by injury or illness exacerbated the loss in muscle mass and leg extension force (1RM) in 28-day bed-rest due to reduced protein synthesis (Paddon-Jones et al. 2006). After a hip fracture, general health of the patients is often poor and comorbidity exists, further complicating the recovery (Keene et al. 1993, Roche et al. 2005, Hawkes et al. 2006).

Poor muscle force has also been reported in chronic diseases, such as osteoarthritis (Rantanen et al. 2003, Rossi et al. 2004), diabetes (Rantanen et al. 1998b, Rantanen et al. 2003) and cardiovascular disease (Rantanen et al. 1998b, Rantanen et al. 2003). In addition, deficits in muscle force exist even 5-10 years after musculoskeletal injury (Seto et al. 1988, Holder-Powell et al. 2000), such as anterior-cruciate ligament (ACL) injury and fracture. For example on average 30 weeks after a hip fracture, patients have less than half the muscle force of healthy age-matched control subjects in both lower-limbs (Sherrington et al. 1998).

The experience of pain is subjective. Due to lack of a standardized measure to assess pain, a range of measures assessing the presence of pain (Al Snih et al. 2005), specific sites with pain (Lamb et al. 1995, Leveille et al. 2002, Wilgen et al. 2003, Herrick et al. 2004, Onder et al. 2006), and the severity of pain (Lamb et al. 1995, O'Reilly et al. 1998, Lamb et al. 2000, Leveille et al. 2001, Steultjens et al. 2001, Leveille et al. 2002, Wilgen et al. 2003, Onder et al. 2006) have been used. For example, the severity of pain may be assessed using categorical responses, such as no, mild and severe (Lamb et al. 1995, Morrison et al. 2003, Onder et al. 2006), continuous scales, such as visual analogue scales (Steultjens et al. 2001, Wilgen et al. 2003), or something in between (O'Reilly et al. 1998, Lamb et al. 2000, Leveille et al. 2001, Leveille et al. 2002, Dasch et al. 2008). Despite the large range of measures used to assess pain, non-specific pain (Leveille et al. 2001, Leveille et al. 2002, Al Snih et al. 2005, Onder et al. 2006) or pain specific to a disease or injury (Lamb et al. 1995, O'Reilly et al. 1998, Steultjens et al. 2001, Herrick et al. 2004, Heuts et al. 2004) have consistently been associated with impairments such as poorer muscle force and mobility limitation. Pain is a frequent problem in hip fracture patients immediately after surgery (Morrison et al. 2003) as well as up to 12 months later (Herrick et al. 2004, Williams et al. 2006, Dasch et al. 2008). After hip fracture, pain is associated with poorer recovery in ADL (Morrison et al. 2003, Herrick et al. 2004, Williams et al. 2006, Dasch et al. 2008) and mobility function (Morrison et al. 2003), and muscle strength (Herrick et al. 2004).

Although pain may be association with inflammation or neural inhibition (Hurley et al. 1997, O'Reilly et al. 1998, Stevens et al. 2003), an important underlying mechanism for functional impairments may be avoidance of certain behavior due to pain or fear for pain (Vlaeyen et al. 2000, Steultjens et al. 2002, Heuts et al. 2004). Avoidance may reduce the level of physical activity (Vlaeyen et al. 2000, Steultjens et al. 2002), which has consequences for physical performance, and may thus reduce muscle strength and increase mobility limitation. Fear for pain or (re)injury may have long-term consequences and thus maintain chronic pain disability (Vlaeyen et al. 2000). However, the relationship between pain and disability may be either direct (Lamb et al. 2000, Leveille et al. 2007) or indirect through impairments such as reduced muscle strength (O'Reilly et al. 1998, Vlaeyen et al. 2000, Steultjens et al. 2002, Al Snih et al. 2005). Also other fear, such as fear for falls, may lead to avoidance behavior and thereby reduce physical performance in a similar way (Delbaere et al. 2004). After a hip fracture, patients are likely to develop fear for falls, which may thus affect their recovery and mobility function (Jarnlo et al. 1991b, Petrella et al. 2000).

Muscle power, similarly as muscle force, may be affected by disease, injury and pain (Lamb et al. 1995, Barker et al. 2004), however, this has not been studied extensively. In addition to the systemic effects, disease, injury and pain may also have a local effect on muscle strength, this will be discussed later.

2.1.5 Asymmetrical deficit in lower-limb muscle strength

In most studies, muscle strength is measured in one lower-limb only, usually the stronger or dominant limb, or the average or sum of the strength in both lower-limbs is used for analysis. However, in older people a side-to-side difference in lower-limb muscle strength, that is an asymmetrical deficit in muscle strength, may exist. The prevalence and consequences of a large asymmetrical deficit have not been studied extensively. A study by Hunter et al. (2000), including a sample of healthy community-dwelling women between 20 and 89 years old, calculated that the average difference between the dominant and non-dominant lower-limb in isometric knee extension force was on average 5% (Hunter et al. 2000). Perry et al. (2007) showed that a difference in isometric muscle force and muscle power between the lower-limbs was larger in older (average 14%) than in younger (average 10%) people.

Diseases, injuries and pain affecting one lower-limb only may have a local effect on muscle strength, and therefore cause relative weakness on the affected side especially. In people with unilateral osteoarthritis, before or after knee athroplasty, muscle strength of the affected lower-limb was significantly weaker than muscle strength in the non-affected limb (Robertson et al. 1998, Sicard-Rosenbaum et al. 2002, Mizner et al. 2003, Rossi et al. 2004). The strength difference between the lower-limbs correlated only weakly with pain (Robertson et al. 1998, Mizner et al. 2003). A recent study by Suetta et al. (2007) suggested that in older people with symptomatic osteoarthritis of the hip, rate of force development was affected relatively more (18-25%) than measures not related to velocity characteristics (10-20%). This was at least partly due to deficits in neural activation.

The asymmetrical deficit after unilateral musculoskeletal injuries seems to be very persistent. Up to ten years after musculoskeletal injury, such as ACL rupture and fracture, relatively young and active people have impaired muscle strength in the injured lower-limb compared to the uninjured limb (Seto et al. 1988, Rutherford et al. 1990, Holder-Powell et al. 1999), even when they are pain-free (Holder-Powell et al. 1999). The strength difference between the lower-limbs was independent of time since injury or whether the injury had occurred in the dominant or non-dominant limb (Holder-Powell et al. 1999). The force deficit was at least partly related to reduced muscle mass (Rutherford et al. 1990) and voluntary activation (Urbach et al. 1999) in the affected lower-limb. Although the injured limb may be weaker due to disuse (Rutherford et al. 1990), it seems that the non-affected limb is overused when compared to the limb function of non-injured controls (Hunt et al. 2004).

After hip fracture, the fractured limb remains weaker than the non-fractured lower-limb. One week after surgical fixation of the hip fracture, the distribution of leg extension power over the fractured and non-fractured limb was 30:70 (Lamb et al. 1995). In hip fracture patients two to four weeks after the fracture, isometric and isokinetic knee extension and flexion force in the fractured limb was only 50% of the force in the non-fractured limb (Madsen et al. 1995). Additionally, testing of muscle force with high contraction velocity was impossible in a large portion of hip fracture patients (Madsen et al. 1995). Six to thirty-six months after a hip fracture, slow-velocity isokinetic muscle force was 18% lower in the fractured than in the non-fractured limb (Madsen et al. 2000). On average 30 weeks after a hip fracture, patients had a larger isometric force difference between the lower-limbs than healthy age-matched control subjects (Sherrington et al. 1998).

Pain may also have a local effect on muscle strength. A study of Wilgen et al. (2003) showed that non-specific pain reduced muscle force in the whole limb on the painful side, thus potentially causing asymmetrical deficit. Steultjens et al. (2001) showed that muscle force was most reduced in the muscle groups surrounding the painful joint affected by osteoarthritis.

2.2 Mobility and balance function in older people

Mobility is defined as the ability to move physically. According to this definition mobility includes moving around with (e.g. wheelchair or motorized vehicle) or without aids (e.g. walking). In this study, mobility refers to the ability to move around independently carrying one's own weight, such as in walking. Balance refers to the ability to maintain postural control in an up-right position.

Mobility (Hurley et al. 1998, Onder et al. 2002, Lauretani et al. 2003) and balance (Hurley et al. 1998, Izquierdo et al. 1999, Onder et al. 2002) function decrease with age, which becomes evident through slowing of the performance and experiencing more difficulty. Limitations in mobility, such as poor habitual (Guralnik et al. 2000, Shinkai et al. 2000, Cesari et al. 2005) or maximal (Laukkanen et al. 1995, Shinkai et al. 2000) walking speed, have been found predictive of functional dependence and mortality. Maximal walking speed may be more sensitive in people between the age of 65 and 74, while habitual walking speed may be more sensitive in older people (Shinkai et al. 2000) or people with mobility limitation. Poor balance function, measured using functional tests or body sway, has also been associated with disability and functional dependence (Era et al. 1997, Shinkai et al. 2000, Rantanen et al. 2001). Perceived difficulty in mobility (Laukkanen et al. 1995, Hirvensalo et al. 2000, Fried et al. 2001) and daily activities (Langlois et al. 1996) have been found to predict future disability and mortality.

Mobility limitation (Jarnlo et al. 1991b, Lamb et al. 1995) and impaired balance (Jarnlo et al. 1991a, Lamb et al. 1995, Sherrington et al. 1998) are common in people after hip fracture. Walking ability remains impaired even two years after hip fracture compared to healthy older people (Norton et al. 2000, Kirke et al. 2001). Limitations in mobility and balance, and falls during the first four months after hip fracture are associated with greater functional disability (Whitehead et al. 2003) and predictive of subsequent hospitalization, nursing home placement, and mortality up to two years post-fracture (Fox et al. 1998).

A disturbance in posture or balance may lead to a fall, which is defined as an unintentionally coming to rest on the ground, floor or other lower level. Around 30% of people aged over 65 living in the community fall every year (Kannus et al. 2005b), and the fall incidence increases with higher age and living in residential care facilities (Luukinen et al. 1995). Of the people who fall, about half fall more than once (Nurmi et al. 2002, Kannus et al. 2005b). In about 10-20% of all falls medical attention is needed, and 4-6% of all falls causes a fracture (King et al. 1995, Tinetti et al. 1995, Kannus et al. 2005b). Fall-induced injuries represent one of the most common causes for longstanding pain, functional impairment (Kannus et al. 2005b), loss of independence (King et al. 1995, Tinetti et al. 1997b) and death (King et al. 1995, Kannus et al. 2005a) in older people. Over 75% of the hip fractures are associated with falls (Jarnlo et al. 1991b, Aharonoff et al. 1998). The total and age-adjusted incidence of hip fractures has increased in Finland in the last decades (Kannus et al. 1999, Lönnroos et al. 2006), although a recent study suggested that the increase seems to have leveled off between 1997 and 2004 (Kannus et al. 2006b). However, considering the continuous aging of the population in general, it is likely that the absolute number of hip fractures further increase in the future (Kannus et al. 2006b).

2.2.1 Muscle strength and its association with mobility and balance function

Muscle strength plays an important role in the disablement process as described by Verbrugge & Jette (1994). Pathology, referring to biochemical and physiological abnormalities such as disease, injury or pain, affects specific body systems and may result in impairments such as muscle force and power deficit. The impairments in turn may lead to functional limitations, such as poor walking speed and balance, which in turn may cause disability, which is difficulty in the performance of socially defined roles and tasks, such as ADL activities.

To be able to perform many daily mobility tasks, such as walking, climbing stairs and rising from a chair, a certain amount of muscle force is needed (Young 1986). A major consequence of poor muscle force is that to perform certain daily tasks the maximal force capacity may be nearly approached (Rantanen et al. 1997a, Hortobagyi et al. 2003). Needing to perform at a level close to maximum capacity may result in discomfort and subsequent avoidance of the task (Rantanen et al. 1997a, Hortobagyi et al. 2003). Therefore poor muscle force increases the risk for mobility limitation, disability and even loss of independence (Rantanen et al. 1994, Rantanen et al. 2002, Hortobagyi et al. 2003, Lauretani et al. 2003). With increasing muscle force the performance of such tasks gets easier, and functioning improves. However, the relationship is not linear (Ferrucci et al. 1997, Rantanen et al. 1997a, Rantanen et al. 1998a, Bean et al. 2003); at some point a plateau is reached after which mobility and balance function do not further improve with higher muscle force. Higher muscle force then serves as a reserve capacity that may prevent small decreases in muscle force, for example due to acute illness, to have functional consequences. Poor muscle force has also been identified as underlying factor of poor balance (Ferrucci et al. 1997, Izquierdo et al. 1999, Carter et al. 2002, Bean et al. 2003, Karinkanta et al. 2005) and it is an important risk factor for falls (Coupland et al. 1993, Nevitt et al. 1993, King et al. 1995, Skelton et al. 2002, Perry et al. 2007).

In addition to muscle force, also the ability to produce force quickly is important for certain mobility tasks (Skelton et al. 1994, Foldvari et al. 2000, Suzuki et al. 2001, Bean et al. 2002, Bean et al. 2003), such as climbing stairs. Muscle power, which takes into account both muscle force and contraction velocity, is therefore considered to be more relevant for mobility function than muscle force (Skelton et al. 1994, Foldvari et al. 2000, Suzuki et al. 2001, Bean et al. 2002, Bean et al. 2003). Additionally, Cuoco et al. (2004) showed that power output at a lower percentage (40%) of maximal muscle force was more strongly associated with habitual walking speed than muscle power against a higher resistance (70%), suggesting that especially contraction velocity is of importance. In older people with osteoarthritis, maximal walking velocity correlated with the rate of force production over the first 50 ms in an isometric knee extension (Suetta et al. 2004a). Sayers et al. (2005) showed that in older women, contraction velocity alone explained more of the variance in mobility function (habitual gait speed and short physical function battery) than muscle strength. Potentially, women may rely more on contraction velocity to compensate for their lower overall muscle strength, while men appear to rely relatively more on muscle strength (Sayers et al. 2005). The capacity to produce force quickly, measured as muscle power or the rate of force production, may also be important for balance function (Izquierdo et al. 1999, Bean et al. 2003). Additionally, muscle power has been identified as an important risk factor for falls (Fleming et al. 1991, Skelton et al. 2002, Perry et al. 2007). To prevent a fall and recover from a disturbance in posture, a certain amount of force needs to be generated within a short period of time (Pijnappels et al. 2005). Therefore, the rate of force development and muscle power may be more relevant than maximal muscle force to prevent a fall (Bassey & Short 1990, Izquierdo et al. 1999).

The functional consequences of poor muscle force and power have mostly been studied using cross-sectional study designs, only a limited number of longitudinal studies is available. A study of Rantanen et al. (1999a) showed that handgrip strength in healthy 45- to 68-year-old men was highly predictive of mobility limitation, such as slow habitual walking speed, and mobility and ADL disability 25 years later. Al Snih et al. 2004 showed that in people aged 65 and over lower hand grip strength progressively increased the risk in any self-reported ADL disability over a 7-year period. This gives evidence for a causal relationship. Additionally, it stresses the importance of obtaining high muscle strength in young age and maintaining high strength for as long as possible.

In older people with mobility limitations, for example after hip fracture, mobility function is at least partly related to reductions in muscle strength (Lamb et al. 1995, Madsen et al. 2000, Visser et al. 2000). In addition to muscle strength, other factors underlying mobility limitation include old age (Bohannon et al. 1997, Rantanen et al. 1998a), poor balance (Lamb et al. 1995, Rantanen et al. 1998a, Rantanen et al. 2001), low levels of physical activity (Hirvensalo et al. 2000), and chronic diseases such as stroke and osteoarthritis (Rantanen et al. 1998a, Hirvensalo et al. 2000, Fried et al. 2001, Sicard-Rosenbaum et al. 2002, Rantanen et al. 2003). Fear for falls has been associated with mobility limitation. In addition to reduced walking speed (Maki 1997, Whitehead et al. 2003, Delbaere et al. 2004), fear for falls may cause gait changes, such as decreased stride length, increased stride width and prolonged double support (Maki 1997).

Especially hip fracture patients are at high risk for falls (Shumway-Cook et al. 2005, Stenvall et al. 2006) and a second hip fracture (Schroder et al. 1993) due to the high prevalence of fall risk factors. Risk factors for falls and hip fracture are largely the same; impaired muscle strength (Nevitt et al. 1993, Sherrington et al. 1998, Stel et al. 2003), limitations in mobility (Nevitt et al. 1993, Cummings et al. 1995, Wei et al. 2001, Shumway-Cook et al. 2005) and balance (Sherrington et al. 1998, Stel et al. 2003, Shumway-Cook et al. 2005), and fear for falls (Maki 1997, Sherrington et al. 1998, Stel et al. 2003, Whitehead et al. 2003) often in combination with low bone density (Cummings et al. 1995, Wei et al. 2001, Mikkola et al. 2007). Other common risk factors for falls and hip fracture include old age (Nevitt et al. 1993, King et al. 1995, Shumway-Cook et al. 2005), chronic diseases such as stroke and osteoarthritis (Nevitt et al. 1989, Nevitt et al. 1993, Cummings et al. 1995, King et al. 1995, Sherrington et al. 1998, Stel et al. 2003), impaired cognition (Tinetti et al. 1995), impaired vision (Nevitt et al. 1989, Nevitt et al. 1993, Cummings et al. 1995, Sherrington et al. 1998), use of medication (Nevitt et al. 1993, Cummings et al. 1995, King et al. 1995), previous falls (Nevitt et al. 1989, Nevitt et al. 1993, King et al. 1995, Stel et al. 2003, Shumway-Cook et al. 2005), and pain (Leveille et al. 2002). Although physical inactivity has been identified as a risk factor for falls and hip fracture (Coupland et al. 1993, Gregg et al. 1998, Kujala et al. 2000), vigorous exercise may increase the risk for falls and hip fracture among those with limitations in ADL (Stevens et al. 1997). Especially people with multiple risk factors are at high risk for falls and hip fracture (Nevitt et al. 1993, Cummings et al. 1995).

2.2.2 Asymmetrical muscle strength deficit and its implications for mobility and balance function

Even in young and relatively active people, having one weak lower-limb may have functional consequences. In people with a lower-limb side-to-side force difference due to unilateral musculoskeletal injury, balance was impaired on average ten years after the event (Holder-Powell et al. 2000). Seto et al. (1988) observed that five years after ACL reconstruction, isokinetic muscle force in the injured lower-limb correlated more strongly with function, such as symptoms during mobility activities, than force of the uninjured limb in relatively young people. Additionally, better function was found in those with side-to-side force difference.

In frail and older people, the consequences of poor muscle strength and asymmetrical strength deficit may be more debilitating for mobility and balance function. In two case-control studies, relatively healthy older women with a history of falls (Perry et al. 2007) or frequent falls (Skelton et al. 2002) had a larger asymmetrical deficit in leg extension power. Additionally, in hip fracture patients, it was shown that muscle force and power of the fractured, thus weaker, limb was more strongly associated with mobility function than muscle strength of the non-fractured limb one week and 6-36 months after the fracture (Lamb et al. 1995, Madsen et al. 2000). However, the effects of the asymmetrical deficit on mobility and balance function have not yet been studied in older people. Considering the muscle weakness and large asymmetrical deficit especially in hip fracture patients, it is likely that mobility and balance function will be affected. However, potentially, high muscle strength in one lower-limb may compensate for the deficit in the other lower-limb. Therefore, it is important to study the effects of an asymmetrical deficit while accounting for the level of muscle strength.

2.3 Progressive resistance training in older people

Considering the disablement process interventions acting on the level of impairment may prevent the progression to functional limitation and disability (Verbrugge & Jette 1994). Increasing muscle force and power may thus be beneficial for mobility and balance function as well, especially in older people with a high risk for functional deterioration. Based on current knowledge, progressive resistance training (PRT) is the recommended strategy to increase muscle strength. PRT is performed according to the principle of progressive overload, in which the stress placed upon the body during exercise training is gradually increased to produce greater force (McArdle et al. 2000, Kraemer et al. 2002). Therefore, the training volume and especially the load should be increased throughout the training period (Kraemer et al. 2002). PRT has been included in recommendations for maintaining health and fitness, also for older people. PRT induced improvements in muscle strength are not different in younger and older people (Häkkinen et al. 2000, Häkkinen et al. 2001, Newton et al. 2002).

2.3.1 Training to increase muscle force

The training response is very specific and depends on the exercise stimulus. To improve muscle force and induce muscular hypertrophy in older people it is recommended that exercises are performed with slow-to-moderate velocity (Kraemer et al. 2002). This translates to the concentric contraction lasting approximately 1-2 seconds and the eccentric contraction 1-4 seconds (Fiatarone et al. 1994, Sipilä et al. 1996, Kraemer et al. 2002). Although 2-3 sets of each exercise are usually performed (Fiatarone et al. 1994, Judge et al. 1994, Skelton et al. 1995, Sipilä et al. 1996, Schlicht et al. 2001), it was shown that also a single set of each exercise increases muscle strength in older people (Galvao et al. 2005). After a short accommodation period, exercises should be performed with a resistance of 60-80% of the 1RM for 8-12 repetitions per set (Fiatarone et al. 1994, Judge et al. 1994, Sipilä et al. 1996, Schlicht et al. 2001, Kraemer et al. 2002), which will be referred to as high-intensity training. In-between sets, one to two minutes of rest are recommended (Kraemer et al. 2002). The frequency of the exercise sessions is commonly two to three times per week (Fiatarone et al. 1994, Judge et al. 1994, Sipilä et al. 1996, Schlicht et al. 2001), although one session a week may be enough to maintain or increase muscle strength (Lexell et al. 1995, Taaffe et al. 1999). The duration of the exercise period determines what adaptations occur (Kraemer et al. 2002). For example, in the initial phases of exercise, neural adaptations, e.g. changes in activation of individual muscles and coordination of muscle groups, mainly account for the improvement in muscle strength (Gabriel et al. 2006). The contribution of muscle hypertrophy increases after several weeks of training (Sipilä et al. 1995, Frontera et al. 2003). Adaptations in the muscle fibers, due to changes in protein synthesis and degradation, may additionally change the muscle fiber type composition (Frontera et al. 2003).

Training effects are also very specific with respect to recruitment patterns and neural activation (Caroll et al. 2006, Janzen et al. 2006). Therefore different movement patterns of exercises (including range of motion) induce training specific adaptation. For example, unilateral training enhances mostly muscle strength of the trained limb, while bilateral training enhances bilateral function (Janzen et al. 2006). In unilateral training, cross-education, i.e. a training effect in the non-trained contra-lateral limb, also plays a role (Kannus et al. 1992, Caroll et al. 2006). As many daily tasks require unilateral lower-limb function, unilateral training may be needed to improve functional abilities.

There is good evidence that well designed PRT increases muscle strength. A systematic review of randomized controlled trials (RCT) by Latham et al. (2004) showed that PRT has a large positive effect on muscle strength, despite heterogeneity in the protocols and effects of the studies included. For example, an early RCT of PRT in frail older people (Fiatarone et al. 1994) showed that the 1RM nearly doubled after ten weeks of high intensity (80% of 1RM, three sets of eight repetitions) slow-velocity (6-9 seconds per repetition) resistance training on three days a week. However, training responses are very specific and greater increases in muscle strength are generally found when muscle strength was measured using the same technique as for training (Baker et al. 1994). Therefore, an increase in isometric or isokinetic muscle strength may be an indicator of a more general improvement in muscle strength. For example, in relatively healthy older people, a RCT of 13 weeks of PRT by Judge et al. (1994) showed that the 1RM of the exercises improved by 60-70%, while the improvement in isokinetic muscle force was only 13%. The training consisted of three weekly sessions, with slow-velocity dynamic exercises performed in 2-3 sets of 10-12 repetitions at an intensity of 60-75% of 1RM. An RCT by Sipilä et al. (1996) showed that an 18-week intensive PRT three times a week increased isometric muscle force by 19%. Each exercise was performed in 3-4 sets of 8-10 repetitions at an intensity of 60-75% of 1RM, and slow-velocity dynamic contractions (4-6 seconds in total) were used. A RCT by Skelton et al. (1995) showed that isometric muscle force increased by 25% and leg extension power by 18% after a 12-week PRT of low-to-moderate intensity (three sets of 4-8 repetitions) including one supervised and 2 home-based training sessions a week.

The Latham et al. (2004) review also showed that PRT had a small-to-moderate effect on other impairments and functional limitations, especially walking speed. Studies with high-intensity PRT of 8-12 weeks in the relatively healthy older people either showed an improvement in walking speed (Schlicht et al. 2001) or reported no change (Judge et al. 1994, Sipilä et al. 1996). Balance function did not change after an 8-week high-intensity slow-velocity PRT (Schlicht et al. 2001). However, high-intensity slow-velocity PRT of six months and two years demonstrated a significant improvement in dynamic balance (Nelson et al. 1994, Taaffe et al. 1999). Improvements in mobility function and balance have been reported more consistently after high-intensity PRT in frail people and people with mobility limitations (Fiatarone et al. 1994, Timonen et al. 2002, Seynnes et al. 2004).

2.3.2 Training to increase rate of force development and muscle power

Recently it has been suggested that high-velocity exercises should also be included in strength training programs for older people to improve the rate of force development and muscle power (Kraemer et al. 2002). In these high-velocity protocols, the exercises are performed in the concentric phase as fast as possible (Fielding et al. 2002, Miszko et al. 2003, Sayers et al. 2003) or using a predefined movement velocity usually of less than one second in duration over the full range of motion (Kraemer et al. 2002). The eccentric phase is performed more slowly with a velocity of approximately 1-4 seconds. Prior to 2004, when our research started, four published RCTs demonstrated the effectiveness of a high-velocity power training program by comparing participants of a high-velocity PRT to a non-training control group (Hruda et al. 2003) or to participants of a slow-velocity PRT (Fielding et al. 2002, Sayers et al. 2003) or both (Miszko et al. 2003). A 10-week high-velocity low-intensity power training with three sessions a week, one set of 4-8 repetitions, increased isokinetic concentric and eccentric muscle power at a movement velocity of 180°/s on average by 60% and 40%, respectively (Hruda et al. 2003). Isokinetic concentric and eccentric muscle force increased on average by 25-30% and the timed performance of several mobility tasks improved on average by 31-66%. A 16-week program with three times a week high-velocity training (concentric action as fast as possible) with an intensity of 40% of 1RM and three sets of eight repetitions for each exercise improved functional performance, measured using a battery of functional tasks related to muscle force, flexibility, balance and coordination and endurance (Miszko et al. 2003). Compared to the slow-velocity PRT (concentric action approximately four seconds) with an intensity of 50-80% of the 1RM, the improvement in functional performance was larger in the high-velocity training group, whereas the improvement in muscle force was similar. Additionally, two papers (Fielding et al. 2002, Sayers et al. 2003) compared the effects of a high-velocity power training (concentric phase as fast as possible) to a conventional slow-velocity strength training protocol (concentric phase in two seconds). For both training groups, the 16-week training protocol consisted of three sessions a week and three sets of eight repetitions at a resistance of 70% of 1RM. Muscle force measured as the 1RM improved similarly in both training groups, while muscle power at different levels of resistance improved significantly more in the high-velocity training group (Fielding et al. 2002). Dynamic balance, stair climb time, and self-reported disability improved similarly in both groups, while chair-rise time and gait velocity did not improve by either training (Sayers et al. 2003).

As the increase in power depends on maximal force as well as the velocity of movement, it may be more efficient to include both slow-velocity high-load (60-80% of 1RM) and high-velocity low-load (40-60% of the 1RM) exercises in a training program (Kraemer et al. 2002). Uncontrolled studies using this type of combined strength and power training have shown improvements in muscle force and power, and timed mobility performance (Häkkinen et al. 1998, Häkkinen et al. 2001, Newton et al. 2002).

2.3.3 Training in hip fracture patients

Diseases and injury may lead to deficits in muscle strength through post-traumatic immobilization, inflammation and pain. Especially after hip fracture, increasing muscle strength seems important considering the force deficit commonly found in this population. In general, the effects of progressive resistance training have not been studied extensively in clinical populations. It seems that progressive resistance training is feasible in clinical populations even shortly after surgery (Sullivan et al. 2001, Timonen et al. 2002, Suetta et al. 2004ab). However, conclusions about the safety of training should be made with caution, since adverse effects are poorly reported. After PRT, improvements in muscle strength, mobility and functional performance, pain and fear for falls have been found in different clinical populations, such as shortly after hospitalization (Sullivan et al. 2001, Timonen et al. 2002) and in osteoarthritis (Ettinger et al. 1997, Suetta et al. 2004ab).

Table 1 summarizes the results of all randomized controlled trials including progressive resistance training alone (Mitchell et al. 2001, Binder et al. 2004, Mangione et al. 2005, Miller et al. 2006a) or as part of a broader rehabilitation program (Tinetti et al. 1997a, Tinetti et al. 1999, Hauer et al. 2002) after hip fracture. Only three of them were published prior to the start of our intervention in 2004. Few adverse effects have been reported due to training in patients shortly after hip fracture (Tinetti et al. 1997a, Miller et al. 2006a) or training with a longer delay after hip fracture (Hauer et al. 2002, Binder et al. 2004, Mangione et al. 2005). Thus, it seems that progressive resistance training is feasible in people with a hip fracture. However, with respect to functional improvements the study results are somewhat conflicting. In general, it seems that studies using a higher resistance and volume of training (Mitchell et al. 2001, Hauer et al. 2002, Binder et al. 2004) induced larger improvements in muscle force and power, and mobility and balance function. Additionally, larger changes in perceived difficulty in mobility and daily activities, self-rated health and disability were generally reported.

Considering the likelihood of an extremely large asymmetrical deficit in muscle force and power after hip fracture, returning symmetrical lower-limb muscle strength may be more beneficial for mobility function. However, little

TABLE 1 Randomized controlled trials including supervised progressive resistance training in hip fracture patients.

Reference	Participants (Mean age, time since fracture)	Study groups (n pre-trial→ n post-trial→ n follow-up)	Training frequency / duration Sets / repetitions / resistance	Training effect on muscle strength and power	Training effect on mobility, balance and self-reports
Tinetti et al. 1997a/ 1999	80 years Discharge from hospital or subacute care facility (mean 12 or 98 days)	Multi-component physical and functional therapy (n=148) RT in 84% (70% completed all therapy) SR (n=156)	6M Therabands	Lower extremity strength # ns Upper extremity strength + # *	Mobility function 0 Balance function 0 Self-rated disability 0
Mitchell et al. 2001	80 years Mean 15 days post-fracture	RT, UNI n=40 → n=30 → n=20 SR n=40 → n=29 → n=24	2 * week / 6W 3-6 / 12 / 50-80% 1RM	**Leg extension power Fract** § RT:+154%*(W6) +227%*(W16) C: +55% (W6) + 86% (W16) **Leg extension power Non-fract** § RT:+70%*(W6) +96%*(W16) C: +19% (W6) +22% (W16)	Mobility function 0 Balance function + * (W6,W16) Self-rated physical function + *(W6)
Hauer et al. 2002	81 years 6-8 weeks post-hip surgery	RT + FT n=15 → n=13 Motor placebo activities n=13 → n=11	3 * week / 12W 2-3 / 10 / 70-90% 1RM	**1RM leg press Fract** § RT:+122%*(M3) +122%*(M6) C: +5% (M3) +25% (M6) **1RM leg press Non-fract** § RT:+63%*(M3) +60%*(M6) C: +8% (M3) +20% (M6) **Isom leg extension force Fract** § RT:+61%*(M3) +66%*(M6) C: +12% (M3) +26% (M6) **Isom leg extension force Non-fract** § RT:+20%*(M3) +23%*(M6) C: -7% (M3) +0% (M6)	Mobility function + * (M3) Balance function + * (M3) Self-rated physical function 0

(continues)

TABLE 1 (continues)

Reference	Participants (Mean age, time since fracture)	Study groups (n pre-trial→ n post-trial→ n follow-up)	Training frequency / duration Sets / repetitions / resistance	Training effect on muscle strength and power	Training effect on mobility, balance and self-reports
Binder et al. 2004	80 years Mean 100 days post-surgery	RT, BI n=46 SR n=44	3 * week / 6M M1-3: FT M4-6: RT 1-3 / 6-12 /65-85%	**Isokin knee extension force 60º/s Fract** § RT:+56%* C:+28% **Isokin knee extension force 60º/s Non-fract** § RT:+21%* C:+8% **1RM exercises** (bilateral) § RT:+20-70%* C:+2-10%	Mobility function + * Balance function + * Self-rated physical function, and health + * Self-rated disability - *
Mangione et al. 2005	79 years 7-50.5 weeks post-surgery	RT, UNI n=17 → n=13 Aerobic n=13 Control n=11	1-2 * week / 12W 3 / 8 / 8RM	**Isom leg force** (summed measure) § RT:+23%* C:+6%	Mobility function 0 Self-rated physical function 0
Miller et al. 2006	84 years 7 day post-injury	RT n=25→ n=23 Nutritional n=25→ n=23 Combined n=24→ n=22 Attention control n=26→n=25	3 * week / 12W 2/ 8/ resistance band	**Isom knee extension force Fract** § RT:+225% C:+150% **Isom knee extension force Non-fract** § RT:+40% C:+19%	Mobility function 0

* significant improvement compared to control group
\# effect was not calculated: baseline means not reported
§ effect calculated from means reported compared to baseline values
M = month, W = week
RT= conventional resistance training, FT= functional exercises, SR = standard rehabilitation, C = control group
UNI = unilateral exercises for the lower-limbs, BI = bilateral exercises for the lower-limbs, 1RM= 1 repetition maximum
Isom = isometric, Isokin = isokinetic
Fract = fractured side, Non-fract = non-fractured side
+ improved, - decreased, 0 no change

attention has been paid to the asymmetrical deficit in the training or results reporting. The majority of the studies reported muscle strength of both lower-limbs together (Tinetti et al. 1997a, Tinetti et al. 1999, Binder et al. 2004, Mangione et al. 2005, Miller et al. 2006a). In two studies, the asymmetrical deficit in leg extension power and muscle force (1RM leg press and isometric leg extension) seemed to be reduced after unilateral resistance training (Mitchell et al. 2001) or combined functional and resistance training (Hauer et al. 2002). However, the authors did not report the significance of the change.

Some studies also examined the long-term effects of training. Some weeks to several years after cessation of the training, improvements in muscle strength, and mobility and balance function may be at least partly maintained (Hauer et al. 2001, Mitchell et al. 2001, Hauer et al. 2003), although this was not found in another study (Tinetti et al. 1999).

3 PURPOSE OF THE STUDY

The purpose of this study is to gain more insight into asymmetrical deficit in muscle strength of the lower-limbs in different populations of older people; its prevalence, potential determinants, and consequences for mobility limitation, balance and falls.

In addition, the effects of a resistance training program in a population with alleged asymmetrical deficit will be studied in a randomized controlled trial. The resistance training was specifically aiming to increase muscle force and power of both lower-limbs and to reduce the asymmetrical deficit. Our hypothesis was that increasing muscle strength reduces limitations in mobility and balance according to the theoretical model of the disablement process.

The specific research questions are:

- What is the prevalence of asymmetrical deficit in leg extension power in a population of healthy 63-75-year-old women? (I)
- Is asymmetrical leg extension power deficit associated with mobility limitation, balance (I), and injurious falls (II) in a population of healthy 63-75-year-old women?
- Is asymmetrical leg extension power deficit associated with mobility limitation in 73-96-year-old women recovering from hip fracture? (III)
- What are the determinants of asymmetrical deficit in muscle force, rate of force development and power in the lower-limbs in older men and women six months to seven years after a hip fracture? (IV)
- What are the effects of a strength-power training, specifically designed to reduce the asymmetrical deficit and to increase muscle force and power of both lower-limbs, on lower-limb muscle strength, its asymmetry, balance, mobility limitation and perceived difficulty in mobility and daily activities in men and women six months to seven years after hip fracture? (V)

4 METHODS

4.1 Study design and participants

For this study, data of three larger research projects were used. The Finnish Twin Study on Aging, FITSA, is an epidemiological study that follows a classical twin study design. The data were collected in Jyväskylä between September 2000 and March 2001. HIP-RECOVERY is a clinical study including women recovering from a hip fracture. The data were collected in Oxford in the UK between October 1993 and March 1995. HIP-ASYMMETRY is a study utilizing cross-sectional data and a randomized controlled trial in people with a history of hip fracture. The data were collected in Jyväskylä between August and December of the years 2004 and 2005. The study designs are summarized in Table 2.

4.1.1 Finnish Twin Study on Aging (FITSA; I,II)

The FITSA study is a study of genetic and environmental effects on the disablement process in older, 63-75-years-old, female twins. The twin study design has been described in detail by Tiainen et al. (2004). The study includes monozygotic (n= 103), and dizygotic (n= 114) twin pairs recruited from the Finnish Twin Cohort (Kaprio et al. 1978, Kaprio & Koskenvuo 2002). To be recruited for the study, both individuals in the pair had to agree to participate. Figure 1 shows the flow chart of the recruitment. Assessments were performed in a laboratory and followed by a one-year fall surveillance. In the analyses, the sample was treated as a set of individuals by taking into account the dependency between the sisters. Only participants with valid outcome measures were included in the analyses (n=403-419). Considering that this was a non-clinical population of older women that were community-dwelling, we refer to this population as healthy older women.

TABLE 2 Study designs

Paper	Study	Design	Participants	Age (mean ± SD)	Main outcomes
I	FITSA	**Observational** Cross-sectional (twin study)	**419 women** MZ n= 195 DZ n= 224	63–75 (68.6± 3.4)	LEP and asymmetrical deficit Walking speed Standing balance
II	FITSA	**Observational** One year follow-up (twin study)	**403 women** MZ n= 187 DZ n= 216	63–75 (68.6± 3.4)	LEP and asymmetrical deficit Injurious falls
III	HIP-RECOVERY	**Observational** Three months follow-up	**43 women**	73–96 (82.7± 5.9)	LEP and asymmetrical deficit Walking speed Stair climbing speed
IV	HIP-ASYMMETRY	**Observational** Cross-sectional	**79 participants** Men n= 25 Women n= 54	60–85 (75.3± 6.7)	KET, RFD_{200}, LEP and asymmetrical deficit Lower-limb pain Lower-limb injury burden Lower-limb muscle mass
V	HIP-ASYMMETRY	**Experimental** Randomized controlled trial	**46 participants** Men n= 14 Women n= 32	60–85 (74.0± 6.8)	KET, LEP and asymmetrical deficit Walking speed Dynamic balance Mobility disability

MZ= monozygotic, DZ= dizygotic
LEP= leg extension power, KET= knee extension torque, RFD_{200} =rate of force development over the first 200 ms in isometric knee extension

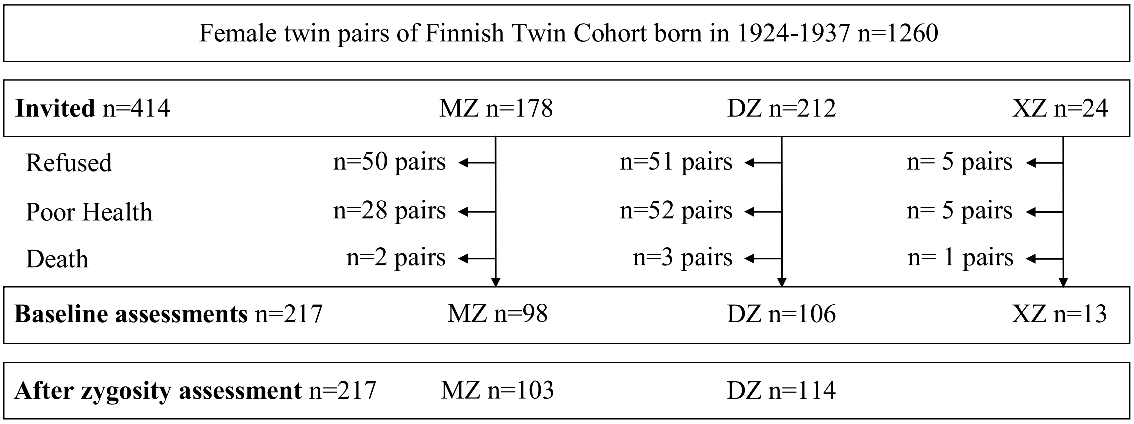

FIGURE 1 Flow chart of the FITSA study. MZ = monozygotic twin pair, DZ = dizygotic twin pair, XZ = twin pair with uncertain zygosity

4.1.2 Women recovering from a hip fracture (HIP-RECOVERY; III)

The HIP-RECOVERY study is a substudy of a larger research project on health and mobility limitation in women with recent surgical repair of a hip fracture. The study is an observational three-month follow-up study. Consecutive admissions of women with surgical fixation of a proximal femoral fracture were recruited for this study using daily admission lists of the John Radcliffe Hospital trauma service. Subjects, admitted from their own home, a relative's home or sheltered housing, were medically assessed for eligibility for the study protocol. In total, 69 women, aged 73-93 years, meeting the eligibility criteria were approached (Figure 2). Exclusion criteria were aged under 70 years, acute physical (e.g. delirium) or mental illness or distress, mental (Hodkinson mental test score of less than 7/10; Hodkinson et al. 1972) or neurological impairment (e.g. stroke or Parkinson), and taking drugs likely to affect neuromuscular function. The hospital provided standard rehabilitation for all participants comprising of inpatient routine physical therapy and pain management, and a standard exercise advice sheet on discharge. The study protocol has been described in detail by Lamb et al. (1995, 2002).

Nineteen patients with a surgical repair of a hip fracture participated in a follow-up study with baseline assessments of mobility and leg extension power on day six and seven after the surgery (week 1) and again 12 weeks later (week 13). Additionally, 24 patients, who had participated in a 6-week randomized controlled trial right after the fracture, were included in the analyses. They participated in identical assessments of mobility and LEP at week 1 and 13. In the RCT, stratified block randomization was used to assign 12 patients to neuromuscular electrical stimulation of the fractured limb (intervention) and 12 patients to placebo stimulation (control). The results of the RCT, reported by Lamb et al. (2002), suggested that the effects of 6-week neuromuscular stimulation were small and not clinically significant. Additionally, the outcome variables used in the current study were similar between the intervention and control groups and those subjects participating only in the follow-up study.

Therefore the data of the follow-up and RCT study were pooled to increase sample size to 43.

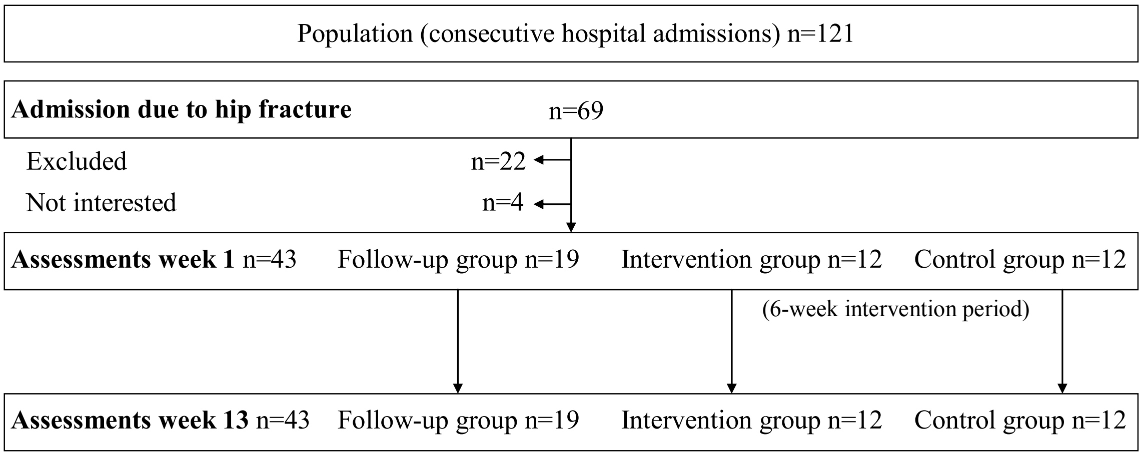

FIGURE 2 Flow chart of the HIP-RECOVERY study.

4.1.3 Men and women with a hip fracture history (HIP-ASYMMETRY; IV,V)

HIP-ASYMMETRY is a research investigating health, functional capacity and rehabilitation of older men and women with a hip fracture history. Cross-sectional data of all participants at baseline were utilized (IV), and the effects of a combined strength-power training aiming to reduce asymmetrical strength deficit were studied in a 12-week randomized controlled trial including all participants without contraindications for training (V; registered as ISRCTN34271567).

To avoid confounding of acute recovery effects, community-living 60-85-year-old men and women with a femoral neck or trochanteric fracture within six months to seven years prior to baseline were invited to participate in the study. In 2004 and 2005, the patient records of the Central Finland Central Hospital were used to identify all 452 patients alive with a hip fracture in the years 1998-2004 and living independently in the Central Finland Health Care District. All of them were informed about the study. Those willing to participate were interviewed over telephone (n=132). We excluded patients with neurological and progressive severe illnesses, amputation or inability to walk outdoors without another person’s assistance. The flow chart of the study is displayed in Figure 3. Eventually, 54 women and 25 men participated in the baseline laboratory measurements. After clinical examination, those without physical (American College of Sports Medicine 2000) or mental (Mini-Mental State Examination score<21; Folstein et al. 1975) contraindications for participation in the strength and power training were randomized into the training (eight men, 16 women) and control group (six men, 16 women). The groups were randomized by blocks of gender and stratified by average age.

Data were collected in two phases due to the small number of eligible subjects in 2004. In 2005, in the same time of year (August-December), the study

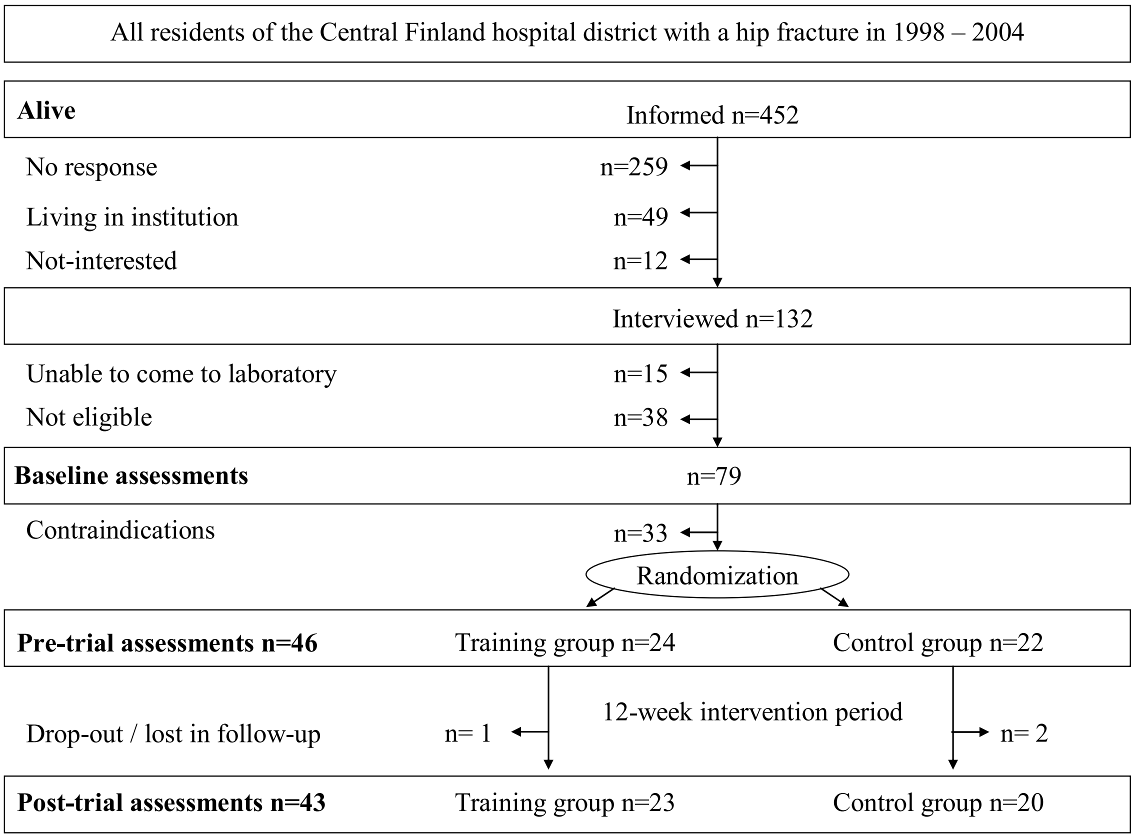

FIGURE 3 Flow chart of the HIP-ASYMMETRY study.

was repeated using the same protocol, infrastructure and staff for the measurements and training; only the recruitment area was enlarged from the city of Jyväskylä and surrounding communities to cover the complete hospital district. The data were pooled for analysis.

4.2 Ethics

The FITSA and HIP-ASYMMETRY study were approved by the Ethics Committee of Central Finland Health Care District. Before the laboratory examinations, the participants were informed about the study and written informed consent was obtained. The HIP-RECOVERY study was approved by the Central Oxford Research Ethics Committee and written informed consent was obtained from participants.

4.3 Measurements

All measurement methods, their reliability and references are listed in Table 3.

4.3.1 Muscle strength

Muscle strength was assessed for both lower-limbs separately. In the FITSA study, participants were tested first on the side of the dominant hand. In the HIP-RECOVERY study, participants were first tested on the non-fractured side. In the HIP-ASYMMETRY study, alternate participants were tested first on the fractured or non-fractured side.

Maximal (peak) voluntary isometric knee extension force was assessed using an adjustable dynamometer chair (Good Strength, Metitur LTD, Palokka, Finland; IV,V). The ankle was attached to a strain-gauge system with the knee angle fixed at 60 degrees from full extension. Participants were encouraged to extend the knee as hard as possible. After two to three practice trials, measurements were performed at least three times until no further improvement occurred. Each contraction was maintained for 2-3 seconds. The inter-trial rest period was 30 seconds. The performance of highest maximal force was used for analysis. Maximal force (N) was registered and maximal knee extension torque (KET; Nm) was calculated using the formula: force in Newton*(chair lever arm in meter*cos 30^{o}) (Sipilä et al. 1996; IV,V). Muscle torque is defined as the force that produces a turning, twisting or rotary moment in any plane about and an axis, such as a joint (McArdle et al. 2000). Maximal rate of force development (N/s) was recorded using the manufacturer's formula (V). In addition, the rate of force development over the first 200 ms of the contraction (RFD_{200}; Nm/s) was derived from the force-time curve (IV).

Maximal leg extension power (LEP; Watt, W) was assessed in all studies using the Nottingham power-rig (Bassey & Short 1990; I-V). The seat position was adjusted for lower-limb length. The participant was seated with the arms folded and one foot was placed on the pedal attached to a flywheel, while the other foot rested on the floor. After one to three practice trials, participants were asked to push the pedal as hard and fast as possible five to ten times, until no further improvement occurred. The inter-trial rest period was at least 30 seconds. The best performance was used for analysis. Due to pain or limitations in knee or hip joint range of motion in the sitting position suggested by the manufacturer, seven (IV) and five (V) hip fracture patients, respectively, were allowed to sit with the back leaning backwards on the backrest and one patient was seated on a cushion of seven cm height. The same position was used for both lower-limbs, and in the pre-and post-trial measurement.

In the FITSA study, participants were stratified based on the level of LEP of the stronger lower-limb and the asymmetrical LEP deficit. Participants with LEP of the stronger limb below median (97 W) were considered to have poor LEP. Participants belonging to the tertile with the largest side-to-side difference in LEP ($\geq$ 17 W) and participants with LEP measured in one lower-limb only were considered to have an asymmetrical deficit.

TABLE 3 Measurement methods and variables used in the study, including references and test-retest reliability.

Variables	Paper	Method and reference	Reliability and reference	Specifics
Muscle strength				
Maximal voluntary isometric KET (Nm)	IV,V	Dynamometer	CV 6%(Sipilä et al. 1996)	Both sides
RFD_{200} in isometric knee extension(Nm/s)	IV	Dynamometer (Aagaard et al. 2002)		Both sides
Maximal LEP (W)	I -V	Nottingham power-rig (Bassey & Short 1990)	CV 6-8% (Tiainen et al. 2005, Lamb et al. 1995)	Both sides
Maximal voluntary isometric handgrip force (N)	IV,V	Dynamometer	CV 6% (Rantanen et al. 1997)	Dominant
Mobility limitation				
10 meter maximal walking speed (m/s)	I	Photocells	CV 5% (Rantanen et al. 1997)	
10 meter habitual walking speed (m/s)	IV,V	Photocells	r=0.90 (Bohannon et al. 1997)	
10 and 50 feet habitual walking speed (m/s)	III	Stopwatch	CV 10% (Lamb et al. 1995)	
Stair climbing speed (steps/s)	III	Stopwatch	CV 9% (Lamb et al. 1995)	
Balance function				
20-sec tandem stance ability (yes/no)	I	Timer		
Dynamic lateral balance test; time (s) and distance (cm)	V	Force plate	Time r=0.81, distance r=0.72 (Sihvonen et al. 2004)	
Fall surveillance				
Injurious falls (n)	II	Fall calendar and telephone interview (Tinetti et al. 1993)		
Self-reports				
Perceived difficulty to walk 2 km (cat)	V	Self-rated	r=0.82 (Laukkanen et al. 1995)	
Perceived difficulty to perform daily activities (cat)	V	Self-rated		
Self-rated health (cat)	V	Self-rated		
Pain				
Summed lower-limb pain on 4 locations (n)	II	Self-rated		General
Hip pain (cat)	III	Self-rated (Keene et al. 1993)		Fractured
Pain in hip (mm)	V	Visual Analogue Scale	r=0.95 (Pohjola 2006)	Both sides
Sum of pain in knee and hip (mm)	IV	Visual Analogue Scale		Both sides

(continues)

TABLE 3 (continues)

Variables	Paper	Method and reference	Reliability and reference	Specifics
Clinical examination				
Chronic medical diseases (n)	I ,II	Self-reports confirmed by physician		
Chronic medical diseases (n)	III	Extracted from medical records		
Chronic medical diseases (n)	IV-V	Medical records and self-reports confirmed by a physician		
Lower-limb injury burden (n)	IV	Medical records and self-reports confirmed by a physician		
Prescription pain medication (yes/no)	IV	Medical records and self-reports confirmed by a physician		
Anthropometry				
Body weight (kg)	I -V	Beam scale		
Body height (cm)	I,II,IV,V	Scale stadiometer		
Lean body mass (kg)	I,IV	Bioimpedance	CV <2% (Sipilä et al. 1996, Völgyi et al. 2008)	
Lower-limb muscle mass (kg)	IV	Bioimpedance		Both sides
Physical activity				
Physical activity (cat)	I,II	Modified from Grimby 1986		
Physical activity (p)	IV,V	Yale Physical Activity Scale; sum index (DiPietro et al. 1993)		

KET = knee extension torque, RFD_{200} = rate of force development in the first 200 ms of isometric knee extension, LEP = Leg extension power
Cat = categorized scale, CV = coefficient of variation

4.3.2 Mobility limitation

Maximal walking speed over 10 meters was assessed in a laboratory corridor (I). The participants were allowed three meters for acceleration. Time was measured using photocells. The participants were instructed to walk as fast as possible, without compromising safety. The faster performance of two trials was recorded. The participants wore walking shoes or sneakers, the test order was the same for each participant, and the resting time between the tests was one minute. Habitual walking speed over 10 meters was assessed in a laboratory with non-slippery floor (V). The participants were allowed one trial and walked on stocking feet. The use of walking aids commonly used for walking inside was allowed. Three meters for acceleration was allowed and time was measured using photocells.

The ability and time to walk over a distance of 10 feet (3.05 meters) safely and at comfortable walking speed was assessed (III). Walking aids were permitted. The walk, timed using a handheld stopwatch, started from stationary position at the start line and ended with crossing the finish line. The fastest time of two trials was recorded. Using a similar protocol, the ability and time to walk a distance of 50 feet (15.25 meters) was assessed.

The ability and time to climb stairs was assessed on a staircase of five steps with handrails on both sides. Time was measured using a handheld stopwatch, starting from the footfall on the first step to the footfall on the top step (III).

Walking speed (m/s; I,III,V) and stair climbing speed (steps/s; III) were calculated for all participants able to complete the walking or stair climbing task without human assistance. To be able to analyze all participants in the HIP-RECOVERY study, those unable to perform the tasks without assistance were assigned a walking (10 feet n=3 and 50 feet n=8) or stair climbing (n=11) speed of 0 m/s or 0 steps/s, respectively.

4.3.3 Balance

The standing balance test was performed with the participant in stocking feet (I). During the tests, the participants were instructed to stand as still as possible in a well-balanced position. The ability to maintain balance for 20 seconds in a tandem position, one foot placed in front of the other with the feet touching, was recorded. The participants were asked to keep their arms down by their sides. Gaze was fixed at a marked point at eye level at a distance of two meters. Timing started when a balanced and safe stance had been attained. The participants were allowed one trial for each test. Correcting a disturbance in balance by moving a foot or leg, or reaching for support with hands was regarded as inability to maintain balance.

Dynamic balance was tested using the Good Balance computerized force platform system (Good Balance, Metitur LTD, Palokka, Finland) (V). Participants were asked to move their center of pressure along a track shown on a computer screen (Sihvonen et al. 2004). The test was started from a well balanced standing position with the center of pressure in the middle. Weight was shifted 10 times between two marks on the left and right with a nine cm distance in-between. The performance time (time used to complete the test) and the distance (the extent of the path traveled by the center of pressure during the test) were measured. After two practice trials, the best of three repetitions (shortest performance time) was chosen for analysis. The test was performed with the participant on stocking feet and the participant was allowed to sit and rest between the trials. An improvement in time (thus speed) and distance (accuracy) indicates that the participants have more confident postural control, while moving near the limits of stability (Sihvonen et al. 2004).

4.3.4 Perceived difficulty in mobility and daily activities

Perceived difficulty in mobility and daily activities were assed using a questionnaire (V). Participants were asked to rate their ability to walk a distance of two kilometers: 1) no difficulty, 2) some difficulty, 3) considerable difficulty, 4) impossible without assistance of another person, 5) impossible even with assistance of another person. For the analysis, a dichotomous variable was created differentiating those with (category 2-5) and without (category 1) difficulty. Participants were also asked to rate their ability to perform daily activities according to the most appropriate category: 1) excellent, 2) good, 3) fair, or 4) poor. For the analysis, a dichotomous variable was created differentiating those rating good or excellent (category 1 and 2) and those rating it as fair or poor (category 3 and 4). In the experimental part of the HIP-ASYMMETRY study, at post-trial, participants were additionally asked to rate the change in ability to walk outdoors and ability to perform daily activities since baseline. The response categories were: 1) improved, 2) no change, 3) decreased.

4.3.5 Health status

Self-rated health

Self-rated health was assessed using a questionnaire (V). Participants were asked to rate their general health according to the most appropriate category: 1) excellent, 2) good, 3) fair, or 4) poor. For the analysis, a dichotomous variable was created differentiating those rating their health as good or excellent (category 1 and 2) and those rating it as fair or poor (category 3 and 4). In the experimental part of the HIP-ASYMMETRY study, at post-trial, participants were additionally asked to rate the change in general health since baseline. The response categories were: 1) improved, 2) no change, 3) decreased.

Diseases and injury

In the FITSA (I,II) and HIP-ASYMMETRY (IV,V) study, a thorough clinical examination was performed. Information on the presence of chronic conditions and use of medication were collected using a standardized questionnaire and confirmed by a physician in the clinical examination. In the HIP-ASYMMETRY study, the medications were transcribed from current prescriptions, and diagnoses were collected from medical records and radiological films. In the FITSA and HIP-ASYMMETRY study, chronic diseases present for at least three months, included cardiovascular diseases (such as ischemic heart disease and hypertension), respiratory diseases (such as asthma and bronchitis), neurological diseases (such as epilepsy and cerebrovascular dysfunction), musculoskeletal diseases (such as knee, hip and foot osteoarthritis), rheumatic diseases, hormonal diseases (such as diabetes and thyroid gland dysfunction), liver or kidney diseases, and cancer. The number of chronic diseases was calculated as a measure of co-morbidity. In the HIP-ASYMMETRY study, the physician confirmed the presence of medical conditions affecting the lower-limbs. The sum of the number of joints affected by osteoarthritis and the number of fractures in the lower-limbs was calculated for each limb as a measure for lower-limb disease and injury burden. The hip fracture was included in the calculation. The use of pain medication prescribed by a physician was registered as a dichotomous variable (yes/no; IV).

In the HIP-RECOVERY study, previous or present history of chronic conditions was confirmed from the medical records. Comorbidity was assessed using a checklist (Buchner et al. 1993) including the items myocardial infarction, angina, cancer, diabetes, past fractures, arthritis hypertension, urinary incontinence, cataracts, and hearing impairment.

Hip fracture status

In the studies including hip fracture patients, the cause of the hip fracture, the fracture pattern, and type of surgical fixation were confirmed from the medical records and radiological films (III-V). In the HIP-RECOVERY study, twenty-two participants (51%) had suffered an intra-capsular fracture that was fixed using hemiarthroplasty (77%) or osteosynthesis (23%). All extra-capsular fractures (n=21) were fixed with osteosynthesis. In the HIP-ASYMMETRY study, the hip fracture was surgically fixed with osteosynthesis in 37 patients (47%) and with arthroplasty in 42 patients (53%). Additionally, in the HIP-ASYMMETRY study, the number of days between the date of hip fracture and 1st August of the year of measurements (2004 or 2005) was calculated and used as the variable for time elapsed since hip fracture. All data were collected within 2-5 weeks from this date.

Pain

In the FITSA study, self-reported presence of pain in the hip, knee, ankle and foot on most days for at least one month during the preceding year was measured with a yes (score 1) or no (score 0) question. A sum index of pain, ranging from 0 to 4, was created as a measure of wide spread pain in the lower extremities.

In the HIP-RECOVERY study, post-operative pain in the fractured hip was assessed using a method developed by Keene et al. (1993). The presence and intensity of pain at rest and on walking was assessed by interview prior to the measurements. Participants were asked to select one category, which best described their pain over the last 24-hours: 1) no pain, 2) occasional or slight pain, 3) pain on initiation of activity, 4) pain with activity, not at rest, 5) constant, yet bearable pain, and 6) constant, unbearable pain. For the analyses, the hip pain measure was dichotomized as follows: categories 1-3 versus categories 4-6.

In the HIP-ASYMMETRY study, participants were asked by means of a questionnaire to indicate the level of pain in the hip and knee on the left and right side during the last week using a visual analogue scale (range 0-100 mm). Hip pain (V) or the sum of hip and knee pain (IV) of each lower-limb was used for analyses.

Contraindications for safe participation

Potential contraindications for participation in the strength-power training (V) were evaluated according to the criteria for exercise participation by the American College of Sports Medicine (2000). In addition to these contraindications, acute conditions such as inflammation were evaluated to ascertain safe participation in the laboratory measurements (I-V). Contraindications for measurements of muscle force and power were checked for each lower-limb separately. Factors, such as pain (painful arthritis), limitations in joint range of motion (endoprostheses) or inability to perform satisfactory performance measurements were considered as exclusion criteria.

4.3.6 Background information

Anthropometry

Body weight (I-V) and height (I,II,IV,V) were measured in the laboratory or at the hospital. Lean body mass and total body fat were assessed using bioelectrical impedance (Spectrum II, RJL Systems, Detroit, MI, U.S.A) using the manufacturer's equation (I,II). In the HIP-ASYMMETRY study, lean body mass and the muscle mass in each lower-limb were estimated using bioelectrical impedance (BC-418, TANITA Corporation, Tokyo, Japan) (IV).

Handgrip force

Maximal voluntary isometric handgrip force of the dominant hand was assessed using an adjustable dynamometer chair (Good Strength, Metitur LTD, Palokka, Finland) and used as an indicator for general force (Rantanen et al. 1999a, Rantanen et al. 2003; IV,V). In the assessment, the dynamometer was fixed to the arm of the chair with the elbow flexed in an angle of 90 degrees. Participants were encouraged to squeeze the handle as hard as possible. The testing protocol was the same as for the isometric knee extension force assessment.

Physical activity

The present status of physical activity was assessed using a self-report scale by Grimby et al. (1986) with slight modifications (I,II). The highest category of the initial scale was divided into two categories separating those participating in regular exercise fitness activities from those active in competitive sports. The 7-point scale ranged from one (hardly any activity) to seven (participation in competitive sports). Participants were considered sedentary if they reported no other activity than light walking once or twice a week.

In the HIP-ASYMMETRY study, the level of physical activity was assessed by interview using the YALE physical activity questionnaire (DiPietro et al. 1993). The questionnaire includes a physical activity dimension sum index, which is the summation of five weighted subindices. Participants were asked how many times they performed vigorous physical activity (weight 5) and leisure walking (weight 4) during the past month and the duration of each physical activity session. The frequency, duration score, and the weight of the respective activity were multiplied. Additionally, participants were asked to estimate the duration of the time spent moving around (weight 3), standing (weight 2) and sitting (weight 1) on an average day in the past month. The duration scores were multiplied by the weight of each subindex.

4.3.7 Fall surveillance

Data on falls and related injuries were collected prospectively for 1-year using monthly fall calendars and telephone follow-up (II; Tinetti et al. 1993). A fall was defined as unintentionally coming to rest on the ground, floor, or other lower level, other than as the consequence of sudden onset of acute illness or overwhelming external force (Kellogg International Work Group 1987). Falls resulting in fracture, bruise, laceration or pain were considered injurious. Two dichotomous variables were created: 'at least one injurious fall' versus 'no injurious falls' and 'recurrent (two or more) injurious falls' versus 'one or no injurious fall'.

4.3.8 Asymmetrical measures

Asymmetrical deficit in muscle strength

In the healthy older women (I,II), the relative LEP difference between the stronger and weaker lower-limb was calculated according to Formula 1 and used as measure for asymmetrical deficit. The value 0% represents equal LEP in both lower-limbs, thus no asymmetrical deficit.

FORMULA 1: $$\frac{|Weak - Strong|}{Strong} \times 100\%$$

In studies III and IV asymmetrical deficit in the different muscle strength measures (KET, RFD and LEP) was calculated according to Formula 2. The value 50% represents equal strength in both lower-limbs, indicating no asymmetrical deficit. Values lower than 50% indicate poorer strength on the fractured side. This formula was used as it creates a situation in which strength deficits are distributed equally around the value of 50% irrespective of whether the deficit is present on the fractured or non-fractured side.

FORMULA 2: $$\frac{Fractured}{Fractured + Nonfractured} \times 100\%$$

Participants in the HIP-ASYMMETRY study were stratified based on baseline asymmetrical deficit in KET, RFD and LEP (IV). Participants with a consistent deficit in muscle strength of the fractured limb (asymmetrical deficit <50% for all measures) were compared to participants with either no asymmetrical deficit or a deficit in the non-fractured lower-limb for at least one of the muscle strength measures. In those with strength measures in one leg only (n=1 for KET and RFD, and n=4 for LEP, respectively); the leg not measured due to pain or limitation in range of motion was considered to be the weaker leg.

In the experimental part of the HIP-ASYMMETRY study, the asymmetrical deficit was calculated according to Formula 3 to bring about an equal distribution of strength deficits. The value 50% represents equal muscle strength in both lower-limbs, indicating no asymmetrical deficit. Values lower than 50% indicate poorer strength in the weaker limb as defined for training (WEAKleg; see paragraph 4.4.1).

FORMULA 3: $$\frac{WEAKleg}{WEAKleg + Stronger} \times 100\%$$

For this summary, the asymmetrical LEP deficit of the FITSA study participants was additionally calculated according to Formula 4 to obtain similar values for comparison with the other studies. All values were 50% (equal muscle strength in both lower-limbs) or below.

FORMULA 4: $$\frac{Weaker}{Weaker + Stronger} \times 100\%$$

Other asymmetrical measures

In the HIP-ASYMMETRY study (IV), the side-to-side differences in lower-limb pain (summed hip and knee pain score), lower-limb disease and injury burden (osteoarthritis and fracture) and lower-limb muscle mass were calculated as asymmetrical measures, in a way that the correlations between the asymmetrical deficit in muscle strength and the other asymmetrical measures were expected to be positive if our hypothesis were true. According to our hypothesis, more intense lower-limb pain, higher lower-limb disease and injury burden and lower lower-limb muscle mass will occur on the same side as the asymmetrical deficit in muscle strength. The asymmetrical lower-limb disease and injury burden and asymmetrical lower-limb pain were calculated according to Formula 5. Asymmetrical lower-limb muscle mass was calculated according to Formula 6.

FORMULA 5: $Nonfractured - Fractured$

FORMULA 6: $Fractured - Nonfractured$

4.4 Strength - power training (V)

In the HIP-ASYMMETRY study, participants without contraindications for the strength-power training participated in the RCT of PRT. The aim of the training was to reduce asymmetrical deficit and to increase force and power of the lower-limb muscles. A 12-week individually tailored training program was organized twice a week (1-1.5 h) in a senior gym for participants of the training group. The training sessions were supervised by an experienced physiotherapist. The training compliance was calculated according to Formula 7.

FORMULA 7: $\frac{SessionsAttended}{SessionsOffered} \times 100\%$

Power calculations performed in advance, indicated that a minimum of 30 subjects should be included in both study groups to detect significant changes in the main outcome measures (muscle force, power, balance) at $\alpha=0.05$ and $\beta=0.20$ (power 80%). Despite the intensive recruitment, our design was slightly underpowered with 22-24 persons per group.

4.4.1 Weaker lower-limb for training

As the purpose of the training was to reduce asymmetrical strength deficit, WEAKleg was defined based on maximal knee extension force, maximal rate of force production, and maximal LEP for each participant in the training and control group. WEAKleg was defined as the lower-limb that had lower values in at least two of the measures. A side-to-side difference larger than 5% in the lower-limbs ((|difference between lower-limbs|/best result)*100%) was considered meaningful. In participants measured in one lower-limb only due to pain, the limb not measured was considered to be WEAKleg. In participants of the training group with conflicting or unclear results for WEAKleg, the 1-repetition maximum (1RM) of the unilateral leg press exercise, estimated during the first training sessions, was used to ascertain the choice. The 1RM was estimated from a 3-6RM test using a conversion table (McDonagh & Davies 1984) for the leg press, knee flexion, and hip abduction and adduction exercises trained with pneumatic resistance equipment (Ab HUR Oy, Kokkola, Finland).

4.4.2 Strength-power training

Each training session included both strength and power exercises and started with a 10-minute warming-up sitting on a chair. Pneumatic resistance equipment was used for the leg press, knee flexion, hip abduction and adduction exercises. Exercises were performed with as large a range of motion (ROM) as possible with pain-free performance. The training equipment allowed for limiting the ROM individually for each lower-limb. The ankle plantarflexion exercises, rising to the toes and returning the heel onto the ground, were performed with a weighted vest in front of a mirror while holding a handrail. WEAKleg was trained first in every exercise, and more sets and repetitions and/or a higher resistance were used.

The first two training sessions were used to familiarize the participants with the facility, equipment and staff. The exercises were performed with very low loads and correct movement technique was assured. In the following sessions, the 1RM was estimated (see paragraph 4.4.1). The assessment, one exercise at a time, was repeated during the weeks six, seven and eight. Throughout the training period, the intensity was increased progressively when tolerated. The intensity was based on the latest 1RM estimation and adjusted individually.

In week seven, isometric force and LEP measurements were repeated for the training group to check whether the asymmetrical deficit still existed. If reversion of the power (n= 6) or force (n= 2) deficit or both (n= 1) had occurred, from week nine onwards, these participants trained the power and/or strength exercises similarly for both lower-limbs according to protocol of WEAKleg (more intensive protocol). One participant had no deficit at baseline and therefore trained both lower-limbs similarly, according the protocol of WEAKleg for the whole period.

A physician was consulted for all pain and other medical symptoms emerging during the training period. This was done to ascertain which of the symptoms were likely to be related to the training and whether they affected the training.

Power training

The power exercises, leg press and ankle plantarflexion, aiming to increase muscle power and movement velocity were performed early in the training session in sets of 12 repetitions. Relatively low resistance was used and the concentric phase of the contraction was performed as fast as possible. The leg press exercise for WEAKleg consisted of 3-4 sets and for the stronger lower-limb of 2-3 sets with a resistance of 40-50% of 1RM. The ankle plantarflexion exercise was performed standing on both legs, for safety reasons, in 2-3 sets using a weighted vest with 0-10% of body weight.

Strength training

The strength exercises aiming to increase muscle force were performed at a slower pace, with fewer repetitions (WEAKleg: 2-3 sets of 8 repetitions; and stronger lower-limb: 1-2 sets of 10 repetitions), and higher resistance. Leg press, knee flexion and hip abduction and adduction exercises were performed with a resistance of 60-80% of 1RM for WEAKleg and 50-70% of 1RM for the stronger lower-limb. From week eight onwards, the leg press strength exercise was performed only once a week due to time restrictions. The ankle plantarflexion strength exercise was performed standing on one leg with 0-15% of bodyweight, if necessary the other foot was allowed to touch the floor for balance.

4.4.3 Control group

The control group did not receive any intervention. Participants were encouraged to continue their lives as usual and maintain their lifestyle habits during the 12-week trial.

4.5 Statistical analyses

For each participant, the absolute change in the LEP and mobility measures over time was calculated according to Formula 8 (III).

FORMULA 8: $Week13 - Week1$

The relative change in KET, LEP, mobility and balance measures between the pre- and post-trial measurements was calculated according to Formula 9 and for the asymmetrical deficit the change in time was calculated according to Formula 10 (V).

FORMULA 9: $\frac{Post - Pre}{Pre} \times 100\%$

FORMULA 10: $Post - Pre$

In the FITSA study, group specific marginal means and 95% confidence intervals (95%CI) of each continuous variable were calculated with general linear univariate analyses of variance with the twin pair variable as a random effects factor to adjust for the dependency between the sisters. The adjusted values were saved and used for further analysis. Categorical variables were entered in the analyses without adjustment. Analyses were performed including and excluding those with only one lower-limb measured for LEP. Since the results were similar, only the analyses including all participants are reported.

In the HIP-RECOVERY study, analyses were performed including and excluding those unable to perform the mobility tasks without assistance of another person. Since the results were similar, only the analyses including all participants are reported.

In the HIP-ASYMMETRY study, statistical tests were first performed separately for men and women. Since the results were similar, the data were pooled to obtain larger sample size. Participants with missing variables in the muscle force and power tests or bioelectrical impedance measurements were dropped from the respective analysis only. For the RCT, all reported results were derived from intention-to-treat analysis. Exclusion of those with poor compliance did not materially change the results.

In all studies, SPSS software was used for analysis and statistical significance was set at $p<0.05$. Normality of data was tested using Kolmogorov-Smirnov tests. Differences between the lower-limbs were tested with paired sample T-tests or Wilcox P tests. Group differences in normally distributed variables were tested with independent T-tests or analyses of variance (ANOVA). Mann-Whitney U tests were used for non-parametric variables, and Kruskal-Wallis or χ^2-tests for categorical variables. Due to slight distortion of the distribution of pain in the non-fractured limb in study IV, pain was tested using parametric and non-parametric tests.

Associations between walking velocity and the LEP measures were analyzed with partial correlation and the group differences were analyzed using a general linear multivariate analysis (two-way ANOVA) (I). The tandem stance ability was analyzed with a general linear univariate analysis to compare the muscle power measures among those able and unable to maintain tandem stance (I). Logistic regression was used to assess the risk of inability to maintain tandem stance (I) and to asses the risk for injurious falls (II). The analyses were adjusted for age, body weight, and body height (I,II). Additionally, in study II, the analyses were adjusted for the number of diseases, the level of physical activity, and lower-limb pain.

Multiple linear regression analysis was used to test whether LEP and asymmetrical LEP deficit were associated with 10 and 50 feet walking and stair climbing speed (III). To identify the combined effects of LEP and asymmetrical deficit, it was therefore decided to use LEP of the non-fractured limb as measure for general LEP in the regression models. Additionally, LEP of the fractured limb was entered as determinant in separate models. Cross-sectional models at week 1 (Model 1-2) and 13 (Model 3-4) as well as longitudinal models (Model 5-6) were constructed to predict walking and stair climbing speed. The longitudinal models were adjusted for baseline walking (Models a-b) or stair climbing (Models c) speed, respectively. Finally, the change in time in LEP of the fractured limb (Model 7), LEP of the non-fractured limb (Model 8) and the asymmetrical LEP deficit (Model 9) were entered separately into regression models and related to the change in walking or stair climbing speed over time. To account for the dependency of change from the baseline level, these models were adjusted for baseline LEP of the fractured or non-fractured lower-limb, respectively, baseline asymmetrical LEP deficit and baseline mobility. In addition, all models were adjusted only for potential confounding variables (age, body weight, pain, and treatment) that had a significant correlation with the LEP or mobility measures in univariate analysis.

Multiple linear regression analysis was used to predict the level of asymmetrical deficit in KET, RFD_{200} or LEP, respectively (IV). The asymmetrical lower-limb pain, lower-limb disease and injury burden, and lower-limb muscle mass variables were entered as predictors in the models. Only the final models including significant determinants are shown. Additionally, the models were adjusted for potential confounders (age, gender, time since fracture, type of fixation of the hip fracture, and prescribed pain medication) one at a time as the sample size did not allow for simultaneous inclusion.

In the experimental study (V), the analyses were adjusted for the year of participation as a precaution to account for potential effects of factors such as group dynamics. Training effects were analyzed as group-time interaction (IA) derived from repeated measures ANOVA. Additionally, the difference between the mean (and 95%CI) relative change in the training and control group (effect) was calculated. The perceived change in mobility and daily activities, and the perceived change in self-rated health from pre- to post-trial were tested using cross-tables with McNemar tests (within-group change) and χ^2-tests (group difference).

5 RESULTS

5.1 Sample characteristics

Table 4 shows characteristics of the women in all three samples. In FITSA (I,II), the women were on average 68.6 ± 3.4 year-old, and they had on average 2.4 ± 1.1 chronic diseases. The participants were stratified based on LEP of the stronger lower-limb and the asymmetrical deficit. Table 5 shows that participants with higher LEP were somewhat younger than those with poor LEP. Additionally, their body weight and lean body mass were higher and they were taller compared to those with poor LEP. A higher proportion of the women in the groups with poor LEP reported no more than light walking once or twice a week as physical activity (sedentary; 31-41%) compared to those in the group with higher LEP (18-21%; $p<0.001$). There was no difference in physical activity level in the groups with and without asymmetrical deficit ($p=0.931$). The prevalence of pain in the lower-limbs was similar over the groups (29-39%; $p=0.600$ for LEP of the stronger limb and $p=0.237$ for asymmetrical deficit). The prevalence of any disease or category of diseases did not differ among the participants.

TABLE 4 Participant characteristics of the women in all samples; women one week after hip fracture surgery (HIP-RECOVERY; III), women ½-7 years after hip fracture (HIP-ASYMMETRY; IV), and healthy older women (FITSA; I,II).

	HIP-RECOVERY		HIP-ASYMMETRY (Women)		FITSA	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
Age (yr)	43	82.7 ± 5.9	54	76.0 ± 6.2	419	68.6 ± 3.4
Body weight (kg)	43	59.9 ± 12.2	54	68.0 ± 11.2	419	70.0 ± 10.4
Body height (cm)	-	-	54	159.0 ± 5.8	419	158.6 ± 5.7
Lean body mass (kg)	-	-	48	42.9 ± 4.4	418	46.0 ± 4.1
Chronic diseases (n)	43	1 (0-4)*	53	3.5 ± 1.9	418	2.4 ± 1.1
Time since fracture (d)	43	7	54	1485 ± 659	-	-

* Median (range)

TABLE 5 Characteristics of the healthy older women (FITSA; I,II) stratified based on leg extension power (LEP) and the asymmetrical (Asym) deficit. Poor LEP was defined as LEP of the stronger lower-limb below median (high LEP: above median), and asymmetrical deficit as the tertile of the highest absolute side-to-side LEP difference and those with LEP measured on one side only (without asymmetrical deficit: two tertiles of smaller LEP difference).

	Poor LEP				High LEP						
	Asym Deficit (n=73)		Without Asym Deficit (n=133-134)		Asym Deficit (n=96)		Without Asym Defit (n=116)		1	2	3
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	p	p	p
Age (yr)	68.8	68.0-69.7	69.3	68.7-69.9	68.0	67.3-68.7	68.0	67.5-68.6	0.281	<0.001	0.004
Body Weight (kg)	68.5	66.5-70.5	67.8	66.2-69.3	71.9	70.2-73.7	71.7	70.0-73.3	0.993	0.018	0.091
Body Height (m)	1.58	1.57-1.59	1.57	1.57-1.58	1.60	1.59-1.61	160	1.60-161	0.298	0.007	0.047
Lean body mass (kg)	44.8	43.9-45.6	44.4	43.7-45.0	47.5	46.8-48.2	47.5	46.8-48.2	0.697	<0.001	0.001
Chronic Diseases (n)	2.4	2.2-2.7	2.5	2.3-2.7	2.4	2.2-2.6	2.2	2.1-2.4	0.164	0.588	0.295

1 test of difference between those with and without asymmetrical deficit
2 test of difference between those with poor and high LEP
3 test of difference between all 4 groups

In the HIP-RECOVERY study (III), the participants were on average 82.7 ± 5.9 year-old and had a median of 1 chronic disease with a range from 0 to 4 (Table 4). At one week after surgical repair of the hip fracture, 12% of the participants experienced no pain, 40% occasional or slight pain, 23% pain on initiation of activity, 14% pain with activity, 7% constant yet bearable pain and 5% constant unbearable pain in the fractured hip. At week 13, 31% of the women reported no pain, 57% occasional or slight pain, and 12% pain on initiation of activity.

For comparison with the first two data sets, the characteristics of the HIP-ASYMMETRY study at baseline are reported first for the women only (Table 4). The women were on average 76.0 ± 6.2 year-old, and they had on average 3.5 ± 1.9 chronic diseases. On average over 4 years had passed since the hip fracture. Table 6 displays the characteristics of the pooled sample of the men and women in the study (IV). They were on average 75.3 ± 6.7 year-old and on average over 4 years had passed since the hip fracture. Twenty-two patients (28%) used pain medication prescribed by a physician.

Additionally, participants of the HIP-ASYMMETRY study without contraindications for the training participated in the randomized controlled trail (V). Table 6 shows that the physical characteristics at baseline were not different for the training and control group. Participants were on average 73.8-year-old and on average over 4 years had elapsed since the hip fracture. In 83% of the participants the fractured limb was WEAKleg. In the training and control group, the level of pain in the hip of WEAKleg (34.8 ± 6.9 mm and 39.6 ± 7.1 mm, respectively) was significantly ($p<0.009$) higher than in the stronger lower-limb (5.0 ± 3.7 mm and 15.2 ± 5.7 mm, respectively) at baseline. However, the intensity of the pain in the hip in WEAKleg ($p=0.632$) and the stronger limb ($p=0.131$) was not significantly different between the two groups.

5.2 Leg extension power, asymmetrical deficit and mobility

LEP

Figure 4 displays LEP of the women in the three study projects. In the healthy women (I,II), mean LEP in the weaker lower-limb was 86.3 ± 28.1 W and that in the stronger lower-limb 100.2 ± 30.3 W ($p<0.001$). The relative LEP difference between the stronger and weaker lower-limb was on average 15 ± 9%. The asymmetrical LEP deficit, calculated for this summary as the ratio of LEP of the weaker lower-limb to the sum of LEP in both lower-limbs, was on average 43.6 ± 8.1% (range 29.6 – 50.0%).

In the HIP-RECOVERY study (III), mean LEP of the fractured limb was 22.2 ± 15.5 W and LEP of the non-fractured lower-limb was 52.5 ± 24.3 W one week after hip fracture surgery (Figure 4; $p<0.001$). The asymmetrical deficit ranged between 9 and 57%, being on average 28.5 ± 10.2%. Twelve weeks later, LEP of the fractured limb had on average doubled (44.1 ± 21.4 W; $p<0.001$), while LEP of the non-fractured limb had increased by 30% (65.5 ± 28.7 W;

TABLE 6 Baseline physical characteristics of the men and women ½-7 years after hip fracture (IV). Group differences between those with (asymmetrical deficit for all strength measures <50%) and without a consistent strength deficit on the fractured side (IV), and between those in the training and control group of the randomized controlled trial (V) were tested with independent T-tests.

	IV	IV			V		
	All (n=79) Mean ± SD	Consistent deficit (n=37) Mean ± SD	No consistent deficit (n=35) Mean ± SD	T-Test# P	Training group (n=24) Mean ± SD	Control group (n=22) Mean ± SD	T-Test§ p
Age (yr)	75.3 ± 6.7	73.7 ± 7.8	76.5 ± 5.4	0.075	73.8 ± 6.6	74.1 ± 7.2	0.882
Time since hip fracture (d)	1544 ± 740	1556 ± 812	1607 ± 693	0.778	1587.7 ± 736.2	1551.0 ± 857.2	0.877
Body weight (kg)	71.1 ± 12.2	73.6 ± 12.4	69.2 ± 12.4	0.140	71.1 ± 11.0	72.5 ± 12.0	0.671
Body height (m)	163.3 ± 9.0	165.3 ± 9.7	161.5 ± 7.1	0.062	1.72 ± 0.1	1.77 ± 0.1	0.223
Lean body mass (kg)	47.7 ± 9.2	49.3 ± 10.2	46.1 ± 8.0	0.174			
Chronic diseases (n)	3.2 ± 2.0	3.0 ± 2.0	3.3 ± 1.9	0.584	2.8 ± 1.4	2.3 ± 1.4	0.180
Physical activity * (p)	36.8 ± 20.0	40.22 ± 20.6	33.80 ± 18.1	0.165	41.1 ± 20.1	44.0 ± 20.2	0.632
Handgrip strength (N)	229.2 ± 91.3	250.2 ± 102.6	207.9 ± 76.3	0.055	245.5 ± 81.3	251.0 ± 96.0	0.835

* Sum index of the YALE physical activity questionnaire
# difference between the groups with and without a consistent deficit
§ difference between the training and control group

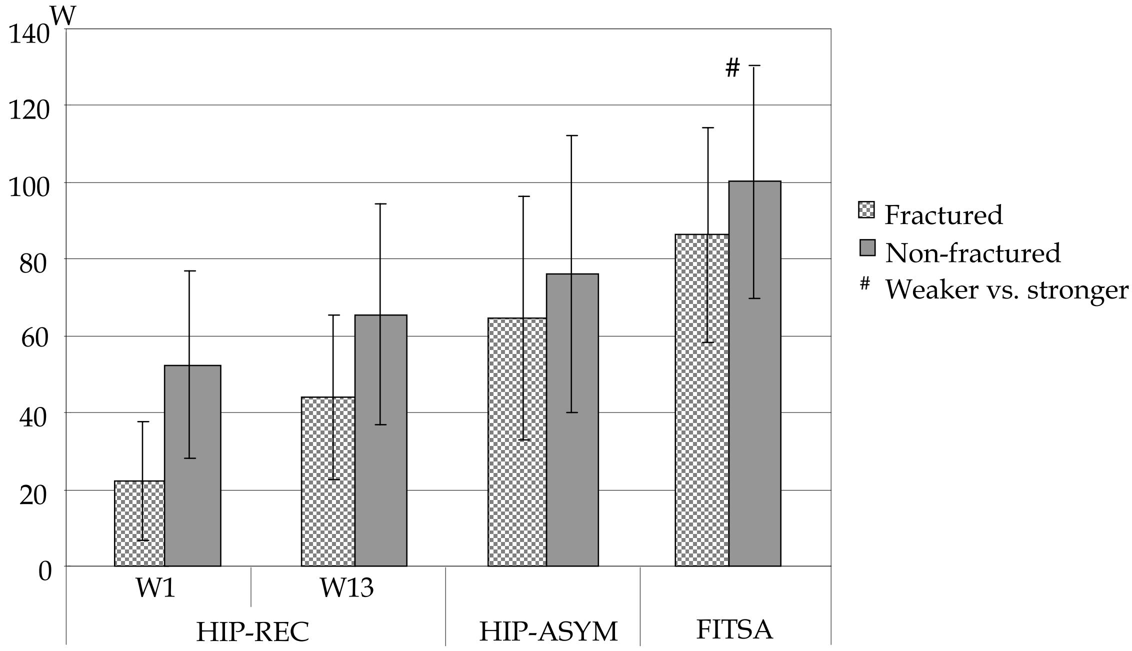

FIGURE 4 Mean (± standard deviation) leg extension power (LEP) of the lower-limbs in the women of all samples; women one (W1) and 13 weeks (W13) after hip fracture surgery (HIP-REC; III), women ½-7 years after hip fracture (HIP-ASYM; IV), and healthy older women (FITSA; I).

p<0.001). However, LEP of the fractured limb remained significantly impaired in comparison to the non-fractured limb (p=0.001). At week 13, asymmetrical deficit had reduced, to an average of 40.4 ± 8.6% (range 15.0–59.7%).

In women of the HIP-ASYMMETRY study, on average four years after hip fracture, LEP was on average 64.6 ± 31.7 W in the fractured limb and 76.1 ± 36.0 W in the non-fractured lower-limb (p<0.001; Figure 4). The asymmetrical deficit ranged between 32.3 and 53.6%, and was on average 45.7 ± 5.1%. In the pooled sample of men and women, LEP was on average 84.2 ± 44.3 W in the fractured limb and 101.4 ± 54.4 W in the non-fractured limb (p<0.001; IV). The asymmetrical deficit was on average 45.4 ± 5.5%, with a range from 32.3 to 62.0%.

Walking speed

Figure 5 displays the mean walking velocity in the women of the three study projects. Mean maximal walking speed over 10 meters was 1.7 ± 0.3 m/s in the healthy older women (I). In the HIP-RECOVERY study (III), habitual walking speed was on average 0.18 ± 0.12 m/s over 10 and 50 feet one week after hip fracture surgery. However, three women (7%) were unable to perform the 10 feet, and eight women (19%) the 50 feet walking test without assistance of the measurer. Including these participants, average walking speed, was 0.16 ± 0.12 m/s over 10 feet and 0.15 ± 0.13 m/s over 50 feet. At week 13, all participants were able to perform the walking tests. Average walking speed had improved significantly compared to week 1 (p<0.001) and was 0.57 ± 0.29 m/s and 0.58 ± 0.30 m/s over 10 and 50 feet, respectively. In the women of the HIP-ASYMMETRY study, average habitual walking speed over 10 meters was 0.9 ± 0.2 m/s. In the pooled sample, walking speed was on average 1.0 ± 0.3 m/s.

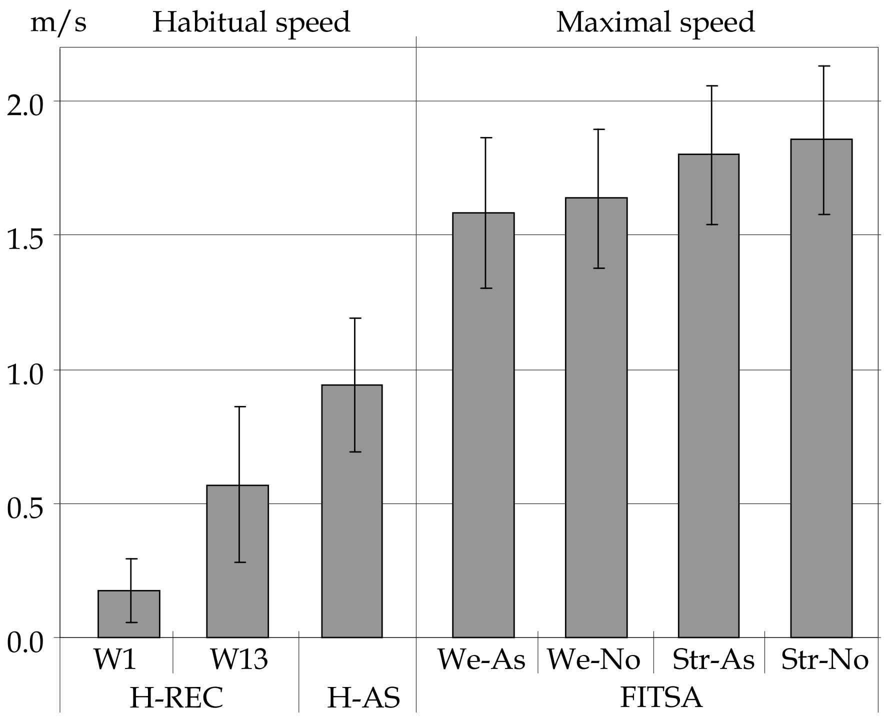

FIGURE 5 Mean (± standard deviation) walking speed over 10 feet and 10 meters, respectively, in the women of all samples; women one (W1) and 13 weeks (W13) after hip surgery (H-REC; III), women ½-7 years after hip fracture (H-ASYM; IV), and healthy older women stratified based on leg extension power (LEP) and the asymmetrical deficit (FITSA; I). Poor LEP (We) was defined as LEP of the stronger lower-limb below median (high LEP (Str) above median), and asymmetrical deficit (As) as the tertile of the highest absolute side-to-side LEP difference and those with LEP measured on one side only (without asymmetrical deficit (No): two tertiles of smaller LEP difference).

Stair climbing

Of the women recovering from hip fracture (III), 11 women (26%) were unable to perform the stair climbing test without assistance of the measurer one week after surgery. The mean stair climbing speed was excluding those unable to perform the task 0.49 ± 0.32 steps/s and including all participants 0.36 ± 0.35 steps/s. At week 13, all participants were able to perform the stair climbing test and the average stair climbing speed (1.06 ± 0.58 step/s) had improved significantly compared to week 1 ($p<0.001$).

5.3 Leg extension power, asymmetrical deficit, and its associations with mobility, balance and falls

5.3.1 Healthy older women (I, II)

Walking speed (I)

Higher LEP in the stronger and weaker lower-limb were associated with higher maximal walking speed ($r=0.45$ $p<0.001$ and $r=0.48$ $p<0.001$, respectively) after adjustment for age, body height and body weight. Additionally, larger asymmetrical LEP deficit was associated with slower walking speed (r= - 0.23, p<0.001).

Figure 5 shows the mean maximal walking speed in the groups based on LEP of the stronger lower-limb and the asymmetrical deficit. Walking speed was highest among those with high LEP and without asymmetrical LEP deficit, and decreased with decreasing LEP and increasing asymmetrical LEP deficit. Multivariate analysis showed that, after adjustment for age, body height and body weight, the variables of LEP of the stronger limb (p<0.001) and the asymmetrical LEP deficit (p=0.027) were independent predictors of walking speed without an interaction effect (p=0.573).

Standing balance (I)

Fifty participants (12% of the sample) were unable to maintain tandem stance for 20 seconds. After adjustment for age, body height and body weight, those unable to maintain tandem stance had poorer LEP in the stronger (88.5 W, 95%CI 82.0 – 95.0 W) and weaker (72.9 W, 66.4 – 79.4 W) lower-limb than those who were able (103.7 W, 101.0 – 106.4 W, p<0.001; and 89.4 W, 86.6 – 92.2 W, p<0.001; respectively). Additionally, those unable to maintain balance had a larger asymmetrical LEP deficit (18.8%, 15.7 – 21.9%) than those able (14.0%, 12.7 – 15.4%). Of those with poor LEP, 69% with asymmetrical deficit was able to maintain tandem stance for 20 seconds compared to 82% of those without asymmetrical deficit. Of those with high LEP, 90% with asymmetrical deficit and 92% of those without asymmetrical deficit were able to maintain tandem stance. Logistic regression analysis revealed that for participants with poor LEP, the risk for inability to maintain tandem stance was nearly 6-fold greater in those with asymmetrical LEP deficit and nearly 3–fold greater in those without asymmetrical LEP deficit compared to the risk among those with high LEP and without asymmetrical LEP deficit (reference group; Figure 6). Among those with high LEP, asymmetrical LEP deficit was not associated with an increased risk.

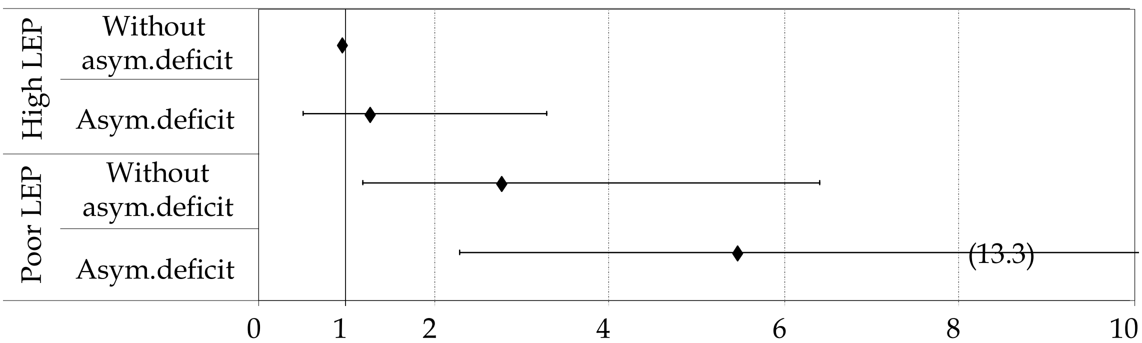

FIGURE 6 Odds ratio for not being able to maintain balance in a tandem stance position for 20 seconds in healthy older women stratified based on leg extension power (LEP) and the asymmetrical deficit (I). Poor LEP was defined as LEP of the stronger lower-limb below median (high LEP: above median), and asymmetrical (asym.) deficit as the tertile of the highest absolute side-to-side LEP difference and those with LEP measured on one side only (without asymmetrical deficit: two tertiles of smaller LEP difference).

Injurious falls (II)
During the one-year follow-up, 111 participants reported in total 171 injurious falls. Of those with asymmetrical LEP deficit, 22% reported a single injurious fall and 12% recurrent injurious falls. For those without asymmetrical LEP deficit, the corresponding figures were 18% and 5%, respectively. The relative risk for at least 1 injurious fall was 1.7 and for recurrent injurious falls 2.4 among those with asymmetrical LEP deficit compared to those without (Figure 7). Adjusting for potential confounders did not materially change the estimates.

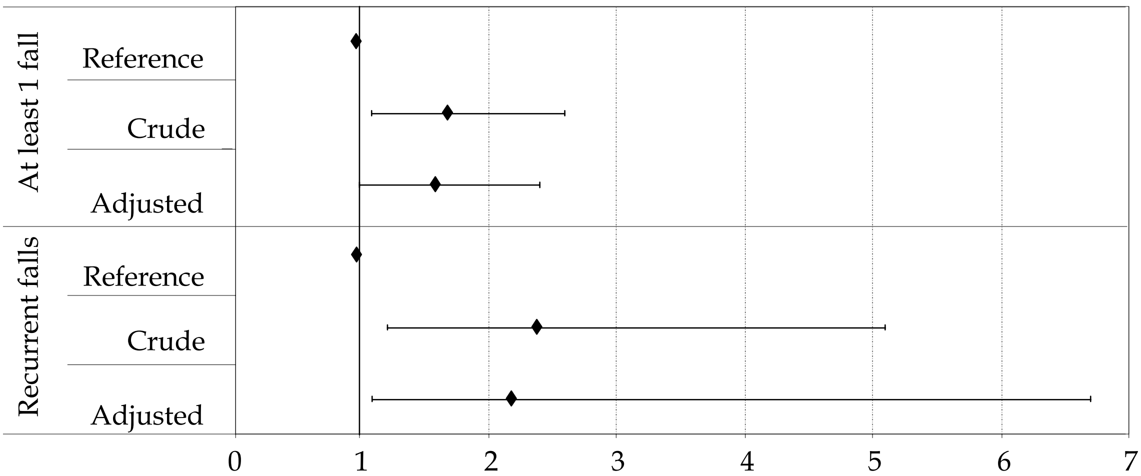

FIGURE 7 Odds ratio for the incidence of at least one injurious fall (≥ 1) or recurrent injurious falls (≥ 2) in the 1-year follow-up in healthy older women with asymmetrical leg extension power (LEP) deficit in reference to those without. Asymmetrical LEP deficit was defined as the tertile of largest side-to-side difference and those able to perform LEP testing in one leg only (without: two tertiles of smaller side-to-side difference). Crude and adjusted (age, body weight and height, number of diseases, physical activity and lower extremity pain) analyses are shown (II).

5.3.2 Women recovering from a hip fracture (III)

Mobility
Cross-sectional linear regression analyses showed that at week 1 and 13 after hip fracture surgery, poorer LEP of the fractured and non-fractured lower-limb correlated with slower 10 and 50 feet walking and stair climbing speed (Table 7). Additionally, larger asymmetrical deficit was associated with slower stair climbing speed (Models 2c and 4c). In the longitudinal analysis, baseline LEP of the non-fractured limb also predicted mobility function 3 months later, while the asymmetrical deficit in these models and LEP of the fractured limb did not (Table 8). Adjustment for potential confounders (age, body weight, and pain in model 1,2 and 5, age and pain in model 3, and age and body weight in model 4 and 6) did not materially change the estimates (data not shown).

The increase in LEP of the fractured limb was associated with the increase in walking and stair climbing speed (Models 7; Table 9). The increase in LEP of the non-fractured limb was not associated with the increase in any mobility task (Models 8). The decrease in asymmetrical LEP deficit was associated with the

TABLE 7 Cross-sectional multiple linear regression models predicting walking speed (m/s) over 10 (a) and 50 (b) feet or stair climbing speed (c; steps/s) at week 1 and 13 after hip fracture surgery (III). Leg extension power (LEP) of the fractured limb (model 1 and 3) or the combination of LEP of the non-fractured lower-limb and asymmetrical (asym) LEP deficit (model 2 and 4) were entered into the models as determinants.

	Week 1						Week 13					
	Model 1			Model 2			Model 3			Model 4		
	R^2	β	p	R^2	β	p	R^2	β	p	R^2	β	p
a) **10 feet walking speed**	0.237		0.001	0.331		<0.001	0.258		0.001	0.346		<0.001
LEP fractured limb		0.487	0.001		-	-		0.508	0.001		-	-
LEP non-fractured limb		-	-		0.531	<0.001		-	-		0.616	<0.001
Asymmetrical LEP deficit		-	-		0.232	0.080		-	-		0.140	0.304
b) **50 feet walking speed**	0.244		0.001	0.330		<0.001	0.272		<0.001	0.303		0.001
LEP fractured limb		0.494	0.001		-	-		0.522	<0.001		-	-
LEP non-fractured limb		-	-		0.525	<0.001		-	-		0.560	<0.001
Asymmetrical LEP deficit		-	-		0.346	0.064		-	-		0.098	0.470
c) **Stair climbing speed**	0.210		0.002	0.234		0.005	0.377		<0.001	0.387		<0.001
LEP fractured limb		0.458	0.002		-	-		0.614	<0.001		-	-
LEP non-fractured limb		-	-		0.349	0.016		-	-		0.615	<0.001
Asymmetrical LEP deficit		-	-		0.343	0.018		-	-		0.402	0.004

TABLE 8 Longitudinal multiple linear regression models predicting walking speed (m/s) over 10 (a) and 50 (b) feet or stair climbing speed (c; steps/s) at week 13 after hip fracture surgery (W13; III). Baseline (W1) leg extension power (LEP) of the fractured limb (model 5) or the combination of LEP of the non-fractured lower-limb and asymmetrical LEP deficit (model 6) were entered into the models as determinants. Additionally, the models were adjusted for baseline mobility.

		Model 5			Model 6		
		R^2	β	p	R^2	β	p
a)	**10 feet walking speed W13**	0.263		0.002	0.356		0.001
	LEP fractured limb W1		0.256	0.107		-	-
	LEP non-fractured limb W1		-	-		0.448	0.006
	Asymmetrical LEP deficit W1		-	-		0.020	0.881
	10 feet walking speed W1		0.337	0.036		0.221	0.166
b)	**50 feet walking speed W13**	0.283		0.001	0.372		<0.001
	LEP fractured limb W1		0.142	0.361		-	-
	LEP non-fractured limb W1		-	-		0.365	0.020
	Asymmetrical LEP deficit W1		-	-		-0.048	0.717
	50 feet walking speed W1		0.447	0.006		0.339	0.035
c)	**Stair climbing speed W13**	0.254		0.003	0.311		0.002
	LEP fractured limb W1		0.267	0.090		-	-
	LEP non-fractured limb W1		-	-		0.354	0.018
	Asymmetrical LEP deficit W1		-	-		-0.024	0.866
	stair climbing speed W1		0.322	0.042		0.332	0.035

TABLE 9 Multiple linear regression models predicting the change (Δ) in walking speed (m/s) over 10 (a) and 50 (b) feet or stair climbing speed (c; steps/s) between week 1 and 13 after hip fracture surgery. The change in leg extension power (LEP) of the fractured (model 7) and non-fractured (model 8) lower-limb, and the change in asymmetrical LEP deficit (model 9) were entered as determinants into the models. Additionally, the models were adjusted for the respective baseline (W1) LEP and mobility measures (III.)

		Model 7			Model 8			Model 9		
		R^2	β	p	R^2	β	p	R^2	β	p
a)	Δ **10 feet walking speed**	0.172		0.059	0.213		0.054	0.188		0.087
	Δ LEP fractured limb		0.475	0.001		-	-		-	-
	Δ LEP non-fractured limb		-	-		0.177	0.238		-	-
	Δ Asymmetrical deficit		-	-		-	-		0.105	0.623
	LEP fractured limb W1		0.336	0.030		-	-		-	-
	LEP non-fractured limb W1		-	-		0.534	0.004		0.512	0.006
	Asymmetrical LEP deficit W1		-	-		0.014	0.927		0.094	0.656
	10 feet walking speed W1		-0.355	0.022		-0.275	0.134		-0.221	0.229
b)	Δ **50 feet walking speed**	0.182		0.047	0.188		0.087	0.160		0.148
	Δ LEP fractured limb		0.393	0.010		-	-		-	-
	Δ LEP non-fractured limb		-	-		0.177	0.238		-	-
	Δ Asymmetrical deficit		-	-		-	-		0.138	0.522
	LEP fractured limb W1		0.207	0.224		-	-		-	-
	LEP non-fractured limb W1		-	-		0.534	0.004		0.444	0.018
	Asymmetrical LEP deficit W1		-	-		0.014	0.927		0.042	0.847
	50 feet walking speed W1		-0.033	0.845		-0.275	0.134		-0.114	0.534
c)	Δ **Stair climbing speed**	0.322		0.002	0.192		0.082	0.373		0.001
	Δ LEP fractured limb		0.475	0.001		-	-		-	-
	Δ LEP non-fractured limb		-	-		0.157	0.297		-	-
	Δ Asymmetrical deficit		-	-		-	-		0.519	0.015
	LEP fractured limb W1		0.336	0.030		-	-		-	-
	LEP non-fractured limb W1		-	-		0.403	0.015		0.454	0.008
	Asymmetrical LEP deficit W1		-	-		-0.035	0.826		0.335	0.116
	Stair climbing speed W1		-0.355	0.022		-0.323	0.062		-0.327	0.050

increase in stair climbing speed only (model 9c). Since age, body weight and pain were not significantly correlated with the changes in time; further adjustment of the models was not performed.

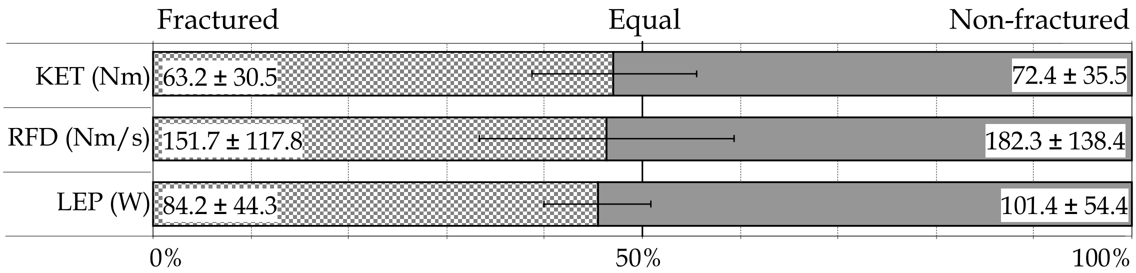

FIGURE 8 Mean (± standard deviation) asymmetrical deficit in isometric knee extension torque (KET), rate of force development (RFD) over the first 200 ms, and leg extension power (LEP). The boxes on the base of the bars representing the fractured and non-fractured lower-limb show the absolute values of the respective strength measures (IV).

5.4 Asymmetrical deficit and its determinants in older men and women with a hip fracture history (IV)

In participants of the HIP-ASYMMETRY study the fractured limb was on average significantly weaker than the non-fractured lower-limb (Figure 8). Additionally, the fractured limb was on average more painful than the non-fractured limb (62.6 ± 58.5 mm vs. 30.9 ± 44.8 mm, respectively; $p<0.001$). The overall disease and injury burden was significantly larger in the fractured than in the non-fractured limb (median 1, range 1-2 vs. 0, 0-2, respectively; $p<0.001$). No difference was observed in the muscle mass of both lower-limbs (7.4 ± 1.4, and 7.4 ± 1.4, respectively; $p=0.575$).

Of the participants, 47% had a consistent strength deficit on the fractured side. Participants with a consistent deficit on the fractured side tended to be older, and taller, and they tended to have higher handgrip force than those without a consistent deficit on the fractured side (Table 6). The type of fixation of the fracture was not different between the groups. For the fractured limb, lower-limb muscle strength and mass were similar in those with and without a consistent strength deficit on the fractured side (Figure 9). However, for the non-fractured limb KET and RFD_{200} were significantly lower and muscle mass tended to be smaller in the group without a consistent strength deficit on the fractured side. For LEP, the group difference for the non- fractured limb was not significant. Lower-limb pain in the fractured and non-fractured limb was similar in both groups. The disease and injury burden of the fractured limb (median 1, range 1-2 injuries, including the hip fracture) was similar in both groups ($p=0.661$). The disease and injury burden in the non-fractured limb was significantly higher (Mann-Whitney U $p=0.015$) in those without (0, 0-2 injuries) than in those with (0, 0-1 injuries) a consistent strength deficit on the fractured side.

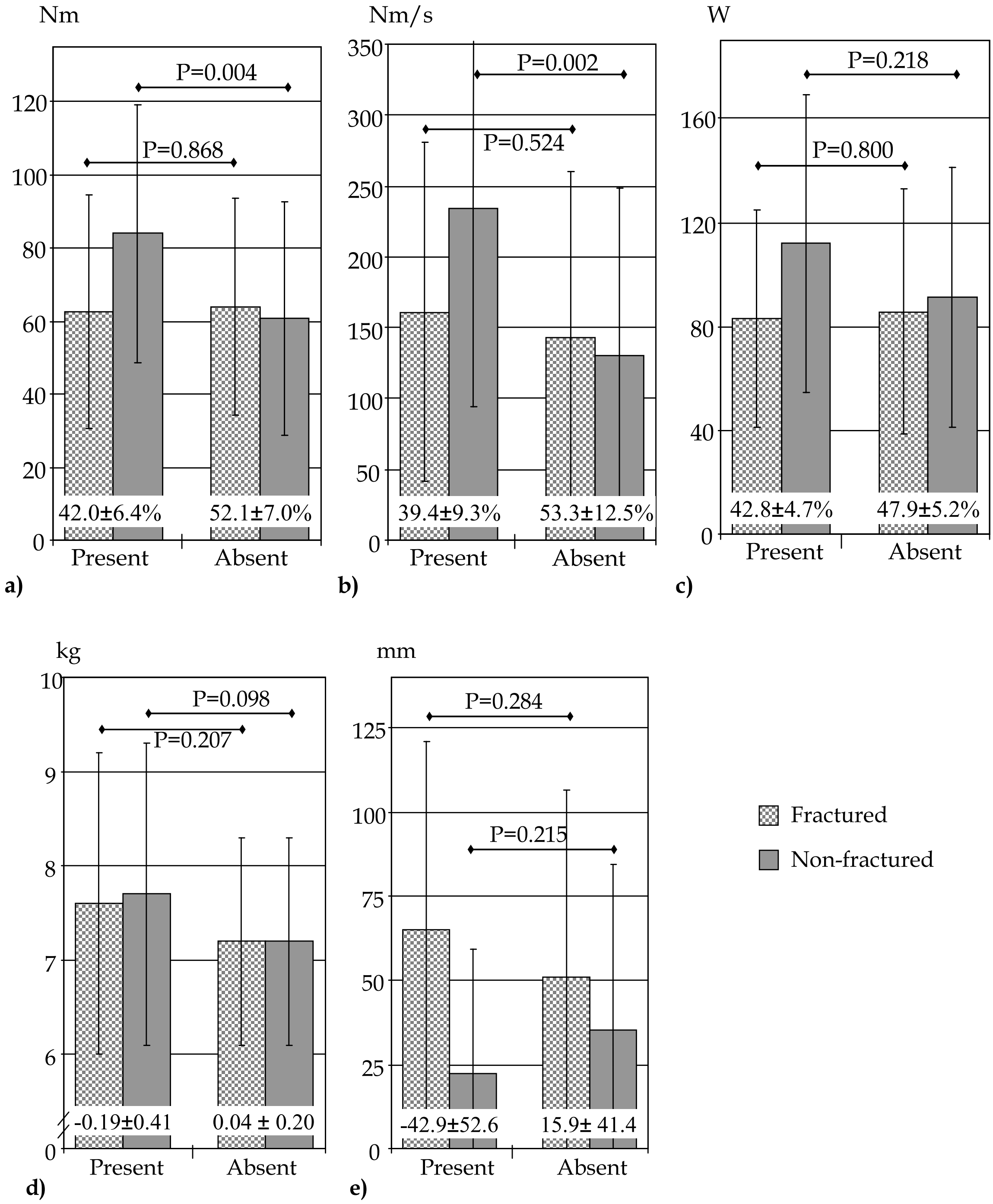

FIGURE 9 Mean (± standard deviation) characteristics of the lower-limbs in participants with a consistent strength deficit on the fractured side (all measures of asymmetrical deficit <50%) present or absent (IV). Group differences (independent T-test) are indicated with horizontal lines. For knee extension torque (a), rate of force development over the first 200 ms (b), and leg extension power (c) the mean (± standard deviation) asymmetrical deficits are noted on the base of the bars. For lower-limb muscle mass (d) and lower-limb pain (e) the mean asymmetrical measures are noted similarly.

Regression analyses revealed that the asymmetrical measures of lower-limb pain, lower-limb disease and injury burden, and lower-limb muscle mass correlated significantly with the asymmetrical deficit in KET and RFD_{200} (Table 10). A smaller strength deficit on the fractured side was associated with more intense pain and higher disease and injury burden affecting the non-fractured limb relative to the fractured limb. Additionally, a smaller strength deficit on the fractured side was associated with lower muscle mass on the non-fractured side relative to the fractured side. The linear regression models explained 43% and 36% of the variation of the asymmetrical deficit in KET and RFD_{200}, respectively.

Asymmetrical LEP deficit was only related to the asymmetrical measure of lower-limb pain. A smaller deficit on the fractured side was associated with more intense pain in the non-fractured limb relative to the fractured limb. The regression model explained 11% of the variation in asymmetrical LEP deficit. Inclusion of potential confounding variables of age, gender, time since fracture, type of surgical fixation, and prescribed pain medication one at a time did not materially change the estimates.

TABLE 10 Crude multiple linear regression models predicting asymmetrical deficit in isometric knee extension torque (KET; N=64), in rate of force development over the first 200ms of isometric knee extension (RFD_{200}; N=64), and in leg extension power (LEP; N=57) (IV). The final models are shown including only significant determinants; the asymmetrical measures of lower-limb pain, lower-limb disease and injury burden and/or lower-limb muscle mass.

		R^2	β	p
a)	**Asymmetrical KET deficit**	0.429		<0.001
	Asymmetrical lower-limb pain		0.284	0.007
	Asymmetrical lower-limb injury burden		0.408	<0.001
	Asymmetrical lower-limb muscle mass		0.380	<0.001
b)	**Asymmetrical RFD_{200} deficit**	0.362		<0.001
	Asymmetrical lower-limb pain		0.259	0.019
	Asymmetrical lower-limb injury burden		0.383	0.001
	Asymmetrical lower-limb muscle mass		0.343	0.002
c)	**Asymmetrical LEP deficit**	0.112		0.009
	Asymmetrical lower-limb pain	0.334	0.009	0.044

5.5 Effects of resistance training in older men and women of the HIP-ASYMMETRY study (V)

Forty-six participants of the HIP-ASYMMETRY study without contraindications for the strength-power training participated in the RCT. During the training period, short-term adjustments for load or training frequency were made in 6 participants after consultation of the physician, in two cases musculoskeletal problems and in one case chest pain were likely to be related to the training. Additionally, one participant developed prolonged radicular pain in the lower-limb after the training period. In two participants poor compliance to the training was caused by health-related problems that were present before the start of the trial, and in one participant due to an unrelated wrist fracture. The training compliance was excellent, being on average 91 ± 15%. Without the three participants with rather poor compliance (48-72%), the training compliance was on average 97 ± 3%.

Sixty-one percent of the participants had a clear and consistent deficit in all laboratory force and power tests. In 83% of the participants the fractured limb was WEAKleg. At baseline, WEAKleg had on average significantly poorer KET and LEP than the stronger lower-limb in both groups (p<0.004; Figure 10).

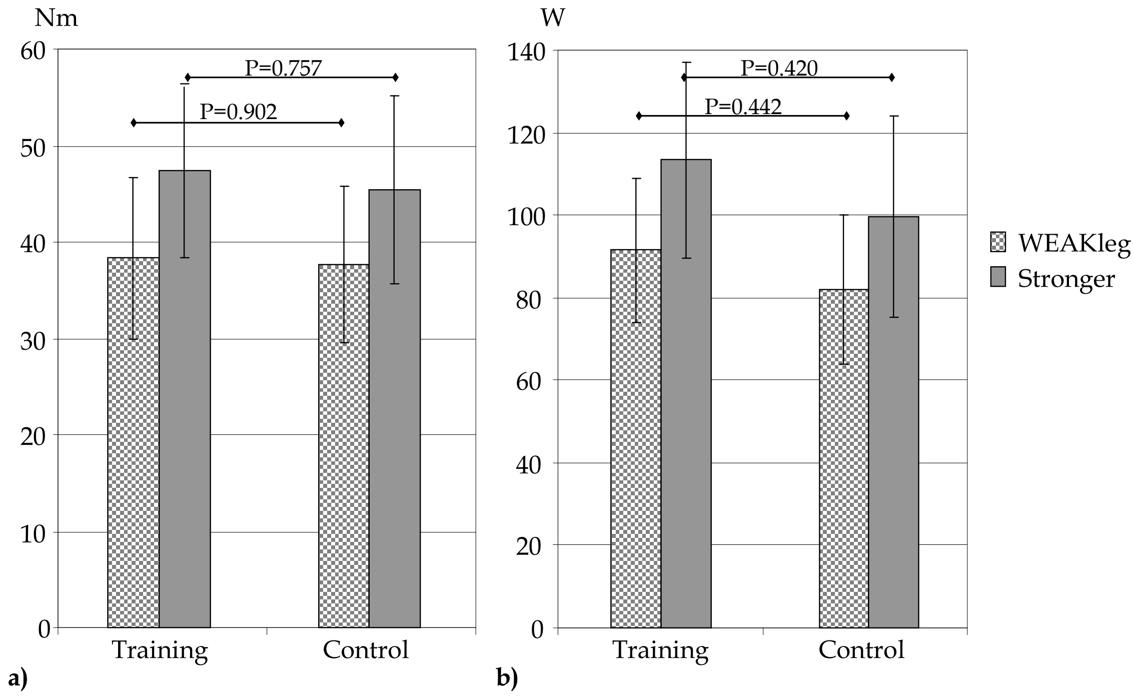

FIGURE 10 Mean (± standard deviation) knee extension torque (a) and leg extension power (b) in the training and control group at baseline (V). WEAKleg was defined as the weaker lower-limb for training based on a side-to-side difference larger than 5% in two out of three baseline strength measures (see paragraph 4.4.1). Group differences (independent T-tests) are indicated with horizontal lines.

5.5.1 Lower-limb muscle strength and asymmetrical deficit

At baseline, there were no significant differences between the training and control group in mean KET and LEP (Figure 10) or the asymmetrical KET (p=0.959) and LEP (p=0.672) deficit (Figure 11). In the training group, WEAKleg provided on average 46% (95%CI: 43 - 48%) of the sum of KET of both lower-limbs. In the control group, the asymmetrical KET deficit was on average 44% (41 - 47%). The LEP deficit was on average 45% (43 - 47%) and 45% (42 - 47%) in the training and control group, respectively.

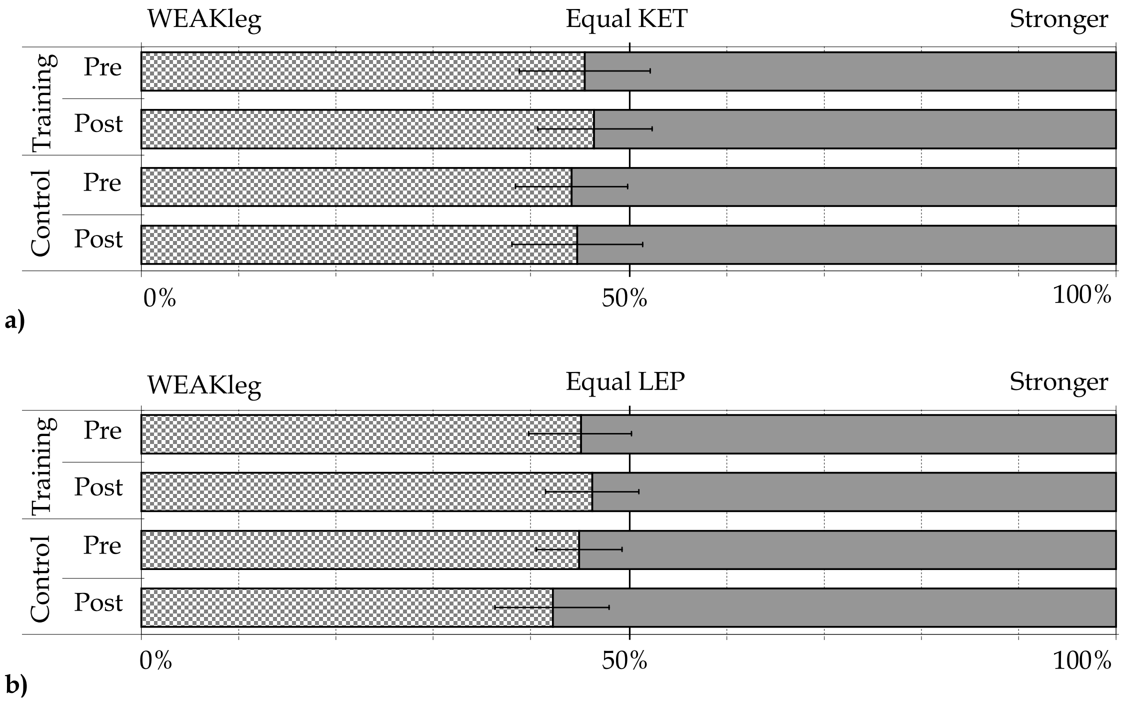

FIGURE 11 Mean (± standard deviation) asymmetrical deficit in isometric knee extension torque (KET; a) and leg extension power (LEP; b) in the training and control group at pre- and post-trial (V). WEAKleg was defined as the weaker lower-limb for training based on a side-to-side difference larger than 5% in two out of three baseline strength measures (see paragraph 4.4.1).

Figure 12 shows forest plots of the effects of the training. KET increased in the training group compared to the control group for both the WEAKleg and the stronger lower-limb (IA p=0.021 and p=0.004, respectively). However, the training had no effect on the asymmetrical KET deficit. The mean improvement in LEP of the WEAKleg tended to be greater in the training group compared to the control group (IA p=0.071), whereas no training effect was observed for LEP of the stronger lower-limb (IA p=0.987). The mean reduction in asymmetrical LEP deficit was significantly greater in the training group compared to the control group (IA p= 0.010).

5.5.2 Limitations in mobility and balance

At baseline, habitual walking speed was similar in the training (1.1, 95%CI: 1.0-1.2 m/s) and control (1.1, 0.9-1.2 m/s) group (p=0.385). The time and distance in the dynamic balance test did not differ between the training (12.0, 10.4-13.6 s; and 182.0, 168-196 cm, respectively) and control (10.7, 9.0-12.4 s; and 177.0, 162-192 cm, respectively) group (p>0.270). No training effect was observed in walking speed (p=0.997) or dynamic balance (distance p=0.996 and time p=0.516; Figure 12).

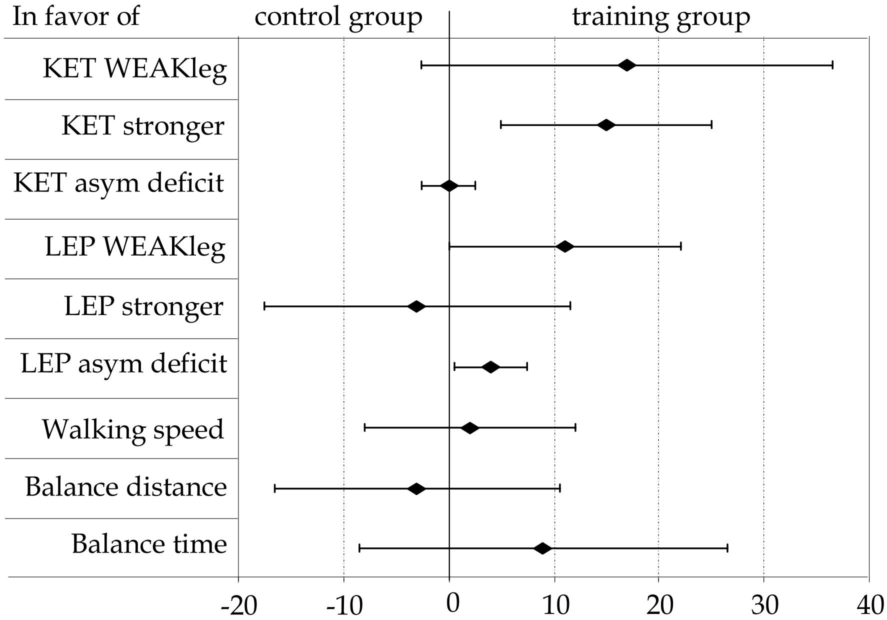

FIGURE 12 The effect of training for isometric knee extension torque (KET) and leg extension power (LEP) of the lower-limbs, the asymmetrical deficit, walking speed, and distance and time in the dynamic balance test (V). The training effect was calculated as the mean difference in percentage of change (95% confidence interval) between the training and control group. WEAKleg was defined as the weaker lower-limb for training based on a side-to-side difference larger than 5% in two out of three baseline strength measures (see paragraph 4.4.1).

5.5.3 Perceived difficulty in outdoor mobility

The number of participants having difficulties in walking two kilometers decreased after training (McNemar p=0.063; Table 11). In addition, an improvement in outdoor mobility was reported by ten and a decrease by two participants of the training group, respectively (χ^2 p=0.016; Figure 13).

5.5.4 Self-rated health and perceived difficulty in daily activities

The number of participants rating fair or poor health decreased after training (McNemar p=0.031; Table 11). An improvement in self-rated health was reported by 12 and a decrease by two participants of the training group, respectively (χ^2 p=0.001; Figure 13). The number of participants rating fair or poor ability to perform daily activities was small at baseline and therefore remained relatively stable (Table 11). However, an improvement in ability to perform daily activities was reported by eight participants of the training group, a decrease was reported by one participant (χ^2 p=0.047; Figure 13).

TABLE 11 Perceived difficulty in outdoor mobility and daily activities, and self-rated health in the training and control group at pre- and post-trial. The within-group changes were tested with McNemar tests and the group differences at baseline with χ^2 tests (V)

	Training			Control			Baseline difference
	Pre-trial n (%)	Post-trial n (%)	McNemar p	Pre-trial n (%)	Post-trial n (%)	McNemar p	χ^2 p
a) Ability to walk 2km			0.063			1.000	1.000
Without difficulty	8 (35 %)	13 (57 %)		7 (35 %)	8 (40 %)		
Difficulties	15 (65 %)	10 (43 %)		13 (65 %)	12 (60 %)		
c) Ability to perform daily activities			0.500			1.000	0.605
Good or excellent	20 (87%)	22 (96%)		17 (81%)	18 (86%)		
Fair or poor	3 (13%)	1 (4%)		4 (19%)	3 (14%)		
b) Self-rated health			0.031			1.000	0.586
Good or excellent	14 (64%)	20 (91%)		16 (76%)	16 (76%)		
Fair or poor	8 (36%)	2 (9%)		5 (24%)	5 (24%)		

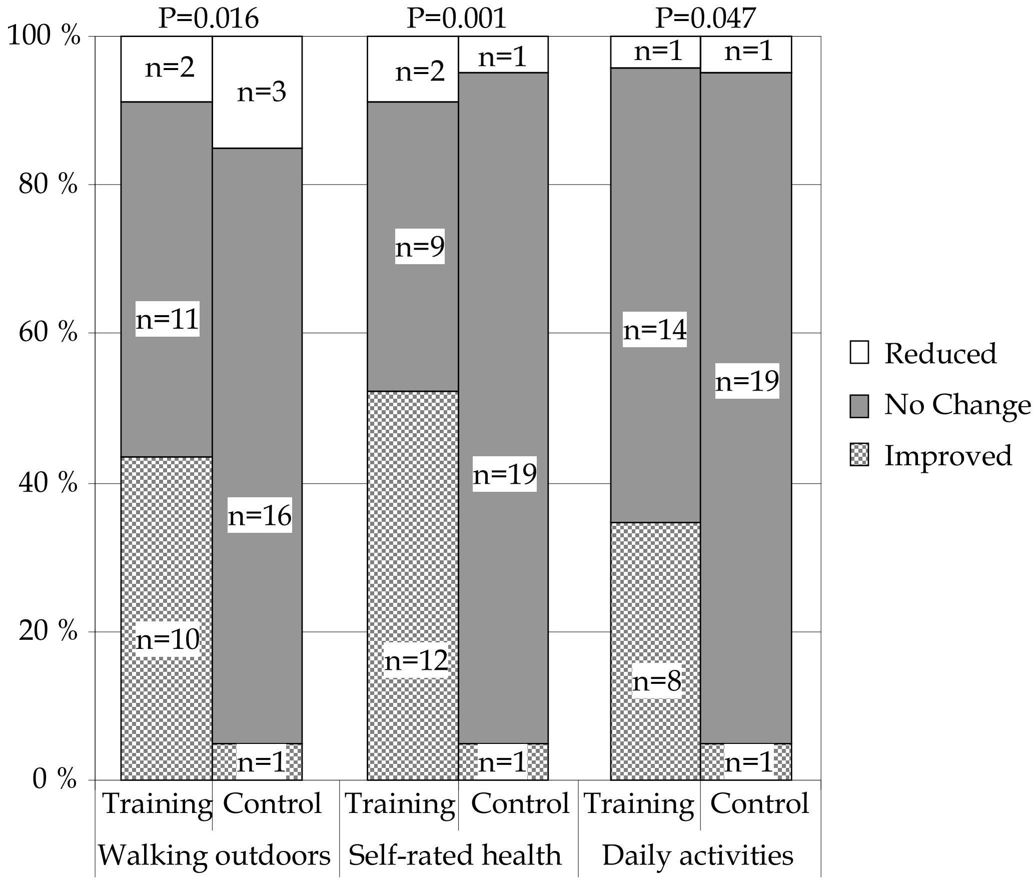

FIGURE 13 Perceived changes between pre- and post-trial in outdoor mobility, and self-rated health and daily activities in the training and control group. The difference between the groups was tested with χ^2 tests (V).

6 DISCUSSION

The aim of this study was to gain insight in asymmetrical lower-limb muscle strength deficit, which is the side-to-side strength difference in the lower-limbs, in healthy older women and in older people with a hip fracture. Its prevalence, potential determinants, and consequences for mobility, balance, and injurious falls were studied. Additionally, the effects of a progressive resistance training program, specifically aiming to reduce asymmetrical deficit in a high-risk population were investigated.

Considerable asymmetrical muscle strength deficit existed in healthy older women as well as patients with a hip fracture. In addition to poor power, asymmetrical deficit compromises mobility and balance function, especially in the more challenging mobility tasks. Improved muscle power of the fractured limb during the first three months after hip fracture correlated with improved mobility function. On average four years after fracture, half of the people had a consistent strength deficit on the fractured side, while the other half had no consistent asymmetrical deficit or a strength deficit on the non-fractured side. Pain, and disease and injury burden affecting the non-fractured limb reduced the strength deficit on the fractured side, resulting in poor strength in both lower-limbs. The strength-power training was feasible in people with a hip fracture history and improved muscle force and power, especially in the weaker lower-limb. The asymmetrical LEP deficit reduced significantly by the training. The training effects on asymmetrical KET deficit and balance were non-significant but positive. Walking speed was not affected, but perceived difficulty in outdoor mobility decreased after training.

6.1 Asymmetrical muscle strength deficit in the lower-limbs and its determinants

Leg extension power was measured in a population of healthy older women. Considerable asymmetrical deficit in leg extension power existed, as the power of the weaker lower-limb was on average 15% lower than that of the stronger lower-limb. In two selected samples of relatively healthy older people with a mean age of 75 and 76 years, respectively, the asymmetrical LEP deficit was on average 5% (Skelton et al. 2002) and 14% (Perry et al. 2007). Additionally, the asymmetrical deficit in isometric knee extension force was on average about 10% (Skelton et al. 2002) and 13% (Perry et al. 2007) in older people. Perry et al. (2007) reported that in younger people the asymmetrical deficit in LEP (10%) was significantly smaller and the asymmetrical deficit in knee extension force (10%) tended to be smaller than in the older people, respectively. The average difference between the dominant and non-dominant lower-limb in isometric knee extension force in a sample of healthy community-dwelling women with a large age range (20-89 years) was on average 5% (Hunter et al. 2000). However, asymmetrical strength deficits may not follow the dominance pattern of the lower-limbs (Skelton et al. 2002).

In our study, muscle power in the non-fractured limb in women one week after surgical repair of hip fracture (HIP-RECOVERY) was about half of the healthy older women (FITSA). The fact that hip fracture patients were older can not entirely explain this difference. It appears that they had low strength even for women of their age (Skelton 1994) and they also had an extremely large asymmetrical deficit, as LEP in the fractured limb was less than half of that in the non-fractured limb. The asymmetrical deficit reduced in the following three months, but remained significant. In the HIP-ASYMMETRY study, among men and women six months to seven years after hip fracture, the fractured limb was still weaker than the non-fractured limb. Asymmetrical deficit was observed in all measures of muscle strength; isometric KET, RFD_{200}, and LEP. Previous studies have shown marked deficits in isometric and isokinetic muscle force in the fractured limb few weeks (Madsen et al. 1995) and six to 36 months after hip fracture (Madsen et al. 2000). Compared to healthy matched controls, isometric muscle force of hip fracture patients was generally poorer and more asymmetrical (Sherrington et al. 1998). In our study, the asymmetrical deficit in LEP was slightly larger than the asymmetrical deficit in RFD_{200} and KET. Potentially, dynamic actions, especially when performed with high velocity, may be more affected by injuries such as hip fracture. Dynamic muscle actions or velocity-related characteristics of muscle contractions were more impaired in people with symptomatic osteoarthritis (Suetta et al. 2007) and in people shortly after hip fracture (Madsen et al. 1995) compared to other strength measures. The fact that the impairments in dynamic actions and explosive contraction velocity exceed the loss in isometric force with age (Bassey & Short 1990, Thelen et al. 1996, Izquierdo et al. 1999, Macaluso et al. 2003, Lanza et al. 2003, Dean et al. 2004, Petrella et al. 2005) also supports the suggestion that power is more sensitive to change.

Six months to seven years after hip fracture half of the men and women had a consistent deficit on the fractured side over all measures of muscle strength in our study. Among the other half, the asymmetrical deficit was not consistent or the strength deficit was on the non-fractured side. The strength measures of the fractured limb were similar in those with and without a consistent deficit on the fractured side. However, those hip fracture patients with a consistent deficit on the fractured side had higher muscle strength in the non-fractured limb than those without a consistent deficit. The results suggest that symmetrical lower-limb muscle strength was not a sign of better recovery, but rather of poor strength in both lower-limbs.

In accordance with other studies (Herrick et al. 2004, Williams et al. 2006, Dasch et al. 2008) pain was present in a large proportion of the people with a hip fracture history. Previously, pain has been suggested to reduce muscle strength in general (Lamb et al. 2000, Steultjens et al. 2002, Al Snih et al. 2005, Onder et al. 2006) and on the painful side in particular (Steultjens et al. 2001, Wilgen et al. 2003). More severe pain correlated with a more asymmetrical knee extension force ratio of the operated and non-operated lower-limb four years after meniscectomy (Ericsson et al. 2006). In our study of men and women four years after hip fracture, a strength (KET, RFD_{200}, and LEP) deficit was associated with more intense pain in the weaker lower-limb. In addition, a deficit in KET and RFD_{200} was independently associated with higher disease and injury burden in the weaker lower-limb. The disease and injury burden was based on the presence of osteoarthritis and fractures. Previous studies have found that both of these conditions correlate with muscle weakness. Impairments in isometric (Madsen et al. 1995, Robertson et al. 1998, Sherrington et al. 1998, Sicard-Rosenbaum et al. 2002, Mizner et al. 2003, Mizner et al. 2005b, Gapeyeva et al. 2007, Suetta et al. 2007) and isokinetic (Madsen et al. 1995, Madsen et al. 2000, Ericsson et al. 2006) muscle force, rate of force development (Gapeyeva et al. 2007, Suetta et al. 2007) and LEP (Robertson et al. 1998) have been reported. Potentially, inflammation (Hedström et al. 2006, Miller et al. 2006b, Paddon-Jones et al. 2006) and neural inhibition (Hurley et al. 1997, O'Reilly et al. 1998, Mizner et al. 2003, Stevens et al. 2003, Mizner et al. 2005b) may play a role in the pathway leading to pain, and disease and injury burden and subsequent muscle strength reduction. Although pain, and disease and injury burden in the fractured limb may increase the strength deficit, the results of our study suggest that a smaller deficit on the fractured side may be the result of more intense pain, and higher disease and injury burden affecting the non-fractured limb. Considering that pain in this study was not directly related to the hip fracture, the associations found in our study may apply for other populations of frail older people with comorbidity in the lower-limbs.

A decrease in muscle strength may be caused by neural and muscular factors (Lamoureux et al. 2001). Usually, it is considered that changes in muscle mass need a longer time than changes in neural activation. In our study, the asymmetrical muscle mass deficit correlated with the asymmetrical deficit in KET and RFD_{200}, suggesting that long-term changes had taken place. This is in accordance with other studies in clinical populations in which the strength deficit in the affected lower-limb was at least partly related to a reduction in muscle mass in the weaker lower-limb (Rutherford et al. 1990, Mizner et al. 2005b, Suetta et al. 2007). Long-term disuse (Berg et al. 1997, D'Antona et al. 2003) and avoidance behavior due to fear for falls (Petrella et al. 2000, Delbaere et al. 2004) or pain (Vlaeyen et al. 2000), and neural inhibition due to pain (Hurley et al. 1997, O'Reilly et al. 1998, Mizner et al. 2003, Stevens et al. 2003, Mizner et al. 2005b) may be involved in the muscle mass reduction. It is logical to suggest that decreased lower-limb muscle mass may mediate the association of lower-limb pain or lower-limb disease and injury burden and lower-limb muscle strength deficit. However, our study shows that lower-limb pain, and lower-limb disease and injury burden also have an effect on the strength deficit independent of muscle mass.

6.2 Consequences of asymmetrical deficit for mobility and balance function

The results of our study indicate that relative weakness of one lower-limb may limit mobility function and decreases the ability to maintain postural stability and counterbalance a significant disturbance in posture. In healthy older women, a large asymmetrical LEP deficit, particularly when accompanied with poor power, was associated with slower walking speed and poorer standing balance. Such limitations in mobility (Laukkanen et al. 1995, Guralnik et al. 2000, Shinkai et al. 2000, Cesari et al. 2005) and balance (Shinkai et al. 2000, Rantanen et al. 2001, Stel et al. 2003) predict future falls, disability, functional dependence and mortality. Additionally, in our study asymmetrical LEP deficit was an independent and strong risk factor for injurious falls in healthy older women. The risk for recurrent injurious falls in the one-year follow-up period was 2.4 times higher in those with asymmetrical deficit compared to those without. Recurrent falls may eventually lead to serious injury that increases the costs for care substantially (Nurmi et al. 2002, Scuffham et al. 2003). For example, the costs for care in the first year after hip fracture were about three times higher than in age and residence matched people without hip fracture from the same neighborhood, and a large part of the costs occurred during the first three months after hospital discharge (Haentjens et al. 2001).

According to my knowledge, only two case-control studies investigating the association of asymmetrical deficit in muscle force and power with falls in relatively healthy older people have been published. Skelton et al. (2002) showed that older women with a history of frequent falls (three or more in the past year) had a larger asymmetrical deficit in leg extension power (16%) than non-falling matched controls (5%). The asymmetrical deficit in isometric knee extension strength tended to be greater in the fallers (17% vs. 10%). In a recent study by Perry et al. (2007), the asymmetrical deficit in LEP was markedly, but not significantly, larger in a group of fallers (one or more falls in the past year; 17%) than in the matched controls (13%). The fallers had large variability in asymmetrical deficit, and a smaller proportion of the fallers had a difference between the lower-limbs of less than 10% compared to the non-falling controls. For isometric dorsiflexion force, the fallers had a significantly larger asymmetrical deficit (26%) than the non-falling older people (17%). Ankle plantar- and dorsiflexor muscles have an important role in restoring balance after a disturbance in posture (Thelen et al. 1996, Suzuki et al. 2001).

Interestingly, a study by Cawthon et al. (abstract 2007) using the same design as our study suggests that a large asymmetrical deficit in LEP of the right and left lower-limb was a significant risk factor for frequent falls, non-spine fractures, and especially hip fractures in a large sample of older men. Together these studies suggest that asymmetrical LEP deficit is a risk factor for falls, especially for frequent and injurious falls.

Muscle force and power are indicators of health and physical function (Rantanen et al. 1999a, Rantanen et al. 1999b, Herman et al. 2005, Portegijs et al. 2007). After a hip fracture, LEP in the non-fractured lower-limb is likely to be a marker of pre-injury health status. LEP of the fractured limb is dependent on the pre-injury health status, but it is impaired due to the trauma and surgery. The asymmetrical deficit is therefore likely to reflect the effects of the injury and surgery, especially when measured shortly after the trauma. Therefore it is not surprising that higher LEP of non-fractured limb measured one week after hip fracture surgery was a significant predictor of better mobility function three months later. This is in line with previous studies, which have found that pre-injury mobility and health status are strong determinants of recovery after fracture (Roche et al. 2005, Hawkes et al. 2006).

Mizner et al. (2005a) showed that three months after knee arthroplasty due to osteoarthritis, isometric knee extension force of the non-affected lower-limb correlated more strongly with mobility function, such as sit-to-stand and stair climbing. A potential explanation may be that people rely more on the non-affected lower-limb. This was shown in people with ACL injury who produced higher power in stationary cycling with the non-affected lower-limb than their matched controls in either lower-limb (Hunt et al. 2004). Reliance on the non-affected side may compromise the ability to restore lower-limb muscle strength on the affected side (Hunt et al. 2004). It may, however, also be a mechanism to compensate for the deficit in the affected lower-limb. In our cross-sectional analyses at week 1 and 13 after hip fracture, poorer LEP of the fractured and non-fractured limb were determinants of poorer mobility function, and a larger asymmetrical LEP deficit was a determinant of slower stair climbing speed, but not of walking speed. Nadeau et al. (2003) previously showed that stair climbing puts a higher demand on unilateral function than level walking. Two recent studies support our findings that asymmetry in walking was found especially in the more demanding motor tasks, such as stair walking, rather than in level walking in older people with asymptomatic knee osteoarthritis (Liikavainio et al. 2007) and middle-aged people 16 years after ACL injury (Porat et al. 2006). Thus the importance of asymmetrical deficit may be task specific.

In our study, during the first three months of recovery from hip fracture, LEP of the fractured limb increased more than the LEP of the non-fractured limb, most probably due to spontaneous recovery. The increase in LEP of the fractured limb between week 1 and 13 was associated with the improvement in all mobility tasks. Although the asymmetrical deficit did not disappear fully, the decrease in asymmetrical deficit contributed significantly to the improvement in stair climbing speed over time. The increase in LEP of the non-fractured limb, however, was not associated with improved walking or stair climbing speed. Other studies in clinical populations have shown that isometric and isokinetic muscle force in the lower-limb affected by hip fracture (Madsen et al. 2000) or ACL injury (Seto et al. 1988) was a better predictor of mobility function than muscle force of the non-affected lower-limb on average 1½ to 5 years after injury. Our results stress the importance of increasing muscle power of the fractured limb after hip fracture to prevent mobility limitation, especially in mobility tasks that require unilateral force production.

6.3 Resistance training effects in older people with lower-limb injury

Our study shows that intensive progressive resistance training, specifically aiming to reduce the asymmetrical strength deficit, is feasible for people six months to seven years after hip fracture as they were able to perform the training protocol with high compliance. Our combined PRT program including high-intensity slow-velocity and low-intensity high-velocity exercises increased muscle force and power. Previous studies have demonstrated that progressive high-intensity resistance training with slow-velocity (Fiatarone et al. 1994, Judge et al. 1994, Sipilä, et al. 1996) or high-velocity (Vos et al. 2005, Caserotti et al. 2008) exercises increases muscle force in older adults. Muscle power increases also by low-intensity high-velocity PRT (Miszko et al. 2003, Vos et al. 2005).

Training programs often do not taken into account asymmetrical strength deficits even in populations where asymmetrical deficit is likely, such as in unilateral osteoarthritis and after hip fracture. One earlier study in patients recovering from unilateral replacement surgery for hip osteoarthritis showed that asymmetrical deficit in strength reverts only with additional unilateral strength training incorporated in the standard rehabilitation protocol (Suetta et al. 2004ab). However, training one lower-limb only is impossible on the long-term. Increasing muscle strength in both lower-limbs, while reducing the asymmetrical deficit, may be more effective. In two earlier studies in people after hip fracture, muscle strength and functional performance improved and the asymmetrical deficit decreased after unilateral training of both lower-limbs (Mitchell et al. 2001) or combined progressive resistance and functional training (Hauer et al. 2002). However, the authors did not report the statistical significance of the reductions in asymmetrical deficit. In an uncontrolled study, Host et al. (2007) reported that the asymmetrical deficit in muscle force was no longer significant after six months of bilateral resistance training. As the intervention started on average three months after the hip fracture (Binder et al. 2004, Host et al. 2007), spontaneous recovery of the fractured limb may have played a role in the increase in muscle force. It has been reported that the largest recovery in function occurs between two to six months after hip fracture with slower recovery in functions involving the lower extremities (Magaziner et al. 2000). In our randomized controlled trial, the asymmetrical LEP deficit decreased significantly by training, but no treatment effect was observed on KET. A larger distinction in training loads for the stronger and weaker lower-limb may be needed to reduce the asymmetrical deficit in KET. It should also be considered that in the weaker and more painful lower-limb, maximal strength is likely to be underestimated (O'Reilly et al. 1998, Lamb et al. 2000, Onder et al. 2006), resulting in relatively lower training resistance than intended for the weaker lower-limb especially. Nevertheless, muscle strength and power of the lower-limbs, especially the weaker limb increased significantly.

According to the disablement process, improvements in muscle strength may reduce limitations in mobility and balance. Considering that an asymmetrical muscle strength deficit may complicate the transfer of weight from one lower-limb to the other, which is important in e.g. walking, a reduction in the asymmetrical deficit may also reduce limitations in mobility and lateral balance. Previous studies have shown that progressive resistance training seems to improve mobility and balance function, especially in more frail people or people with mobility limitations (Fiatarone et al. 1994, Timonen et al. 2002, Seynnes et al. 2004). High-velocity PRT may improve mobility and balance function more than traditional slow-velocity exercises (Miszko et al. 2003, Bottaro et al. 2007), although not consistently reported (Sayers et al. 2003). The optimal resistance is not yet known, however, lower resistance may be more beneficial for improving balance function (Orr et al. 2006). In our study, mobility and balance were not materially affected by training. Despite the hip fracture history, our participants were in relatively good health and were well functioning. Considering that the relationship between muscle strength and mobility is not linear (Ferrucci et al. 1997, Rantanen et al. 1997b, Rantanen et al. 1998a, Bean et al. 2003), improvements in muscle strength do not necessarily transfer to mobility function. Additionally, other factors than muscle strength such as poor balance (Rantanen et al. 2001), fear for falling (Jarnlo et al. 1991b, Petrella et al. 2000, Delbaere et al. 2004) and pain (Lamb et al. 1995, Lamb et al. 2000, Onder et al. 2006) may play an important role in walking, especially.

Poor lateral control of balance is a predictor for falls to the side, which may cause hip fracture (Greenspan et al. 1994, Wei et al. 2001, Kannus et al. 2006a). The non-significant improvement (9%) in time of the test assessing lateral balance in the training group may be functionally relevant in reducing the risk for falls. Hip abductor and adductor muscles, which were trained in this study, play an important role in lateral balance control. Potentially, the improvement in lateral balance may indirectly indicate an increase in muscle strength of the hip abductor and adductor muscles, which were not measured directly. However, potentially adaptation of the distance between the feet (width of the base of support) may have partly masked changes in balance function, as the width was not standardized. Increased confidence may prompt a position with a smaller base of support, generating more challenges for balance control.

In this study, the training reduced the proportion of people reporting perceived difficulties in walking two kilometers. In addition, nearly half of the training group perceived an improvement in outdoor mobility and ability to perform daily activities. Also in other studies including mobility-limited or frail older people similar improvements have been reported after training. Reductions in perceived difficulty in daily activities have been reported after slow-velocity training with low- (Meuleman et al. 2000, Seynnes et al. 2004) or high- (Mitchell et al. 2001, Sayers et al. 2003, Binder et al. 2004, Seynnes et al. 2004) intensity, and after high-velocity training with high-intensity (Sayers et al. 2003). Reduced disability, including measures of mobility function and daily activities, was observed after low-intensity slow-velocity training (Ettinger et al. 1997, Jette et al. 1999). In accordance with Binder et al. (2004) we also observed an improvement in self-rated health. Self-rated health was assessed with a 1-item scale, which is considered to be a relatively stable measure that takes into account different health-related aspects such as age (Leinonen et al. 1998, Jylhä et al. 2001). Self-rated health and perceived difficulty in mobility and daily activities are determinants of quality of life and predictors of disability, loss of independence and death (Laukkanen et al. 1995, Langlois et al. 1996, Hirvensalo et al. 2000, Fried et al. 2001, Gill et al. 2006). Therefore the improvement we observed after the training may be considered clinically relevant for community-dwelling people. Considering that these self-reported measures are placed within the contextual environment in which a person lives, participants may have considered a two-kilometer distance to include slopes, which is more challenging than level walking such as in the laboratory test.

Considering that training-induced changes are task specific, functional and weight-bearing exercises that challenge balance may be more effective to improve mobility and balance function than resistance training alone. Based on the RCTs in hip fracture patients listed in table 1, there is no clear evidence of an additional benefit of combining functional exercises and resistance training for hip fracture patients, as the combined training programs rendered conflicting results with respect to improvements in muscle strength and mobility function (Tinetti et al. 1997a, Tinetti et al. 1999, Hauer et al. 2002). However, a relatively intensive weight-bearing functional training program, including a variety of weight-bearing exercises such as step-ups, in people on average five to seven months after hip fracture may also improve muscle force in the affected lower-limb and mobility function such as walking speed and chair-rise (Sherrington et al. 1997, Sherrington et al. 2004). In healthy older people, Vreede et al. (2005) showed that a 12-week weighted functional training improved physical function, including muscle strength and balance measurements. Additionally, functional training performed according to a low-intensity high-velocity training protocol improved muscle power and several mobility test results more than a low-resistance slow-velocity seated resistance training in frail older women (Bean et al. 2004).

Intensive training, especially in clinical populations, requires careful supervision and individualized protocols. Participation in exercise programs should be preceded by medical screening for contraindications (American College of Sports Medicine 2000). Pain and medical conditions in the lower-limbs make it necessary to adjust the training resistance individually. The ROM of the knee and hip joints may be limited, especially in people with joint replacements, knee osteoarthritis or hip fracture. Resistance training in a sitting position is safe to perform in older people with balance impairments, such as hip fracture patients (Jarnlo et al. 1991a, Sherrington et al. 1998). Acknowledging theses issues, resistance training is generally well tolerated and feasible for people with a history of hip fracture (Tinetti et al. 1997a, Hauer et al. 2002, Binder et al. 2004, Mangione et al. 2005, Miller et al. 2006a). However, people may be more responsive in the rehabilitation phase shortly after major injury, when the asymmetrical deficit is likely to be large.

6.4 Methodological considerations

This study is based on a randomized controlled trial specifically aiming to study the effects of rehabilitation on muscle strength, asymmetrical deficit, and mobility and balance function. In addition, data of two pre-existing studies were used. LEP was measured in all studies according to the same protocol. Therefore the results from the different studies complement each other. The FITSA study is population-based and the sample is thus representative of older women between 63- to 75-years of age. Data on falls were collected prospectively, so that a temporal order between asymmetrical LEP deficit and injurious falls was established, supporting a causal relationship. The HIP-RECOVERY study was an observational study with a longitudinal design. Therefore the effect of asymmetrical deficit and its change in the recovery process during the first months after hip fracture were established. The HIP-ASYMMETRY study consisted of a well defined population of people with a history of hip fracture.

In previous studies, asymmetrical strength deficit after an injury such as hip fracture was most often calculated as the ratio of the side-to-side difference divided by the strength of the non-fractured lower-limb (similar to formula 1) or the ratio of the fractured and non-fractured lower-limb. However, in our study (HIP-RECOVERY and HIP-ASYMMETRY) these formulas were less useful than the formula we used (formula 2), which equally distributes the side-to-side strength difference around the value of 50%, representing equal strength in both legs, irrespective of whether the strength deficit occurs on the fractured or non-fractured side. The values of asymmetrical deficit obtained using this formula are, however, closer to the value of equal strength in the lower-limbs compared to the values obtained with the previously used formulas. The results of the FITSA study show that the mean relative difference of 15% obtained using formula 1 corresponds with a mean deficit of 6% from the value of equal strength in both legs obtained using formula 4 (50 - 44%).

The FITSA and HIP-RECOVERY study consisted of older women only and in the HIP-ASYMMETRY study the majority of the participants were women. The association between muscle strength and mobility function is similar in men and women. For example, the strength requirements for mounting a step are similar in men and women (Rantanen et al. 1996). Therefore it is not likely that the association between asymmetrical strength deficit and mobility function is different in men and women. However, women generally have poorer levels of muscle strength (Rantanen et al. 1996, Petrella et al. 2005, Sayers et al. 2005) and therefore they are at higher risk for mobility limitation (Rantanen et al. 1996, Sainio et al. 2006). Functional consequences due to asymmetrical power deficit may therefore also be more prevalent in women. The distribution of men and women in the HIP-ASYMMETRY study was in accordance with previous studies in older hip fracture patients (Kannus et al. 1999, Roche et al. 2005, Hawkes et al. 2006, Kannus et al. 2006b). Women are more prone to falls and fractures, and they have a lower mortality rate in general and after hip fracture than men.

In FITSA, the women included were mobile and healthy. To be recruited for the study, the participants had to be able to travel independently to the research laboratory from their town of residence. Despite the hip fracture, the men and women in the HIP-ASYMMETRY study were also relatively healthy and well-functioning due to our inclusion criteria (maximum age 85, community-dwelling and able to walk outdoors independently). In the FITSA and HIP-ASYMMETRY study, people with poor mobility and possibly related impairments were more likely to drop out, which, at least to some extent, reduced the variance in muscle power, walking velocity and standing balance. Selective exclusion of persons with more medical problems, limitations in joint range of motion and pain during the leg extension power assessment especially is likely to have weakened the relationships. However, persons were only excluded from the analyses including the respective measure.

The study population of women with a recent hip fracture was recruited using admission lists of a hospital serving a regional function. The study population consisted of rather frail women. One week after hip fracture surgery, part of the women were unable to walk 10 or 50 feet or climb stairs without assistance of another person and they were assigned a walking or stair climbing speed of 0 m/s and 0 steps/s, respectively. Although the change in speed over time may have been overestimated, the overestimation is likely to be marginal, as the performance of other participants was only marginally better at baseline.

In the HIP-ASYMMETRY study, lower-limb pain, and lower-limb disease and injury burden were determinants of asymmetrical lower-limb muscle strength deficit. Unfortunately, we were unable to study whether the severity of the osteoarthritis and fractures affecting the lower-limbs affected the extent of the muscle strength deficit.

Measuring maximal performance in clinical populations is rather challenging, due to their pain and fear for pain. Therefore, maximal muscle force and power may have been underestimated in the studies with hip fracture patients. The training resistance of the weaker lower-limb especially may have been lower than intended in the experimental study. Also the training effect on force and power may have been underestimated. We used standardized dynamometers for the strength assessments rather than 1RM of training equipment, which results in more modest strength gains. The transfer of strength improvements to mobility and balance function may be better with a training program of a longer duration. For example, a six-month and a two-year PRT program improved balance function (Nelson et al. 1994, Taaffe et al. 1999), while shorter programs had no effect (Schlicht et al. 2001).

The sample size was relatively small in the HIP-RECOVERY and HIP-ASYMMETRY study, especially considering the large heterogeneity of hip fracture patients. In the HIP-ASYMMETRY study, 452 people with a hip fracture six months to seven years prior to baseline were informed about the study to obtain the intended sample size of 60 for the randomized controlled trial. However, despite the intensive recruitment, our experimental study was slightly underpowered (46 people). This may partly explain the non-significant improvement in dynamic balance. In accordance with other studies, recruitment of study participants is challenging in clinical populations. For example, Frobell et al. (2007) showed that in order to obtain the intended sample for a randomized controlled trial comparing surgical and non-surgical treatment of ACL injury, the intended sample size needs to be multiplied by 5.5 to provide an estimate of the number of people needed to screen. Our study and a study by Chang et al. 2004 suggest that in RCTs with older more frail people, the numbers needed to screen may need to be even larger, especially if frequent travel is required for the intervention. In general, the most important reason quoted for non-participation in physical exercise of older people is poor health (Hirvensalo et al. 1998), in addition, people with poorer physical performance and self-reported disability have more negative attitudes towards exercise (Bean et al. 2007). Patients with pain may have doubts and concerns about exercise as treatment (Thorstensson et al. 2006).

6.5 Future directions

Based on the results of this study, we conclude that asymmetrical muscle strength deficit in the lower-limbs is an important determinant of mobility limitation and falls in older women. Especially the more complicated mobility tasks and recurrent falls are affected by the asymmetrical deficit. However, the mechanisms in which the asymmetrical deficit affects mobility and balance function should be further studied. For example the relationship between muscle strength and mobility function is linear only in more frail older people. Potentially, a similar relationship may exist for the asymmetrical deficit and mobility as well. Also the importance of the stronger lower-limb in relation to the asymmetrical deficit needs further study.

This study also suggests that lower-limb pain, and lower-limb disease and injury burden are potential causes of strength deficits in older people that may affect lower-limb muscle strength on one side only, as established using cross-sectional data of people on average four years after hip fracture. The causes of asymmetrical deficit should be confirmed in studies with a longitudinal design.

Unfortunately, detecting exact changes due to fractures affecting the lower-limbs is impossible considering the absence of pre-event measures. The effects of changes in unilateral lower-limb pain or muscle strength deficit, for example by intervention, also need further study. Additionally, the effects of such changes in pain and muscle strength on mobility and balance function should be investigated.

The experimental study showed that an intensive PRT is feasible and safe to perform in hip fracture patients. Although muscle force and power improved due to the combined strength and power training, further study is needed to establish whether the asymmetrical deficit can be reversed by training and whether that affects mobility and balance function. A larger difference in the protocols for the stronger and weaker lower-limb may be needed, as pain may reduce muscle strength obtained in maximal measurements for the weaker and more painful lower-limb especially. However, people may be more responsive to the training in the rehabilitation phase shortly after major unilateral injury in the lower-limbs when the asymmetrical deficit is likely to be large. Considering that impairments in muscle strength, mobility and balance remained even years after the fracture, current rehabilitation strategies should be reviewed. Based on the results of this study, it seems that a multi-component rehabilitation program after hip fracture, including progressive resistance training and components such as pain management and strategies to reduce fear for falling, may especially be beneficial.

The results of this study may also have clinical implications. The results stress the importance of treating pain, diseases, and injuries affecting the lower-limbs to prevent further decreases in muscle strength and power, also when only one limb is affected and the risk for asymmetrical deficit increases. Poor muscle strength in one lower-limb may compromise mobility and balance, however, poor strength in both lower-limbs may be more debilitating. Therefore, current rehabilitation strategies after hip fracture and other lower-limb diseases and injuries should be reviewed to prevent decreases in lower-limb muscle strength. Increasing muscle strength by intensive rehabilitation including resistance training and pain management may prevent or reduce limitations in mobility and balance that may lead to loss of independence. Additional components such as reductions in fear for falling or functional training may also be useful as part of rehabilitation, however, this requires further study.

7 MAIN FINDINGS AND CONCLUSIONS

The main findings of the present study can be summarized as follows.

1. This study showed that healthy older women have a considerable asymmetrical deficit in leg extension power, i.e. a large side-to-side difference in lower-limb muscle strength.
2. In hip fracture patients, the asymmetrical deficit in lower-limb muscle power was extremely large especially in the first months after fracture. After a hip fracture, the fractured limb was weaker than the non-fractured limb. Although the asymmetrical deficit reduced over time, even on average four years after a hip fracture an asymmetrical deficit in muscle force, rate of force development and muscle power existed.
3. On average four years after hip fracture, the fractured limb was consistently weaker on the fractured side in about half of the people, while the other half had no consistent asymmetrical deficit or a deficit on the non-fractured side. The presence of osteoarthritis, fractures, and pain affecting the non-fractured limb reduced or even reversed the asymmetrical deficit, resulting in poor muscle strength in both lower-limbs.
4. A large asymmetrical deficit in leg extension power correlated with poor mobility and balance, especially in the more challenging tasks.
5. A large asymmetrical deficit predicted a higher risk for injurious falls, especially recurrent injurious falls.
6. In the hip fracture patients, muscle power in the non-fractured limb one week after surgical repair of the fracture predicted walking and stair climbing speed three months later. However, the improvement in power in the fractured limb, and not the improvement in the non-fractured limb, was associated with the improvement in walking and stair climbing speed over the first three months of recovery. The reduction in asymmetrical deficit was associated with the improvement in stair climbing speed over time.

7 An intensive progressive resistance training program designed to reduce the asymmetrical deficit and to increase muscle force and power of both lower-limbs was feasible for people six months to seven years after hip fracture. Muscle force and power increased by the training, especially on the weaker side. Only the asymmetrical deficit in leg extension power decreased significantly by the training. Training effects on performance-based mobility and balance function were less clear. Perceived difficulty in outdoor mobility and daily activities decreased, and self-rated health improved, after training.

In conclusion, the results of the present study suggest that an asymmetrical deficit in lower-limb muscle strength is common in older women encumbering mobility and balance function. The results additionally stress the importance of the recovery of muscle strength after hip fracture in the fractured limb especially. Lower-limb disease and injury burden, and lower-limb pain seem to play an important role in the development of asymmetrical strength deficits in older people. Intensive progressive resistance training is feasible in people after hip fracture, and it improved muscle strength of the lower-limbs, especially on the weaker side, although the asymmetrical deficit was not clearly affected. People may be more responsive to the training in the rehabilitation phase shortly after major unilateral injury when the asymmetrical deficit is likely to be large. Further study is needed to determine whether a multicomponent rehabilitation program including progressive resistance training and pain management prevents or reduces limitations in mobility and balance after unilateral disease or injury.

YHTEENVETO

Alaraajojen lihasvoiman puoliero iäkkäillä ihmisillä

Ihmisen lihasvoima ja voimantuottoteho (voiman ja liikenopeuden tulo), heikkenevät iän myötä. Tällainen heikkous alaraajoissa on yhteydessä liikkumiskyvyn alentumiseen sekä liikkumiskykyyn liittyviin toiminnan-vajauksiin. Vähäinen fyysinen aktiivisuus, kipu, sairaudet ja vammat heikentävät lihasvoimaa entisestään. Jos kipu, sairaus (esim. nivelrikko) tai vamma (esim. murtuma) kohdistuu vain toiseen alaraajan, se heikentää erityisesti kyseisen raajan lihasvoimaa ja voimantuottotehoa. Seurauksena on alaraajojen lihasvoiman puoliero. Esimerkiksi jopa vuosia lonkkamurtuman jälkeen alaraajojen lihasvoima on yleisesti heikko verrattuna terveisiin henkilöihin. Tämän lisäksi lonkkamurtuman kokeneilla henkilöillä murtunut alaraaja on toista alaraaja selvästi heikompi. Liikkumiskyvyn vaikeudet ovat yleisiä näillä henkilöillä ja ne saattavat liittyä ainakin osittain lihasvoiman heikkouteen. Alaraajojen lihasvoiman puolieron vaikutuksia on tutkittu vain vähän. Tiedetään, että alaraajojen lihasvoimapuoliero on suurempi henkilöillä, jotka kaatuvat useasti tai ovat kokeneet lonkkamurtuman. Murtuneen alaraajan lihasvoima ja voimantuottoteho ovat vahvemmin yhteydessä liikkumiskykyyn kun toisen alaraajan voimat.

Intensiivinen nousujohteinen lihasvoimaharjoittelu lisää iäkkäiden ihmisten lihasvoimaa ja voimantuottotehoa. Voimaharjoittelu saattaa myös parantaa liikkumiskykyä erityisesti niillä, joilla on liikkumiskyvyn vaikeuksia. Kliinisillä ryhmillä voimaharjoittelun vaikutuksia on kuitenkin tutkittu vain vähän ja alaraajojen lihasvoiman puolieroa, esimerkiksi lonkkamurtuman jälkeen, ei ole harjoittelun aikana juurikaan huomioitu. Lihasvoiman lisäämiseen ja alaraajojen lihasvoiman puolieron pienenemiseen suunnattu kuntosaliharjoittelu saattaa olla liikkumiskyvyn ja tasapainon hallinnan kannalta hyödyllisempää kuin perinteinen harjoitusohjelma.

Tässä tutkimuksessa selvitettiin alaraajojen lihasvoiman puolieron yhteyttä liikkumiskykyyn, tasapainoon ja kaatumisiin terveillä iäkkäillä naisilla sekä lonkkamurtumasta toipuvilla naisilla. Alaraajojen lihasvoiman puolieroon yhteydessä olevia tekijöitä selvitettiin henkilöillä, jotka ovat kokeneet lonkkamurtuman keskimäärin neljä vuotta aikaisemmin. Lisäksi selvitettiin voimanopeusharjoittelun vaikutuksia lonkkamurtuman kokeneiden henkilöiden alaraajojen lihasvoimaan, lihasvoiman puolieroon ja liikkumiskykyyn.

Tutkimuksessa hyödynnettiin kahta aikaisemmin koottua aineistoa ja kerättiin uusi kokeellinen tutkimusaineisto. Finnish Twin Study on Aging (FITSA) -tutkimukseen osallistui 419 tervettä 63–75-vuotiasta naista. Vaikka kyseessä on perinteinen kaksoisaineisto, henkilöt käsiteltiin yksilöinä siten, että sisarten välinen riippuvuus huomioitiin analyyseissä. HIP-RECOVERY tutkimukseen osallistui 43 lonkkamurtuman kokenutta 76–93-vuotiasta naista. Heidät tutkittiin viikko ja kolmetoista viikkoa lonkkamurtuman jälkeen. HIP-ASYMMETRY aineisto koostuu miehistä ja naisista, jotka ovat kokeneet lonkkamurtuman puoli - seitsemän vuotta aiemmin (n=79). Ne henkilöt, joilla ei ollut voimaharjoittelun vasta-aiheita (n=46), osallistuivat satunnaistettuun kontrolloituun kokeeseen. Tutkittavat satunnaistettiin kahteen tutkimusryhmään; voima-nopeusharjoitusryhmään (n=24) sekä verrokkiryhmään (n=22).

Kaikissa edellä mainituissa tutkimuksissa mitattiin maksimaalinen alaraajojen ojennuksen voimantuottotehoa molemmista jaloista. Lisäksi mitattiin molempien alaraajojen maksimaalinen isometrinen polven ojennusvoima ja voimantuottonopeus ensimmäisten 200 millisekunnin aikana, maksimaalinen tai tavanomainen kävelynopeus, portaiden nousunopeus, staattinen ja dynaaminen tasapaino sekä alaraajojen lihasmassa. Ulkona liikkumisen ja päivittäisten toimintojen vaikeudet, koettu terveys sekä alaraajojen kipu, -sairaudet ja -vammat arvioitiin. FITSA -tutkimuksessa kerättiin lisäksi vuoden seuranta-aineisto kaatumisista ja niiden aiheuttamista vammoista.

HIP-ASYMMETRY -tutkimuksen harjoitusryhmään satunnaistetut henkilöt osallistuivat ohjattuun 12 viikkoa kestäneeseen voima-nopeusharjoitteluun kahdesti viikossa. Harjoittelun tavoitteena oli lisätä alaraajojen lihasvoimaa ja pienentää alaraajojen lihasvoiman puolieroa. Harjoittelu koostui alaraajojen lihasryhmille suunnatuista nopeus (matala vastus, nopea konsentrinen supistusvaihe) ja voima (korkea vastus; 50–80% arvioidusta 1-toistomaksimista) -harjoitteista. Alkumittausten voimatulosten perusteella määritelty heikompaa alaraajaa harjoitettiin enemmän ja suuremmalla vastuksella kuin vahvempaa alaraajaa.

Tutkimuksen tulokset osoittavat, että terveillä iäkkäillä naisilla heikomman alaraajan voimantuottoteho oli noin 15 % alhaisempi vahvempaan jalkaan verrattuna. Lonkkamurtuman kokeneilla henkilöillä alaraajojen voimantuottoteho oli yleisesti alhaisempi ja lihasvoimapuoliero suurempi kuin terveillä iäkkäillä naisilla. Ensimmäisten kolmen kuukauden aikana lonkkamurtuman jälkeen voimantuottoteho kasvoi erityisesti murtuneella puolella ja puoliero pieneni. Voiman puoliero oli kuitenkin edelleen huomattava kolmen kuukauden ja jopa keskimäärin neljän vuoden kuluttua murtumasta. Keskimäärin neljä vuotta lonkkamurtuman jälkeen puolella tutkittavista murtunut alaraaja oli useilla eri voimatesteillä arvioituna johdonmukaisesti heikompi alaraaja. Toisella puolella tutkittavista taas ei havaittu alaraajojen lihasvoiman puolieroa tai murtuneen alaraajan sijaan toinen alaraaja oli heikompi. Näillä henkilöillä molempien alaraajojen lihasvoimat olivat heikko ja ei-murtuneessa alaraajassa oli myös enemmän kipua tai muita vaivoja. Kaiken kaikkiaan kipu, nivelrikko ja murtumat sekä pieni lihasmassa olivat yhteydessä kyseiseen alaraajan lihasvoiman heikkenemiseen. Alaraajoihin kohdistuva kipu oli ainoa voimantuottotehon puolieroa selittävä tekijä.

Tutkimus osoitti, että suuri alaraajojen lihasten voimantuottotehon puoliero oli yhteydessä hidastuneeseen kävelynopeuteen ja heikentyneeseen tasapainoon. Lisäksi voimantuottotehon puoliero oli yhteydessä vammoja aiheuttaviin kaatumisiin. Ensimmäisen kolmen kuukauden aikana lonkkamurtuman jälkeen molempien alaraajojen voimantuottoteho oli yhteydessä kävelynopeuteen sekä portaiden ylösnousunopeuteen. Jos ei-murtuneen alaraajan voimantuottoteho oli matala viikko lonkkamurtuman jälkeen, ennusti se huonoa kävelynopeutta vielä kolmen kuukauden kuluttuakin murtumasta. Alaraajojen lihasten suuri voimantuottotehon puoliero oli yhteydessä hitaaseen portaiden ylösnousunopeuteen sekä viikko että 13 viikkoa murtuman jälkeen. Lisäksi murtuneen alaraajan voimantuotto-tehon lisääntyminen sekä lihasvoiman puolieron pieneneminen ensimmäisen kolmen kuukauden aikana murtuman jälkeen olivat yhteydessä lisääntyneeseen portaiden ylösnousunopeuteen.

HIP-ASYMMETRY tutkimuksen kokeellinen osa osoitti, että yli 60-vuotiaat henkilöt, joilla on ollut lonkkamurtuma, pystyvät osallistumaan varsin turvallisesti ohjattuun intensiiviseen voima-nopeusharjoitteluun. Harjoitusryhmän osallistumisprosentti oli korkea eikä harjoittelun aikana tai sen seurauksena ilmennyt vakaavia harjoitteluun yhteydessä olevia komplikaatioita. Alaraajojen ojentajalihasten lihasvoima ja voimantuottoteho, erityisesti heikommalla puolella, lisääntyivät harjoittelun seurauksena. Lisäksi alaraajojen välinen voimantuottotehon puoliero pieneni merkitsevästi harjoitusryhmäläisillä verrokkeihin verrattuna. Harjoitteluun osallistuneiden henkilöiden dynaaminen tasapaino parani, mutta havaittu muutos ei eronnut verrokkiryhmässä havaitusta muutoksesta tilastollisesti merkitsevällä tavalla. Kävelynopeuteen harjoittelu ei vaikuttanut. Ulkona liikkumisen ja päivittäisten toimintojen vaikeudet vähenivät ja koettu terveys parani harjoittelun seurauksena.

Tutkimuksen tulokset osoittivat, että alaraajojen lihasvoiman puoliero on huomattava myös terveillä iäkkäillä naisilla ja se saattaa hankaloittaa liikkumista ja heikentää tasapainoa. Alaraajojen lihasvoiman puoliero saattaa syntyä alaraajan kivun, alaraajojen sairauksien tai vammojen seurauksena. Niillä lonkkamurtuman kokeneilla henkilöillä, joilla ei havaittu lihasvoiman puolieroa tai, joilla murtuneen alaraajan sijaan toinen alaraaja oli heikompi, oli kipuja sekä sairauksia tai vammoja toisessa alaraajassa. Näillä henkilöillä lihasvoima oli heikentynyt molemmissa alaraajoissa. Tutkimustulokset osoittavat lisäksi, että alaraajojen suurien vammojen, kuten murtumien, jälkeen lihasvoiman parantaminen saattaa olla liikkumiskyvyn kannalta erityisen tärkeää. Lonkkamurtuman kokeneiden henkilöiden alaraajojen lihasvoima ja voimantuottoteho lisääntyivät ja voimantuottotehon puoliero pieneni muutaman kuukauden voimanopeusharjoittelun seurauksena. Tasapainoon ja kävelynopeuteen harjoittelu ei vaikuttanut vaikka harjoitteluun osallistuneet kokivatkin myönteisiä harjoitusvaikutuksia liikkumiskykyyn ja päivittäisistä tehtävistä selviytymiseen. Intensiivinen alaraajojen lihasvoimaa lisäävä ja voimanpuolieroa vähentävä harjoittelu olisi syytä aloitetaan heti, kun se on murtuman jälkeen turvallista. Lonkkamurtuman jälkeisen kuntoutuksen tulisi voimaharjoittelun lisäksi sisältää kivunhoitoa ja harjoitteita, jolla voidaan parantaa tasapainoa ja vähentää kaatumisen pelkoa. Alaraajojen lihasvoimapuolieron ehkäisemiseen tulisi myös kiinnittää huomiota muiden alaraajojen sairauksien ja vammojen yhteydessä.

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