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COUNTERACTING SARCOPENIA AND FUNCTIONAL DECLINE

THROUGH RESISTANCE EXERCISE

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Acknowledgements – Dankwoord

> *"Training to the point of muscular failure may be necessary*
>
> *to optimize motor unit recruitment and thus to enhance the hypertrophic response"*

Of hoe één van de basisideeën in ons onderzoek naar de effecten van krachttraining plots ook van toepassing bleek voor het succesvol afronden van een doctoraat. Het is van minimaal belang welk traject je volgt. Het maakt niet uit of je nu één of vijf artikels gepubliceerd hebt. Dé noodzakelijke voorwaarde om *full motor unit recruitment* of je publieke verdediging te bereiken, is simpelweg doorgaan tot uitputting. Niet stoppen wanneer je denkt (het) moe te zijn, maar die laatste inspanning toch leveren. Al het potentieel trachten aan te sturen.

> *"All training sessions were closely supervised by qualified fitness instructors*
>
> *and participants were verbally encouraged to continue the exercises until failure"*

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> *"After climbing a great hill, one only finds that there are many more hills to climb."*
>
> *(Nelson Mandela)*

English summary

The aging of population poses many challenges to our society. A major public health concern is the age-related decline in functionality, which threatens the independency and quality of life of older adults. This functional decline has been shown to be associated with the phenomenon of sarcopenia, first introduced by dr. I.H. Rosenberg as the age-related decrease in skeletal muscle mass.

As our understanding of the complex process of aging progresses, proposed definitions of sarcopenia go beyond a decrease in muscle mass, including a reduction in muscle strength, in muscle power (the ability to generate force quickly), and in functional performance. Maintenance or even gain in muscle mass at age does not necessarily prevent muscle weakness. Previous findings imply that muscle power and the ability to develop a high velocity during muscle contraction are strong predictors of everyday function of older adults, whereas muscle mass seems less decisive for activities of daily living. Thus, for the detection of preclinical functional limitations, attention should also be paid to force-velocity characteristics of skeletal muscle. However, there is a paucity of research regarding the relationship between these force-velocity characteristics, muscle mass and functional limitations in older adults.

Resistance training is widely recognized as an important countermeasure against muscle atrophy, muscle weakness and functional decline. In order to maximize gains in muscle strength and mass, international guidelines currently recommend training at high external resistances (70-85% of one repetition maximum (1RM)). However, the use of such high resistances may sometimes be contraindicated in older adults, suggesting that low-resistance exercise protocols might be more suitable. To date, research remains inconclusive on whether low-resistance exercise is as effective as high-resistance exercise in inducing hypertrophy and strength gains in older adults. There is some evidence that achieving maximal effort in training protocols may be necessary to maximize training-induced gains.

This doctoral thesis consists of two chapters. In **chapter 1**, we focus on gaining a better insight in the relationship between force-velocity characteristics, muscle mass and functional performance in elderly persons. **Chapter 2** investigates the feasibility and the effects of strength training at different external resistances on muscle performance and functional capacity.

In **chapter 1**, discussed in *paper 1* of this doctoral thesis, the main objective was to determine the relative contribution of muscle strength, force-velocity characteristics and muscle mass to functional performance. Subjects were 123 elderly women (aged 79.67 ± 5.25 years). The results emphasize the role of muscle strength and speed of movement of the knee extensors in everyday

function of elderly women. Muscle mass, however, was not an independent determinant of functional performance when included in the same regression model as muscle strength, suggesting that muscle mass primarily contributes to functional performance through its association with muscle strength. This highlights the importance to focus on several aspects of muscle function in addition to muscle mass, not only when identifying persons at risk for functional limitations but also when designing exercise interventions to prevent functional decline.

Chapter 2 of this doctoral thesis consists of two subchapters.

Subchapter 2.1 (*paper 2*) explored the feasibility of an experimental high-repetition low-resistance exercise protocol in young adults, so that it could be fine-tuned before applying it to older adults. *Paper 2* additionally investigated the impact of external resistance and maximal effort in strength training programs on muscle strength and force-velocity characteristics in young adults (N = 36). Two low-resistance exercise protocols were created and compared to high-resistance exercise (HI_{max}) over a 9-week training period: one low-resistance protocol ending in maximal effort (LO_{max}), one low-resistance protocol without achieving maximal effort (LO). All training groups performed one set of 10 to 12 repetitions, but training intensity differed between groups. HI_{max} trained at a resistance of 80% of 1RM ending in maximal effort; LO trained at a resistance of 40% of 1RM without achieving maximal effort; LO_{max} trained at a resistance of 40% of 1RM (similar to LO), preceded by a fatiguing protocol of 60 repetitions at 20% of 1RM. No rest was provided between sets, which led to maximal effort in LO_{max}. The findings in *paper 2* suggest that training until maximal effort, probably resulting in optimal activation of the muscle, is needed to optimize strength gains in low-resistance exercise protocols. Interestingly and unexpectedly, the experimental high-repetition low-resistance exercise protocol (LO_{max}) showed promising and advantageous results on dynamic strength and speed of movement.

Subchapter 2.2 (*papers 3 and 4*) aimed at comparing the effects of high- and low-resistance exercise on muscular and functional outcomes in older adults (N = 56). In *paper 2*, LO_{max} appeared to be effective in inducing strength gains in young adults, but it remained to be elucidated whether this exercise protocol was also effective in older adults. In addition, the resistance exercise protocols in *paper 2* did not allow for conclusions on whether or not the increase in resistance at the end of a single low-resistance exercise set (see LO_{max}) is crucial for optimal effects. Therefore, two low-resistance exercise protocols were created and compared to high-resistance exercise (HIGH) in *papers 3 and 4*: one high-repetition low-resistance protocol (LOW) in which external resistance is kept constant within one session, one mixed high-repetition low-resistance protocol (LOW+) in which resistance was increased after 60 repetitions (similar to LO_{max}

in *paper 2*). All protocols were designed to end in maximal effort. *Paper 3* focused on the immediate post-intervention effects after 12 weeks of training, whereas *paper 4* evaluated the residual adaptations 24 weeks after the end of the intervention. *Paper 4* additionally investigated the long-term exercise adherence of participants in HIGH, LOW and LOW+. The results of **subchapter 2.2** suggest that high- and low-resistance exercise protocols until muscle failure are equally able to counteract the age-related declines in muscle mass, basic muscle strength (isometric and isokinetic strength at low speed) and functional performance. Our data also suggest the importance of long-term maintenance of resistance exercise behavior for increasing or maintaining muscle mass and muscle function, but indicate that various aspects of muscle strength and functional performance remain elevated for several months after the end of a supervised training intervention. When compared at follow-up, low-resistance exercise until muscle failure appears to be as effective as high-resistance exercise for maintaining training-induced neuromuscular and functional adaptations. These findings point out that it is time to re-think or at least nuance the high-resistance training philosophy that has gone unchallenged for decades. Low-resistance exercise is valuable in older age as alternative to high-resistance exercise. However, long-term maintenance of resistance exercise behavior remains a challenge among older adults.

Dutch summary – Samenvatting

De algemene voortschrijdende trend van vergrijzing leidt tot een zorgwekkende toename van het aantal ouderen dat fysiek niet langer in staat blijkt om dagdagelijkse taken onafhankelijk te verrichten. Deze vorm van fysieke fragiliteit is geassocieerd met sarcopenie, wat voor het eerst gedefinieerd werd door dr. I.H. Rosenberg als de leeftijdsgebonden daling in spiermassa.

Naarmate ons inzicht omtrent de complexiteit van het verouderingsproces toeneemt, wordt het duidelijk dat de aanvankelijk enge definitie van sarcopenie veel ruimer gezien moet worden. Immers, veroudering gaat ook gepaard met een daling in spierkracht en in spierpower (het snel kunnen produceren van kracht). Men heeft zelfs aangetoond dat het behoud van spiermassa op leeftijd niet voldoende is om spierzwakte tegen te gaan. Meer nog, spierpower en de capaciteit van de spieren om hoge snelheden te halen bij spiercontracties blijken cruciale factoren te zijn in de fysieke prestatie van ouderen, terwijl spiermassa minder doorslaggevend is voor dagdagelijkse activiteiten. Voor het identificeren van ouderen met een verhoogd risico op het ontwikkelen van functionele beperkingen, moet er dus aandacht gegeven worden aan krachtsnelheids-karakteristieken van de spier. Er is echter op dit moment nood aan verder onderzoek naar de relatie tussen krachtsnelheidskarakteristieken, spiermassa en functionele beperkingen bij ouderen.

Om de leeftijdsgebonden daling in spiermassa, spierkracht en functionaliteit tegen te gaan, wordt krachttraining naar voor geschoven als de beste methode. Om optimale winsten in spierkracht en spiermassa te realiseren, stellen internationale richtlijnen een belasting van 70-85% van het individueel krachtmaximum (one repetition maximum = 1RM) voorop. In de praktijk blijken heel wat ouderen, omwille van fysieke beperkingen (bv. gewrichtspijn), echter vaak niet in staat om te trainen met deze relatief hoge weerstand. Krachttraining aan lage weerstand zou dus meer geschikt kunnen zijn voor ouderen. Echter, tot op heden blijft het onduidelijk of krachttraining aan lage weerstand even effectief kan zijn bij ouderen voor het induceren van spierhypertrofie en krachtwinst als krachttraining aan hoge weerstand. Wel is er reeds indicatie dat het bereiken van lokale spiervermoeidheid cruciaal kan zijn in het maximaliseren van krachttrainingsadaptaties.

Deze doctoraatsthesis bestaat uit twee hoofdstukken. In **hoofdstuk 1** wordt er gefocust op het verwerven van inzicht in de relatie tussen krachtsnelheidskarakteristieken, spiermassa en functionele beperkingen bij ouderen. In **hoofdstuk 2** worden de haalbaarheid en de spier- en functionele adaptaties van verschillende krachttrainingsprotocollen onderzocht.

De hoofddoelstelling van **hoofdstuk 1**, wat u kan lezen in *paper 1* van deze doctoraatsthesis, was het bepalen van de relatieve bijdrage van spierkracht, krachtsnelheidskarakteristieken en

spiermassa tot functionaliteit. De proefgroep bestond uit 123 oudere vrouwen (leeftijd = 79.67 ± 5.25 jaar). De resultaten van deze studie benadrukken de rol van spierkracht en bewegingssnelheid van de knie-extensoren in functionele taken bij oudere vrouwen. Spiermassa was daarentegen geen onafhankelijke determinant van functionaliteit wanneer het geïncludeerd werd in hetzelfde regressiemodel als spierkracht, wat erop wijst dat de associatie tussen spiermassa en functionaliteit hoofdzakelijk te wijten is aan de link tussen spiermassa en spierkracht. Dit beklemtoont het belang van spierfunctie, meer nog dan dat van spiermassa, voor het identificeren van personen met een verhoogd risico op functionele beperkingen en voor het ontwikkelen van trainingsinterventies gericht op preventie van functionele achteruitgang.

Hoofdstuk 2 van deze doctoraatsthesis bestaat uit twee subhoofdstukken.

Subhoofdstuk 2.1 (*paper 2*) onderzocht de haalbaarheid van een experimenteel krachttrainingsprotocol aan lage weerstand en een groot aantal herhalingen bij jongvolwassenen, zodat het bijgestuurd kon worden alvorens het toe te passen bij ouderen. Daarenboven onderzocht *paper 2* de impact van externe weerstand en lokale spiervermoeidheid op spierkracht en krachtsnelheidskarakteristieken in krachttrainingsprogramma's bij jongvolwassenen (N = 36). Twee krachttrainingsprotocollen aan lage weerstand werden ontwikkeld en vergeleken met krachttraining aan hoge weerstand (HI_{max}) over een trainingsperiode van 9 weken: één protocol aan lage weerstand waarbij getraind werd tot vermoeidheid (LO_{max}), één protocol aan lage weerstand waarbij niet getraind werd tot vermoeidheid (LO). Alle trainingsgroepen voerden één set uit van 10 tot 12 herhalingen, maar de trainingsintensiteit verschilde tussen de groepen. HI_{max} trainde aan een weerstand van 80% van 1RM en voerde herhalingen uit tot vermoeidheid; LO trainde aan een weerstand van 40% van 1RM zonder door te gaan tot vermoeidheid; LO_{max} trainde aan een weerstand van 40% van 1RM (idem als LO), maar dit werd voorafgegaan door een protocol van 60 herhalingen aan 20% van 1RM. Er was geen rust toegestaan tussen sets, zodat LO_{max} ook trainde tot vermoeidheid. De bevindingen van *paper 2* suggereren dat trainen tot lokale spiervermoeidheid, wat waarschijnlijk resulteert in een optimale activatie van de spier, noodzakelijk is om krachtwinsten te optimaliseren in trainingsprotocollen aan lage weerstand. Het experimentele krachttrainingsprotocol aan lage weerstand en een groot aantal herhalingen vertoonde veelbelovende resultaten op dynamische spierkracht en bewegingssnelheid.

Subhoofdstuk 2.2 had als doel om de effecten van krachttraining aan hoge en lage weerstand te vergelijken met betrekking tot spier- en functionele adaptaties bij ouderen (N = 56). In *paper 2* bleek LO_{max} effectief om krachtwinsten te induceren in jongvolwassenen, maar het was nog onduidelijk of dit protocol ook effectief zou zijn bij ouderen. Bovendien lieten de krachttrainingsprotocollen in *paper 2* niet toe om te concluderen of het verhogen van de

weerstand op het einde van het protocol (zie LO_{max}) noodzakelijk is voor optimale effecten. Daarom werden er opnieuw twee krachttrainingsprotocollen aan lage weerstand ontwikkeld en vergeleken met krachttraining aan hoge weerstand (HIGH) in *papers 3 en 4*: één protocol met een groot aantal herhalingen waarin de weerstand constant bleef tijdens een trainingssessie (LOW), één protocol met een groot aantal herhalingen waarin de weerstand verhoogd werd na 60 herhalingen (LOW+) (gelijkaardig aan LO_{max} in *paper 2*). Alle trainingsprotocollen eindigden ditmaal in lokale spiervermoeidheid. In *paper 3* werden de resultaten na 12 weken training gerapporteerd, terwijl in *paper 4* nagegaan werd welke adaptaties behouden bleven 24 weken na het einde van de interventie. Daarenboven werd in *paper 4* onderzocht in welke mate onze interventies geleid hadden tot een blijvende deelname aan krachttraining op lange termijn. De resultaten van **subhoofdstuk 2.2** tonen dat krachttraining aan hoge en lage weerstand tot lokale spiervermoeidheid even effectief zijn in het tegengaan van leeftijdsgebonden dalingen in spiermassa, spierkracht en functionaliteit. Onze data duiden ook op het belang van het volhouden van krachttraining voor het verbeteren of behouden van spiermassa en spierfunctie, maar ze geven ook aan dat verschillende neuromusculaire en functionele adaptaties na het beëindigen van een gesuperviseerd trainingsprogramma nog gedurende meerdere maanden gedeeltelijk behouden blijven. Dit behoud in spierkracht en functionaliteit is gelijk na krachttraining aan hoge of lage weerstand. De studie onderstreept hiermee dat de huidige krachttrainingsfilosofie, waarbij hogere weerstanden als beter beschouwd worden, in vraag gesteld of op zijn minst genuanceerd moet worden. Krachttraining aan lage weerstand is waardevol bij ouderen als alternatief voor krachttraining aan hoge weerstand. Het blijft wel een uitdaging voor ouderen om krachttraining langdurig vol te houden.

PART 1

GENERAL INTRODUCTION AND OUTLINE

The aging of the population is emerging worldwide as a major demographic trend. In one sense, it represents a human success story of increased longevity. However, it also poses many challenges to our society (63). A major public health concern is the age-related decline in functionality, which threatens the independency and quality of life of older adults. This functional decline has been shown to be associated with sarcopenia (9,57,59,80). It is clear that effective interventions are needed to counteract sarcopenia and functional decline. This introduction will first focus on the definition of sarcopenia and its relationship with functional outcomes.

1. Sarcopenia and functional decline

1.1. Towards an operational definition of sarcopenia

What is sarcopenia? What once seemed a simple Greek translation of 'poverty (penia) of flesh (sarx)', is nowadays an evolving concept with researchers worldwide striving for a consensus definition and for recognition of the condition among geriatricians (1,39).

The term sarcopenia was introduced by dr. Irwin Rosenberg and was originally defined as the age-related loss in skeletal muscle mass (35,98,99). Sarcopenia is considered as a normal part of the biological aging process (23). It is not a disease in itself, but illness can accelerate the age-related loss in muscle mass and thus aggravate sarcopenia (100). Functional decline will occur when an individual has lost enough muscle mass to cross a threshold for disability.

In 1998, Baumgartner and colleagues were the first to propose an operational definition of sarcopenia based on skeletal muscle mass (9). They summed the lean mass of the four limbs, measured by means of Dual energy X-ray Absorptiometry (DXA), and defined this as appendicular skeletal muscle mass (ASM). A skeletal muscle mass index (SMI) was then calculated as $ASM/height^2$ (kg/m²). Individuals with a SMI of two or more standard deviations (SD) below the sex-specific mean SMI of a young reference population (Rosetta Study (46), 7.26 kg/m² for men and 5.45 kg/m² for women) were defined as sarcopenic. Delmonico and colleagues (30) used the SMI proposed by Baumgartner (9), but redefined the cutpoints. Individuals were classified as sarcopenic if their value fell into the sex-specific lowest 20% of the distribution of the index in the Health ABC Study. These cutpoints (7.25 kg/m² for men and 5.67 kg/m² for women) were very similar to those of Baumgartner (9). Several other cutpoints for sarcopenia have been proposed, strongly depending on the method used for determination of muscle mass as well as on the reference population used (for an overview, see Bautmans et al. (11)).

Sarcopenia is nowadays considered as a dynamic process characterized by progressive and generalized loss in muscle mass and muscle function with a risk of physical disability. The

abovementioned criteria to operationalize sarcopenia were thus not able to capture the whole spectrum of sarcopenia as the indexes were only based on muscle mass. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) recommended the use of both low muscle mass and low muscle function (strength or performance) for the diagnosis of sarcopenia (28). An algorithm based on the preliminary screening of low usual gait speed (≤ 0.8 m/s) and low handgrip strength (≥ 2SD below the mean reference value) was proposed to identify sarcopenia in clinical practice. If at least one of both measurements is impaired, DXA-analysis of muscle mass is recommended. If the skeletal muscle mass index falls ≥ 2SD below the mean reference value, the individual is considered sarcopenic. Although important steps towards a consensus definition of sarcopenia have been taken, a global consensus on the use of the term sarcopenia has not yet been achieved (82).

The prevalence of sarcopenia is dependent on the population studied and the definition used. Bautmans et al. give an overview of prevalence values covering several continents and races (11). The New Mexico Elder Health Survey by Baumgartner et al. (9) showed that prevalence of sarcopenia increased from 13-24% in persons under 70 years of age to >50% in persons over 80 years of age.

Similar to the ongoing debate on the diagnostic criteria for sarcopenia, the underlying mechanisms of the age-related changes in the muscle are not yet clearly understood. Multiple, interrelated factors appear to be involved in the onset and the progression of sarcopenia. Among others, these factors include genetic susceptibility, alterations in protein synthesis, changes in the hormone and cytokine signaling, nutrition, physical activity levels, and increased oxidative stress (39,82).

1.2. Aging of muscle

1.2.1. Age-related changes in muscle mass and morphology

Total muscle mass has been shown to peak at the age of about 24 years, with only a modest decrease (10%) between 24 and 50 years of age (33). From the fifth decade on, an annual decrease in muscle mass of about 1% is reported (33,68,82), resulting in a total decrease of about 40% in muscle mass between the ages of 24 and 80 years (33).

One of the factors contributing to age-related muscle atrophy is a loss in motor units. A motor unit consists of a single motor neuron and the muscle fibers innervated by its branches (Figure 1).
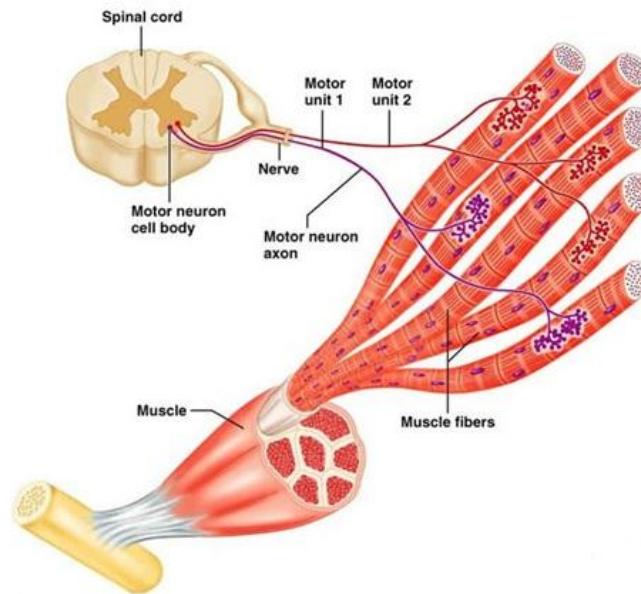
Figure 1. The motor unit, consisting of a single motor neuron and the muscle fibers innervated by its branches. Adapted from Marieb (76).

Slow motor units contain the smallest number of fibers and consist of type I fibers. These fibers contract with relatively slow velocity and generate low force, but are fatigue-resistant. Fast motor units generate more force and have higher contraction velocities, but are less fatigue-resistant. They contain a higher number of fibers and consist of type II fibers.

With aging, the number of both slow and fast muscle fibers decreases, with an accelerated loss in the number of fast muscle fibers (34,68). Muscle fibers are lost via denervation. De-innervated fibers will either be re-innervated by the surviving motor units or will disappear. Re-innervated fibers then change their fiber type to that of the motor unit, resulting in a net conversion of type II fibers to type I fibers (68). In addition to this fast-to-slow fiber type transformation, there appears to be an age-related selective atrophy of the type II fibers (34,68). These age-related morphological changes result in the weakening and slowing of muscles.

1.2.2. Age-related changes in muscle strength and power

Although muscle mass accounts for a small fraction (< 10%) of the loss in muscle strength and power (i.e. the ability to generate force quickly), it is far from the sole or even primary explanatory variable (24,31,82). Muscle strength declines with advancing age at an average rate of 2 to 4% per year. These decline rates are 2-5 times greater than the loss in muscle mass (31,82). Declines in muscle power are even more dramatic and start earlier in the aging process than the declines in muscle mass and strength (25,56,69,92). Furthermore, maintenance or gain in muscle mass does not necessarily prevent age-related declines in muscle strength and power (75).

This dissociation between the loss in muscle mass and in muscle strength and power can partly be explained by the abovementioned selective atrophy and denervation of the type II fibers. In addition, neural changes, such as a decline in motor unit recruitment and in motor unit discharge rates, contribute to this dissociation (24).

1.3. Relationship between sarcopenia and functional performance

Increased clinical and epidemiological interest in sarcopenia is related to the hypothesis that aging of muscles results in functional limitations and subsequent disability among elderly (96). Supporting this hypothesis, several cross-sectional studies established a significant association between low muscle mass and physical disability (9,57-59,80).

Although numerous reports support the importance of muscle mass in (the onset of) functional limitations, evidence suggests that muscle mass primarily contributes to functional performance through its association with muscle strength (75,116). In comparison with muscle strength, muscle mass is a weak and inconsistent predictor of functional performance. Lauretani and colleagues demonstrated that knee extension isometric torque and handgrip strength were strong predictors of poor mobility, defined either as walking speed < 0.8 m/s or inability to walk at least 1km without difficulty. Calf muscle area was much less decisive (70). Data from the Korean Longitudinal Study on Health and Aging revealed that muscle mass was not associated with physical performance in weak older adults. This study concluded that measures of muscle strength may be of greater clinical importance in weak older adults than muscle mass (62). In line with these findings, a previous study from the Health, Aging and Body Composition database showed that quadriceps and grip strength, and not muscle mass, were predictive of mortality (85). As muscle power decreases earlier and more precipitously with aging, a series of studies have focused on the relationship between muscle power and functional performance in older adults. These studies showed that muscle power explained more of the variability in functional performance than muscle strength (12,13,41). More specifically, the velocity component of muscle power appeared to be crucial in functional and balance performance in older adults (26,29,78,89,102).

1.4. Prevention or treatment of sarcopenia?

It is better to prevent or at least postpone the loss in muscle mass and muscle function rather than to try to restore it in old age when functional limitations and disability are already prominent. In theory, the target populations for preventive interventions are those people who are at risk of developing a specific condition. In the context of sarcopenia, this is particularly

difficult as the definition of sarcopenia is still lacking consensus and as every living being is exposed to this age-related phenomenon (23). It should by now be clear that, instead of solely focusing on muscle mass, muscle strength and power deserve attention in the prevention of functional decline.

Current evidence suggests that no nutritional, pharmacological or behavioral intervention has been proven to be as efficacious against sarcopenia as resistance exercise (2). Therefore, this introduction will mainly focus on the potential benefits of resistance exercise.

2. Resistance exercise as countermeasure against sarcopenia

2.1. Adaptations to resistance exercise

Despite the deteriorating effect of aging, muscles remain trainable even in old age (85,86,106). Previous research concluded that muscles, even of old (17,45) or elderly (38) individuals, have the potential to increase in size and strength in response to high-resistance exercise training. These results clearly indicate that we should never accept muscle aging as an unalterable process of loss (90).

Resistance exercise induces a wide range of morphological and neural adaptations. The primary morphological adaptations involve an increase in the cross-sectional area of the whole muscle and of the individual muscle fibers, with a preferential hypertrophy of type II fibers. Neural adaptations are essentially changes in coordination and learning that facilitate improved recruitment and activation of the involved muscles during a specific strength task. These adaptations involve increased motor unit recruitment and firing frequency, increased motor unit synchronization, and decreased antagonist co-activation (43). It is generally accepted that early strength gains (4 to 6 weeks) following resistance exercise are predominated by neural adaptations. As the duration of training increases, muscle hypertrophy also contributes to the strength and power gains observed (40).

2.2. Resistance exercise prescription

2.2.1. Program design and training variables

A resistance training program can be described by many training variables. These training variables serve as a framework of one specific resistance training session. The choices made regarding each training variable result in specific adaptations (40). Fleck and Kraemer determined five training variable clusters: choice of exercise, order of exercise, training intensity, training

volume and rest period lengths between sets and exercises (40). Training intensity and volume are considered as the principle program variables (112).

Training intensity is reflected by the load or resistance used. Other training variables or factors such as loading form, training to failure, speed of contraction, psychological factors, interset recovery, order of exercise, and number of sessions per day are related to the training intensity (112). The training load or resistance can be prescribed in different ways: as an absolute load lifted per repetition (in kg), as a specified number of repetition maximum (RM), or as a specified percentage of the 1RM. The RM represents the heaviest load or resistance that can be lifted for a specified number of times. Prescribing the RM (i.e. using the actual repetitions performed to dictate the load and not vice versa) is probably the easiest method for determining the resistance. Typically, a training RM target (such as 10RM) or RM target zone (a range such as 8-12RM) is used. As the strength level increases over time, the resistance is adjusted so that the number of repetitions completed is unchanged. This method reduces the chance of "over-" or "undershooting" the desired training zone (40,112).

Research has supported a basis for an RM continuum (Figure 2) (32). While training with loads corresponding to 1-6RM might be most beneficial for increasing maximal strength and power, 6-12RM appears to be most effective for increasing muscular hypertrophy. Lighter loads (15$^+$RM) have smaller effects on maximal strength, but are preferable for local muscular endurance (40).
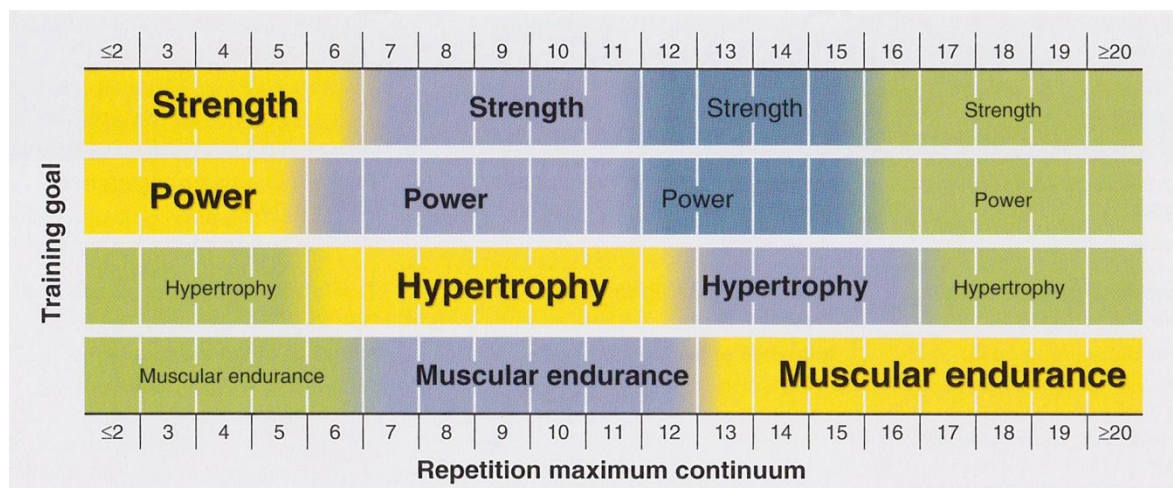
Figure 2. The repetition maximum continuum, adapted from the National Strength and Conditioning Association (83).

Training volume is the total work performed in a specified time. It is generally calculated as: (a) total repetitions = sets x repetitions per set; or (b) volume load = sets x repetitions per set x resistance used (% 1RM) (65,112). One aspect of training volume that has been intensively

studied is the number of sets performed per exercise. A meta-analysis of Krieger demonstrated that multiple sets are associated with greater hypertrophy and strength gains than a single set, in both trained and untrained individuals (66,67). However, it may be argued that multiple sets of resistance exercise do not facilitate additional neuromuscular adaptations compared to a single set during the early phase of training (first 10 weeks) in previously untrained individuals (21).

2.2.2. Current recommendations for resistance exercise

Current guidelines for health-related resistance exercise training have been developed by the American College of Sports Medicine (ACSM). These guidelines recommend training each major muscle group for 2-4 sets on 2-3 days a week. To improve muscular strength, mass, and endurance, a resistance that allows an individual to complete 8-12 repetitions per set should be used. This translates to a resistance of about 60-80% of the 1RM. For older adults, the guidelines suggest to begin with a resistance training program conducting more repetitions (10-15) at 60-70% of 1RM (6). Recommendations for maximizing muscle hypertrophy in untrained individuals are as follows: performing 8-12 repetitions per set with a resistance of 70-85% of the 1RM for 1-3 sets per exercise (7).

2.2.3. Periodization of resistance training

Chapter 1.3 of this introduction highlighted the importance of muscle power in the daily functioning of older adults. If the goal of fitness instructors is to increase independence and reduce the probability of falls in older adults, they should consider adding power to the training goals in program designs. Strength training at very high resistances (1-6RM, see Figure 2) or at lower resistances with the intention to develop the highest possible speed during exercise is preferred to increase muscle power and speed of movement. However, although not documented, both the use of very high resistances (>80% 1RM) as well as ballistic (explosive, moving as fast as possible) training techniques might increase the risk for injuries in untrained older individuals. In line with this concern, a previous 12-week intervention study in older adults reported that the dropout rate was more than twice as high in a power training group than in a traditional strength training group (118).

When training for power, a proper periodization design is warranted. This design starts with training cycles that target muscular hypertrophy and strength in order to toughen the tissues in preparation for the added stress of power training. The following chapters of this introduction, as well as the outline of this doctoral thesis, will focus on targeting hypertrophy and muscle strength as prerequisites for speed and power production.

2.3. High-resistance exercise in older adults: overview and challenges

In 1988, Frontera et al. reported that high-resistance exercise training can induce gains in strength and size of the quadriceps muscle of older men aged between 60 and 72 years (45). Since then, numerous studies have documented the benefits of high-resistance exercise in older adults, even in elderly individuals over 90 years of age (38). Table 1 summarizes the results of some of the recent studies that have investigated the effects of high-resistance exercise on muscle strength and size of the quadriceps (3,10,15,16,19-21,36,37,47,51,53,61,64,72,94,95,101,104,105,109, 110,113) and used program designs that correspond to the current guidelines described in chapter 2.2.2 (6,7). All of these studies designed a resistance exercise program with a frequency of 2-3 times a week, where subjects performed 1-4 sets of 8-15 repetitions per exercise at high external resistances (≥70% of 1RM).

Despite the well-documented benefits of high-resistance exercise in old age, therapists still remain skeptical about the use of such high resistances in older adults (2). It has been demonstrated that high-resistance exercise, when appropriately performed or supervised, does not cause orthopedic and cardiovascular problems even in older adults (49). However, adverse events appear to be reported more often in strength training trials that apply high-resistance exercise as compared to lower-resistance exercise in older adults (73). Exercise protocols consisting of lower resistances might thus be more suitable in older adults. The following chapter will discuss a theory that questions the necessity of high external resistances for optimal effects on neuromuscular adaptations.

Table 1. Effect of high-resistance training on muscle strength and size of the quadriceps muscle in older adults

Authors	Subjects			Training program						% change		
	Age	Gender	N	Exercise	Duration (weeks)	Sessions per week	Sets	Repetitions	% of 1RM	1 RM	MVC	CSA
Ades et al. 2005	73	F	21	LE, LP	24	3	1-2	10	80	47	-	-
Bautmans et al. 2005	69	M/F	31	LP	6	3	3	10	70	83	-	-
Binder et al. 2005	83	M/F	50	LE, LP	12	3	3	8-12	70	43	-	-
Bogaerts et al. 2007	67	M	30	LE, LP	52	3	1-2	8-15	8-15RM	-	13	3.8
Candow et al. 2006	59-76	M	29	LP	12	3	3	10	70	22-31	-	-
Candow et al. 2011	60-71	M	17	LE, LP	22	3	3	10	10RM	-	-	11
Cannon et al. 2010	60-78	F	15	LE	10	3	1-3	10	75	27	20	9
Fatouros et al. 2005	71	M	14	LE	24	3	2-3	8	80	99	-	-
Fatouros et al. 2006	71	M	14	LP	24	3	3	8	80	63	-	-
Galvao and Taaffe 2005		M/F	28	LE, LP	20	2	1-3	8	8RM	9-17	9-26	-
Harris et al. 2004	61-85	M/F	18	LE, LP	18	2	3	9	9RM	64	-	-
Henwood and Taaffe 2006	70	M/F	22	LE, LP	8	2	3	10	75	22	-	-
Kalapotharakos et al. 2005	65	M/F	11	LE	12	3	3	8	80	76	-	10
Kosek et al. 2006	60-75	M/F	25	LE, LP, S	16	3	3	8-12	8-12RM	33-49	-	-
Lemmer et al. 2007	70	M/F	21	LE, LP	24	3	1	15	75	24-26	-	-
Reynolds et al. 2007	66	M/F	13	LP	16	3	2	10-12	75	102	-	-
Roelants et al. 2004	64	F	20	LE, LP	24	3	2-3	10-15	10-15RM	-	18	-
Sayers et al. 2010	70	M/F	13	LE, LP	12	3	3	8-10	80	26	-	-
Seynnes et al. 2004	82	M/F	22	LE	10	3	3	8	80	57	-	-
Slivka et al. 2008	80-86	M	6	LE	12	3	3	10	70	41	-	2.5
Strasser et al. 2009	74	M/F	15	LP	24	3	1-2	10-15	10-15RM	15	-	-
Taaffe et al. 2009	65-84	M/F	13	LE, LP	24	2	3	8	75	33-68	-	NS
Tarnopolsky et al. 2007	65-85	M/F	18	LE, LP	24	2	3	12	75	31-49	14-22	-

M = male; F = female; LE = leg extension; LP = leg press; S = squat; 1RM = one repetition maximum; MVC = (isometric) maximal voluntary contraction; CSA = muscle cross-sectional area; NS = non-significant.

2.4.   Motor unit activation and the size principle

The mechanisms underlying neuromuscular adaptations involve many factors, that is, mechanical, metabolic, endocrine and neural factors (48). A well-documented key issue is the external resistance at which the training is performed (27,42,79). As mentioned previously, international guidelines, supported by the repetition maximum continuum in Figure 2, recommend training at high resistances (>60% of 1RM) for gains in muscle strength and mass (6). This high-resistance training philosophy has gone unchallenged for decades. But is the use of such high resistances really necessary to optimize neuromuscular adaptation?

Motor units will only adapt to exercise if they are recruited during exercise. Thus, if the training goal is to optimize neuromuscular gains, the main focus of resistance exercise should be to recruit as much motor units as possible (full motor unit recruitment). Henneman's size principle of motor unit recruitment states that, when the central nervous system recruits motor units for a specific activity, it starts with the smallest, more easily excited, least powerful motor units (type I) and progresses to the larger, more difficult to excite, most powerful motor units (type II) to maintain or increase force (22,52) (Figure 3). The statement that recruitment of the larger motor units is only possible with high resistances or when high forces are needed (40), appears to be based on a misapplication of the size principle (22). Of course, a non-fatiguing isometric contraction at 20% of the individual's maximum will recruit less motor units than a non-fatiguing isometric contraction at 80% (4). However, when a submaximal weight is lifted to the point of failure, initially recruited motor units will fatigue and recruitment of larger motor units is required to maintain the force necessary to complete any RM set. According to the size principle, it simply requires a maximal or near maximal effort to reach (near) full motor unit recruitment (22). Maximal effort is typically reached at the end of a series of repetitions when the subject is no longer able to perform an additional repetition. For example, 12RM describes a set where the 12th repetition is a maximal effort, with the inability to execute a 13th repetition.

The size principle thus presents a theoretical framework for low-resistance exercise as an alternative to high-resistance exercise, by suggesting that reaching maximal effort might be more important than the use of high resistances.
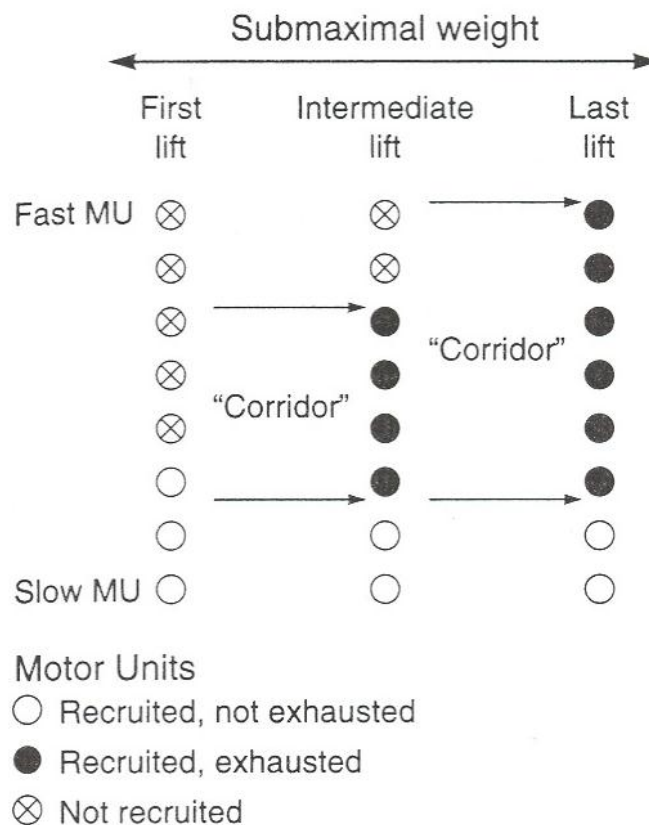
Figure 3. The size principle of motor unit recruitment, adapted from Zatsiorsky (117). The "corridor" represents the motor units that are subjected to the training stimulus.

2.5. Low-resistance exercise: an alternative to high-resistance exercise?

Several studies already pointed out the importance of muscle fatigue (or maximal effort) in the optimization of neuromuscular adaptations. Schott et al. revealed that long continuous isometric contractions appeared to be superior compared to short intermittent isometric contractions for gains in muscle size and strength after 14 weeks of training (103). Rooney et al. reported a significantly greater increase in muscle strength following 6 weeks of resistance exercise in a strength regimen without rest (6RM) compared to a strength regimen at similar resistance but with a 30 second rest period between each of the 6 contractions (97). In line with these findings, Goto et al. demonstrated that a 12-week resistance exercise regimen at 10RM induced greater hypertrophy and strength gains when performed with no rest compared to with a 30 second rest period at the midpoint of a set (48).

Supporting the theoretical framework of the size principle, studies in young adults provide evidence for similar hypertrophy and strength gains following low-resistance exercise as compared to high-resistance exercise. Mitchell et al. found that low-resistance exercise (30% of 1RM) can elicit equivalent hypertrophy in healthy young men as high-resistance exercise (80% of

1RM), as long as maximal effort is achieved (81). These findings contradict a study by Campos and colleagues, in which 8 weeks of resistance exercise at 20-28RM, contrary to resistance exercise at 3-5RM and at 9-11RM, did not induce hypertrophy (18). However, when the 8-week resistance training program of Campos et al. was replicated in a subsequent study, substantial hypertrophy was found in both the high- and low-resistance training group (71). With regard to strength gains, results in literature seem to differ depending on the testing equipment. Maximal strength gains measured with sophisticated motor-driven dynamometers suggest no difference between high- and low-resistance exercise (81). On the contrary, 1RM strength gains appear to be greater after high-resistance exercise, probably due to neural adaptations specific to the trained movement (8,18,81,108).

Meta-analyses in older adults still seem to suggest that higher training resistances are superior to lower resistances for improving maximal strength but not necessarily for functional performance (93,106). However, the diversity of training protocols in study designs complicate the comparison between high- (>60% of 1RM) and low-resistance (<60% of 1RM) exercise training. Some of the studies did not reach maximal effort at the end of an exercise set (14,54,91,111), others did not match volume load between training groups (36,104). To the best of our knowledge, only one study compared hypertrophic gains after 24 weeks of strength training at high (80% of 1RM) or low resistance (50% of 1RM). None of the training groups showed improvements in muscle mass (115).

To conclude, previous studies in young adults seem to underpin low-resistance exercise, as long as maximal effort is reached, as an alternative to high-resistance exercise. More training studies with proper design are needed in older adults.

2.6. Long-term neuromuscular adaptations to low-resistance exercise

Older adults might be more prone to training interruptions because of lack of motivation or health-related issues. Additional data on residual muscular adaptations after cessation of high- and low-resistance exercise interventions are necessary in order to increase our understanding of longer-term training benefits. Only few studies have published data concerning the influence of training resistance on muscle strength (36,50,114) and muscle mass loss (114) following a detraining period in older adults. However, the results of these studies remain inconclusive. While Harris et al. reported that training resistance had no effect on the magnitude of strength loss or retention after a period of detraining (50), Fatouros et al. suggested that strength gains are maintained for a longer period of time after high-resistance exercise compared to low-resistance exercise (36). Tokmakidis et al. found, despite greater declines in muscle strength, greater

retention in muscle strength and mass after a detraining period following high-resistance exercise than following moderate-resistance exercise (114). It should be noted that only in the study of Fatouros et al., resistances below 60% of 1RM were used (36).

A typical aspect of the abovementioned detraining studies is that participants were asked to quit resistance exercise as soon as the guided intervention had ended. However, by restricting participants to continue resistance exercise, the opportunity is lost to obtain valuable information on long-term exercise adherence. Taking into account the psychological and motivational factors associated with high- and low-resistance exercise protocols might increase our understanding of long-term exercise adherence among older adults. It can be hypothesized that if older persons experience more pleasure when training at a certain degree of external resistance, their long-term adherence would increase, hereby limiting the detraining effects. However, current literature lacks information on this topic.

3. Objectives and general outline of the thesis

This doctoral thesis is a compilation of four scientific articles, among which three published in and one submitted to an international peer-reviewed journal. It consists of two chapters. **Chapter 1** aims at gaining a better insight in the relationship between force-velocity characteristics, muscle mass and functional performance in elderly persons. **Chapter 2** investigates the feasibility and the effects of strength training at different external resistances on muscle performance and functional capacity.

In all four papers, we chose to concentrate on the knee extensor muscles in particular for the following reasons. First, literature showed that aging is associated with a greater decline in lower than in upper limb muscle size and strength (44,60,84). The knee extensors in particular appear to be more susceptible to age-related atrophy than other thigh muscles (74). Second, the knee extensors are crucial in a variety of functional tasks (55,88). In addition, knee extensor strength seems to be important to maintain bone health of the proximal femur and spine and might thus be crucial in the prevention of hip fractures related to osteoporosis (77).

A brief description of the rationale and the objectives of each of the chapters is provided in the following paragraphs. An overview of the study sample and measurements included in the different papers is provided in Table 2.

3.1. Chapter 1: Relationship between force-velocity characteristics of the knee extensors and functional performance

As discussed earlier, previous findings imply that muscle power and the ability to develop a high velocity during muscle contraction are strong predictors of everyday function of older adults, whereas muscle mass seems less decisive for activities of daily living (12,13,41,75,116). Attention should thus be paid to force-velocity characteristics of skeletal muscle, instead of solely to muscle mass, for the identification of older adults at risk for functional limitations (see chapter 1 of the introduction). The main objective of *paper 1* was to determine the relative contribution of muscle strength, force-velocity characteristics and muscle mass to functional performance. After identification of the muscle parameters that contributed most to functional performance, a secondary objective of *paper 1* was to identify threshold values for these parameters below which functional difficulties start to occur. Especially for muscle power and speed-related parameters, previous research has not yet identified such threshold values.

In order to meet these postulated objectives, the study sample needed to be carefully selected. It is imperative to include a heterogeneous sample of older individuals across a broad range of the functional performance spectrum. The study sample should thus include both individuals with and without functional limitations. We decided to recruit institutionalized elderly. However, if we had restricted our recruitment to nursing homes only, our focus would inevitably have been on subjects who already experience a lot of functional problems. That is why we additionally included assisted living facilities and cloistered communities. In assisted living facilities, elderly individuals without major dependency in basic activities of daily life live in independent units, but are offered a broad range of services (meals, house-cleaning, primary care at home, etc.). Use of these services is not required, but is available on demand. A cloistered life is based on religious motives and is clearly different from assisted living. However, cloistered communities often consist of elderly individuals and are characterized by coordinated services within the community. This allows for individuals to function independently to some extent, while having access to selected services. Most subjects (83.7%) were recruited from assisted living facilities and cloistered communities. As it is important that persons at risk for functional difficulties can be detected at an early stage, our study sample is consistent with our aims by primarily including individuals who were close to or just entering the early stages of functional limitations. For practical reasons, given that the cloistered communities consisted of women only, we decided to focus on women in *paper 1*. However, as sarcopenia poses a threat to the independence of both men and women, both sexes will be included in the studies of chapter 2.

3.2. Chapter 2: Resistance exercise as countermeasure against sarcopenia and functional decline

Chapter 2 of this doctoral thesis consists of two subchapters.

Subchapter 2.1 aimed at investigating the impact of external resistance and maximal effort in strength training programs that improve neuromuscular performance. To the best of our knowledge, little is known about the effects of low-resistance exercise protocols, in particular high-repetition protocols, in older adults. Therefore, we decided to first explore the feasibility of an experimental high-repetition protocol in young adults. **Subchapter 2.1** resulted in *paper 2*.

As previously stated in the introduction, there are reasons to believe that equivalent gains in muscle strength can be achieved with low-resistance exercise compared to high-resistance exercise, as long as a sufficient number of repetitions is performed. To further examine the importance of maximal effort in low-resistance strength training regimens, a randomized controlled experiment was designed in which two low-resistance exercise protocols for the knee extensors were created: one low-resistance protocol without achieving maximal effort (LO), one low-resistance protocol ending in maximal effort (LO_{max}). These low-resistance exercise protocols were compared to high-resistance training (HI_{max}) in *paper 2*. All training groups performed one set of 10 to 12 repetitions, but training intensity differed between groups. HI_{max} trained at a resistance of 80% of 1RM ending in maximal effort[a] (5); LO trained at a resistance of 40% of 1RM without achieving maximal effort; LO_{max} trained at a resistance of 40% of 1RM (similar to LO), preceded by a fatiguing protocol of 60 repetitions at 20% of 1RM. No rest was provided between sets, which led to maximal effort in LO_{max} (Figure 4).

This training experiment of 9 weeks allowed us to fine-tune the exercise protocols before applying it to older adults. *Paper 2* can therefore be considered as 'a proof of concept' for an alternative low-resistance exercise protocol. However, its findings will not be able to answer the main question of this doctoral thesis: 'Is low-resistance exercise a good alternative to high-resistance exercise for improving muscle mass and muscle function in older adults?'

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[a]The exercise protocol in HI_{max} was designed according to the 7th edition of the ACSM's guidelines (5). These guidelines suggest performing at least one set of 8 to 12 repetitions to the point of volitional fatigue for healthy individuals and differ slightly from the 9th edition of the ACSM's guidelines (6), described in chapter 2.2.2 of the introduction.
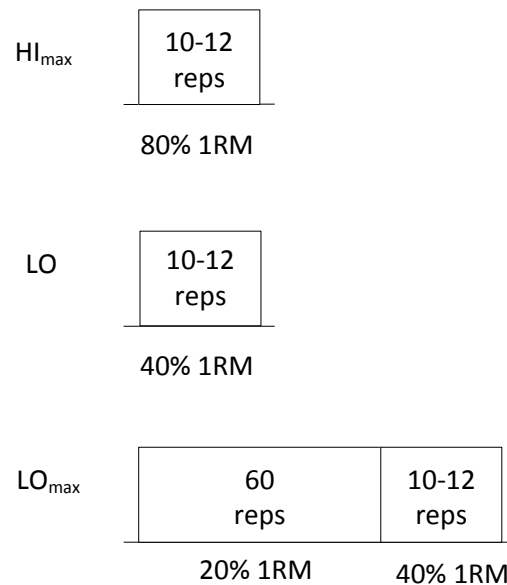
Figure 4. Resistance exercise protocols in *paper 2*.

Subchapter 2.2 will address this latter research question. This subchapter aimed at comparing the effects of high- and low-resistance exercise on muscular and functional outcomes in older adults. We chose here to focus on healthy community-dwelling older adults (N = 56), as they represent an important target population for preventing or at least postponing the loss in muscle mass and muscle function. The next phase of intervention trials could be to test the effects of low-resistance among elderly geriatric patients who are already functionally limited. But this aim was not included in the current doctoral thesis.

The resistance exercise protocols in *paper 2* do not allow for conclusions on whether or not the increase in resistance at the end of a single low-resistance exercise set (see LO_{max}) is crucial for optimal effects. Therefore, two low-resistance exercise protocols were created and compared to high-resistance exercise (HIGH) in *papers 3 and 4*: one high-repetition low-resistance protocol (LOW) in which external resistance is kept constant within one session, one mixed high-repetition low-resistance protocol (LOW+) in which resistance was increased after 60 repetitions (similar to LO_{max} in *paper 2*).

All training protocols were designed to end in maximal effort and to be equal in volume load (Figure 5). HIGH performed two sets of 10 to 15 repetitions. Resistance was initially set at about 80% of one repetition maximum (1RM). LOW performed one set of 80 to 100 repetitions. Resistance was initially set at about 20% of 1RM. LOW+ performed a fatiguing protocol of 60 repetitions at an initial resistance of 20% of 1RM, immediately followed (no rest) by 10 to 20 at an initial resistance of 40% of 1RM.
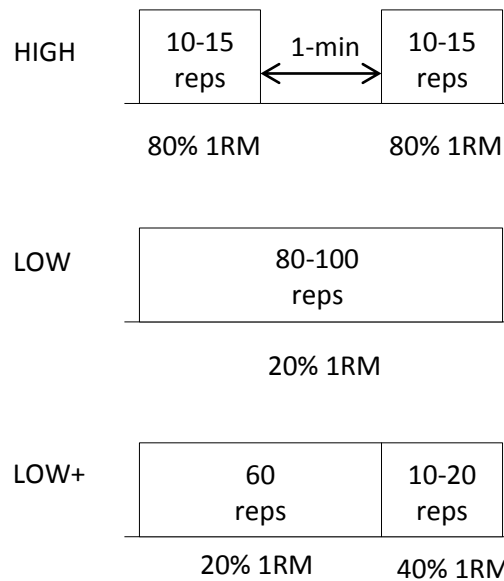
Figure 5. Resistance exercise protocols in *papers 3 and 4*.

Paper 3 focused on the immediate post-intervention effects of 12-weeks resistance exercise training on muscular and functional outcomes. If performing repetitions to the point of momentary muscle fatigue is sufficient to reach (near) maximal motor unit recruitment, and thus to activate type II muscle fibers, all exercise protocols would be expected to be effective in improving muscle mass, muscle strength, and force-velocity characteristics. However, it might be possible that, in addition to muscle fatigue, a mechanical stimulus is needed to activate type II muscle fibers, especially when training at very low external resistances (protocols with many repetitions). If that is the case, increasing the resistance in LOW+ at the end of a high-repetition protocol should allow this group to obtain better effects than LOW on muscle mass, muscle strength, and force-velocity characteristics.

Paper 4 focused on 24-week follow-up data after the 12-week resistance training program. The first objective was to compare the persistence of muscular and functional adaptations in HIGH, LOW and LOW+, 24 weeks after the intervention had ended. During follow-up, no strict detraining period was applied. Thus, subjects were free to decide whether or not they continued strengthening exercise at their own expense post-intervention. The second objective was to investigate how many participants continued strength training after cessation of the intervention and whether or not this number differed between HIGH, LOW, and LOW+. Attention was paid to motivation and self-efficacy. Differences in motivation could lead to differences in longer-term exercise adherence, and this should be taken into account when determining the effectiveness of exercise protocols to counteract age-related muscular and functional declines. In addition, the perceived barriers for continuing strength training were examined.

Table 2. Overview of the study sample and measurements included in the different papers

| | Chapter 1 | Chapter 2 | | |
| | | Subchapter 2.1 | Subchapter 2.2 | |
	paper 1	*paper 2*	*paper 3*	*paper 4*
Study sample	Institutionalized women (N = 123) 79.7 ± 5.3 yrs	Young adults (N = 36; 21m, 15f) 21.8 ± 2.1 yrs	Older adults (N = 56; 26m, 30f) 68.0 ± 5.0 yrs	
CT-scan				
Muscle volume upper leg	X		X	X
Biodex dynamometer: knee-extensor measurements				
Isometric strength	90°	90°	90°, 120°, 150°	120°
Speed of movement	0%, 20%, 40%, 60%	20%, 40%, 60%	20%, 40%, 60%	
Isokinetic strength	60°/s	60°/s	60°/s, 180°/s, 240°/s	60°/s, 180°/s, 240°/s
One repetition maximum strength				
Leg extension		X	X	X
Leg press			X	X
Local muscular endurance				
Leg extension			X	X
Functional performance				
Modified Physical Performance Test	X		at baseline	
6-min walk test			X	X
Maximal gait speed			X	X
30-second chair sit-to-stand test			X	X
5-times chair sit-to-stand test			X	X
Timed up-and-go test			X	X
Psychological processes				
Positive/negative feelings related to exercise				X
Multi-dimensional self-efficacy questionnaire				X
Behavioral regulations in exercise questionnaire - 2				X

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PART 2

RESEARCH ARTICLES

Relationship between force-velocity characteristics of the knee extensors and functional performance

Force-velocity characteristics of the knee extensors:

an indication of the risk for physical frailty in elderly women

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Abstract

Objective: To examine the relationship between muscle strength, speed of movement, muscle mass and functional performance in elderly women and to determine optimal threshold values below which physical frailty occurs. *Design:* Cross-sectional survey. *Setting:* University-based laboratory. *Participants:* Institutionalized women (N = 123) aged 79.67 ± 5.25. *Interventions:* Not applicable. *Main Outcome Measures:* Force-velocity characteristics of the knee extensors were evaluated with isometric, isokinetic, and ballistic tests on a Biodex dynamometer. Static peak torque ($PT_{stat90°}$), dynamic peak torque ($PT_{dyn60°/s}$), maximal speed of movement (SoM – unloaded) and speed of movement with standardized resistance of 20% (S_{20}), 40% (S_{40}), and 60% (S_{60}) of $PT_{stat90°}$, were recorded. Muscle mass of the upper leg was determined by computed tomography. Modified Physical Performance Test (mPPT) was used to assess functional performance. *Results:* Force-velocity characteristics (r varied between 0.31 and 0.68) and muscle mass (r = 0.41) were significantly correlated with functional performance (P < 0.05). In a forward stepwise regression model, only SoM and $PT_{stat90°}$ remained independently associated with mPPT (R^2 = 0.49), with SoM accounting for the majority of the variance. The threshold value that optimally differentiates between women with mild (mPPT-score of 25 to 31) or without (mPPT-score ≥ 32) physical frailty, was 350°/s for SoM and 1.46Nm/kg for $PT_{stat90°}$. Sensitivity and specificity ranged from 74% to 77% and from 71% to 77%, respectively. *Conclusions:* SoM is a key component in the onset of functional difficulties in elderly women. Exercise interventions specifically targeting muscle power (by including exercises at high velocities) might thus be crucial to prevent functional decline.

Keywords: frail elderly; muscle strength; sarcopenia

Introduction

As life expectancy continues to rise worldwide, age-related loss of function and mobility have become a major public health issue, threatening the independency and quality of life of older adults. The phenomenon of sarcopenia, first introduced by dr. I.H. Rosenberg (38,39) as the age-related decrease in skeletal muscle mass, is found to be a strong predictor of this physical frailty (18,33,36). Early detection of persons at risk is thus crucial in developing an effective strategy to avoid a dramatic increase of the incidence of sarcopenia and physical frailty in a graying society.

As our understanding of the complex process of aging progresses, various definitions of sarcopenia have been proposed. These definitions go beyond a simple decrease in muscle mass, including a reduction in muscle strength, in muscle power (the ability to generate force quickly), and even in functional performance (1,2,15). Although the loss in muscle mass contributes to

some of the loss in strength and power, it is far from the sole explanatory variable (12). Declines in strength and power take place to an even greater degree than the loss in muscle mass (17,34,41), and maintenance or gain in muscle mass at age do not necessarily prevent degeneration in strength and power (11,21). Evidence for this discrepancy can be found in both morphological and neural changes in the aging muscle. With regard to muscle morphology, muscle power and strength are highly affected by a selective atrophy and denervation of the type II muscle fibers (29). In addition, neural changes, such as a decline in neural recruitment and in motor unit discharge rates, also result in a loss of muscle strength and power, apart from muscle atrophy (12).

Previous studies imply that muscle power and the ability to develop a high velocity during muscle contraction are strong predictors of everyday function of older adults (13,16,40), whereas muscle mass is less decisive for activities of daily living (31,44). Thus, for the detection of preclinical functional limitations, attention should be paid to force-velocity characteristics of skeletal muscle. Currently, measurements of total-body or appendicular skeletal muscle mass are the most commonly used techniques to identify sarcopenia (5,27). However, it is clear that measurements solely based on muscle mass may not be sensitive enough to detect early deficits in muscle function.

Therefore, in the present study, standardized tests on a motor-driven dynamometer were used to evaluate muscle strength and force-velocity characteristics of the knee extensor muscles, in addition to measurements of leg muscle mass. It is widely accepted that the knee extensors are of major importance in a variety of functional tasks (26,35). Nevertheless, there is no consensus about the level of loss in muscle strength and force-velocity at which subjects encounter functional performance deficits. The aim of this study was to identify force-velocity characteristics of the knee extensors associated with a reduced functional performance and to determine the contribution of several muscle parameters to physical frailty in elderly women. It was hypothesized that, by comparing force-velocity characteristics of elderly women without physical frailty and elderly women with mild physical frailty, a threshold value could be determined below which physical frailty occurs.

Methods

Participants

Elderly women aged 70 years and older, living in nursing homes, assisted living facilities or cloistered communities, were enrolled in this study. Most participants (83.7%) were recruited from assisted living facilities and cloistered communities, consistent with our aim to primarily

identify individuals who were close to or just entering the early stages of physical frailty. In these facilities, elderly individuals live relatively independently but have access to a broad range of services when needed. Exclusion criteria were cognitive impairment in the opinion of an independent physician and all pathologies that prohibit maximal strength testing, such as severe cardiovascular disease, artificial hip or knee on the test side, acute hernia, infection or tumor. One hundred twenty-three elderly women participated in this study. The study was approved by the University's Human Ethics Committee in accordance with the declaration of Helsinki. All participants gave written informed consent.

Outcome measurements

Muscle mass. Axial slices of the right upper leg were measured by a multislice computed tomography scan (Siemens Sensation 16; Forchheim, Germany) and were analyzed with the program 'Volume' (Siemens). A 3mm-thick axial image was obtained at the midpoint of the distance between the medial edge of the greater trochanter and the intercondyloid fossa of the femur. This procedure was repeated 3cm above and 3cm below the midpoint. Standard Hounsfield Units ranges for skeletal muscle (0-100) were used to segment muscle tissue area (20). Muscle mass (MM) was estimated as the cumulative muscle volume (cm³) of the three slices. Corrections were made for bone marrow. In previous research, test-retest reliability evaluated in 12 older men yielded an intraclass correlation coefficient of 0.99 (8). All measurements were executed by one expert radiologist in the University Hospital.

Force-velocity characteristics. Force-velocity characteristics of the knee extensors were evaluated by means of a Biodex Medical System 3 dynamometer (Biodex Medical Systems; Shirley, NY). Tests were performed unilaterally on the right side, unless there was a medical contraindication. Subjects were seated with the hip fixed between 90° and 100° of flexion during the test. The upper leg, the hips, and the shoulders were stabilized with safety belts. The rotational axis of the dynamometer was aligned with the transversal knee-joint axis and was connected to the distal end of the tibia with a length-adjustable rigid lever arm.

On the one hand, the absolute performance characteristics of the knee extensors were determined by three basic tests: an isometric test (knee angle 90°), an isokinetic test at 60°/s and a 'maximal', unloaded, ballistic knee extension test. This procedure allowed to quantify strength of the knee extensors in the absence of speed (isometric) and during slow-dynamic contraction (isokinetic at 60°/s), as well as to record the highest possible speed developed by the subject in the absence of external resistance (with the exception of the weight of the lever arm of the dynamometer).

On the other hand, relative force-velocity characteristics were recorded by equating the maximal strength (isometric value) of each individual to hundred percent. Subsequently, three ballistic tests were performed with a constant external resistance (isotonic conditions) that equals 20%, 40% and 60% of the maximal strength (isometric value), respectively. The results of these tests were quantified by means of the maximal speed (°/s) developed over the full range of motion.

The total protocol, as described below, was performed twice.

Isometric test. – Subjects performed twice a maximal voluntary isometric contraction of the knee extensors over a 5-second period. The knee joint angle was 90°. The isometric contractions were separated by a 20-second rest interval. The static peak torque (Nm) was recorded as the isometric strength performance ($PT_{stat90°}$). The intraclass correlation coefficient (ICC) for test-retest reliability, recorded in older adults, was 0.96.

Ballistic test. – Subjects performed four ballistic tests for the knee extensors. They were asked to extend the lower leg as quickly as possible from a knee joint angle of 90° to 160°. This test was performed once without external resistance on the lever arm (unloaded), followed by three identical tests with a controlled resistance on the lever arm: 20%, 40%, and 60% of the individual isometric maximum, respectively. In each of these conditions, the speed of movement (°/s) was recorded. The maximal speed recorded in the unloaded tests was defined as the maximal speed of movement (SoM). The maximum speed recorded at the loading of 20%, 40%, and 60% was reported as S_{20}, S_{40} and S_{60} respectively. The ICC for test-retest reliability, recorded in older adults, ranged from 0.91 to 0.96.

Isokinetic test. – Subjects performed a series of three consecutive maximal isokinetic flexion-extension movements at a velocity of 60°/s. They were instructed to cover the full range of motion during movement (knee joint angle of 90° to 160°). Maximal dynamic strength ($PT_{dyn60°/s}$) was defined as the peak torque (Nm) during these series of knee extensions. The ICC for test-retest reliability of dynamic strength, recorded in older adults, was 0.91.

__Functional performance.__ Functional performance related to daily activities was assessed with the modified Physical Performance Test (mPPT), an objective and well-validated assessment of degree of physical frailty. This test battery consists of nine functional items and correlates with degree of disability, loss of independence and early mortality (10,19,22,28).

Seven items were derived from the physical performance test described by Reuben and Siu (37): (i) lifting a book from waist height to a shelf at shoulder level, (ii) putting on and taking off a coat, (iii) picking up a penny from the floor, (iv) turning 360°, (v) walking 15 m, (vi) ascending one flight of stairs, and (vii) climbing four flights of stairs. These seven items were combined with (viii) the chair rise test and (ix) the Romberg test for balance described by Guralnik and co-workers (23).

The score of each item ranged from 0 (the inability to complete the task) to 4 (the highest level of performance), with a summary performance score (mPPT-score) of maximum 36 points. Binder and co-workers (7) found for the mPPT-score a test-retest reliability of 0.96. In accordance with previous research (10), subjects were divided in three frailty categories: 'not frail' (32-36, n = 34), 'mildly frail' (25-31, n = 70) and 'moderately frail' (17-24, n = 19).

Statistical analyses

To standardize, muscle mass, isometric strength, and dynamic strength values were divided by individual body weights in kilograms (cm^3/kg and Nm/kg). Descriptive statistics were calculated for subject characteristics. One-way analysis of variance (ANOVA), with frailty group as independent variable, and Bonferroni post hoc testing were used to evaluate differences between groups. The normal distribution of all parameters was evaluated by means of the Kolmogorov-Smirnov test. Pearson correlation coefficients were used to determine whether muscle mass, muscle strength, and speed of movement were significantly associated with functional performance.

In addition, all muscle variables (independent variables) were entered in a multiple forward stepwise regression model to determine the contribution of each variable to functional performance (dependent variable). Variance inflation factor (VIF) was used to examine collinearity. In line with previous research (40), only variables with a VIF of less than 2.0 were included in the same equation. Because muscle mass, strength, and speed of movement measurements might show a curvilinear relationship with functional performance (6), we explored if the inclusion of both linear and quadratic terms was necessary. Therefore, quadratic bivariate regressions between each muscle parameter and functional performance were obtained. A quadratic term was included in multiple regression, only if it was significant in bivariate regression.

Finally, to define functionally relevant threshold values, receiver operating characteristic (ROC) curves were obtained for each muscle characteristic that significantly contributed to the model. As it is imperative that persons at risk for functional difficulties can be detected at an early stage, our categories of 'not frail' and 'mildly frail' (i.e. starting to have functional limitations) were applied in the ROC curves to define 'good' and 'poor' functionality, respectively. Across the entire range of possible cut-points, ROC curves were plotted to compare the probability of a correct prediction among the 'mildly frail' women (sensitivity, true positives) with the probability of an incorrect prediction among the women who were 'not frail' (1-specificity, false positives). From

these ROC curves, diagnostic threshold values were identified as those yielding the most favorable compromise between specificity and sensitivity (31).

All statistical tests were performed with SPSS software version 16.0 (SPSS Inc., Chicago, IL). Level of significance was set at $P < 0.05$.

Results

Subject characteristics are described in Table 1. All variables were normally distributed at $P < 0.01$.

Table 1. Subject characteristics (mean ± SD) and differences between frailty categories by One-way Analysis of Variance and Bonferroni post hoc testing

Variable	All subjects (N = 123)	Not frail (n = 34)	Mildly frail (n = 70)	Moderately frail (n = 19)
Age, yrs	79.7 ± 5.3	76.7 ± 4.8	80.0 ± 4.7*	83.9 ± 4.6*†
Body mass, kg	65.3 ± 10.8	64.1 ± 10.3	65.2 ± 10.8	67.7 ± 11.7
Body height, m	1.56 ± 0.06	1.57 ± 0.06	1.56 ± 0.07	1.55 ± 0.05
mPPT-score	28.6 ± 4.5	33.44 ± 1.16	28.4 ± 1.8*	20.5 ± 2.2*†
MM, cm³/kg	1.10 ± 0.18	1.20 ± 0.15	1.08 ± 0.17*	0.98 ± 0.18*
$PT_{stat90°}$, Nm/kg	1.37 ± 0.39	1.70 ± 0.40	1.31 ± 0.29*	1.01 ± 0.28*†
$PT_{dyn60°/s}$, Nm/kg	1.04 ± 0.33	1.29 ± 0.27	1.02 ± .26*	0.68 ± 0.30*†
S_{60}, °/s	109 ± 40	117 ± 39	113 ± 39	82 ± 38*†
S_{40}, °/s	157 ± 47	180 ± 28	158 ± 46*	112 ± 50*†
S_{20}, °/s	244 ± 55	277 ± 41	245 ± 43*	182 ± 69*†
SoM, °/s	320 ± 62	365 ± 43	318 ± 48*	242 ± 65*†

Abbreviations: mPPT = modified Physical Performance Test; MM = muscle mass, $PT_{stat90°}$ = static peak torque; $PT_{dyn60°/s}$ = dynamic peak torque; S_{60}, S_{40}, S_{20} = speed of movement at 60%, 40%, 20% of $PT_{stat90°}$; SoM = maximal speed of movement
*significantly different from 'not frail', †significantly different from 'mildly frail', $P < 0.05$

The mPPT-score showed moderate to high correlations with all muscle parameters. With regard to speed of movement during ballistic tests, these correlations became stronger when external loadings decreased and thus when speed of movement increased. Importantly, maximal speed of movement showed the highest correlation with functional performance ($r = 0.68$, $P < 0.05$) (Table 2). ANOVA and Bonferroni post hoc testing additionally revealed significant differences between the three frailty categories for the majority of the muscle parameters ($P < 0.05$) (Table 1).

Quadratic bivariate regression was found to be significant for the relationship between mPPT-score and four muscle parameters: MM, $PT_{stat90°}$, $PT_{dyn60°/s}$ and S_{40} ($P < 0.05$). For these parameters, both a linear and a quadratic term were included in the multiple regression.

Table 2. Pearson correlations of muscle parameters with score on the modified Physical Performance Test (mPPT) for 123 women

	MM, cm³/kg	$PT_{stat90°}$, Nm/kg	$PT_{dyn60°/s}$, Nm/kg	S_{60}, °/s	S_{40}, °/s	S_{20}, °/s	SoM, °/s
mPPT	0.41*	0.57*	0.61*	0.31*	0.48*	0.58*	0.68*

Abbreviations: mPPT = modified Physical Performance Test; MM = muscle mass; $PT_{stat90°}$ = static peak torque; $PT_{dyn60°/s}$ = dynamic peak torque; S_{60}, S_{40}, S_{20} = speed of movement at 60%, 40%, 20% of $PT_{stat90°}$; SoM = maximal speed of movement
*significant at $P < 0.05$

Results of multiple regression analysis with mPPT-score as dependent variable and all muscle characteristics as independent variables are shown in Table 3. Two variables could be included in the same model (VIF < 2.0) and contributed independently to the prediction of the mPPT-score (model R^2 = 0.49): maximal speed of movement and isometric strength. None of the quadratic terms remained significant.

Table 3. Forward stepwise regression analysis with mPPT-score as dependent variable

Variable	Standardized β	P-value	Change in R^2	F (of Change)	VIF
SoM, °/s	0.524	<0.001	0.458	102.36	1.623
ISO, Nm/kg	0.247	0.003	0.038	8.93	1.623

Abbreviations: mPPT = modified Physical Performance Test; SoM = maximal speed of movement; $PT_{stat90°}$ = static peak torque
Adjusted model R^2 = 0.487

As SoM and $PT_{stat90°}$ were found to be significant contributors to functional performance, the ROC method was used to select the diagnostic threshold value of these muscle parameters for the identification of persons at risk for functional limitations. Two curves were obtained by setting several diagnostic threshold values within the range of the muscle variable and plotting the true positive rate (sensitivity, y-axis) versus the false positive rate (1-specificity, x-axis) for each value (Figure 1). The area under the curve (AUC), reflecting the discriminating power of the screening test, was 0.765 (CI = 0.667-0.863) for maximal speed of movement and 0.786 (CI = 0.694-0.879) for isometric strength, respectively.

The optimal diagnostic cut-points were selected based on the most favorable trade-off between sensitivity and specificity (Table 4). These cut-points were set at 350°/s for SoM and at 1.46Nm/kg for $PT_{stat90°}$.
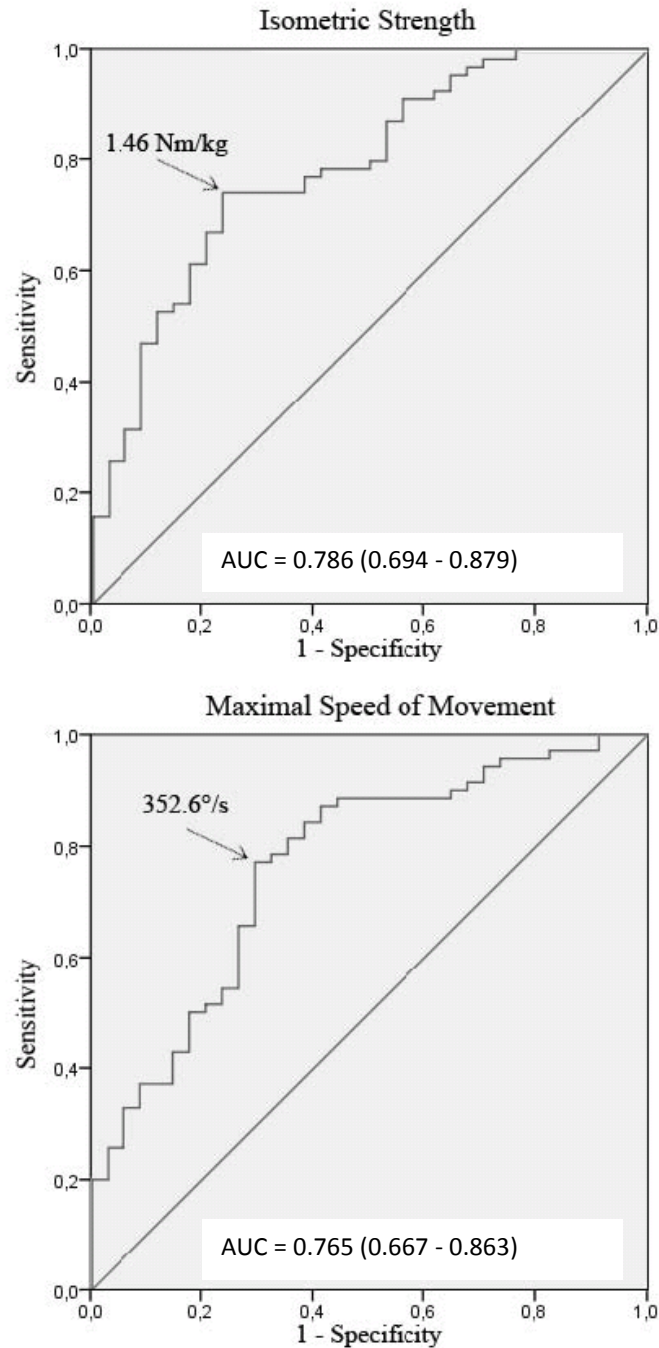
Figure 1. Receiver operating characteristic curves created for the identification of participants with functional limitations based on isometric strength and maximal speed of movement values of the knee extensors. Both curves are the graphical representation of the trade-off between the true positive (sensitivity) and false positive rates (1-specificity) for every possible cut-point. The area under the curve (AUC) indicates the overall discriminative value for both muscle parameters. The arrows represent the threshold values yielding the best compromise between sensitivity and specificity.

Table 4. Optimal threshold values for unloaded speed of movement and isometric strength of the knee extensors in the identification of persons at risk for functional limitations

Muscle parameter	Threshold value	Sensitivity	1 - Specificity
Maximal speed of movement, °/s	352.6	0.771	0.294
Isometric strength, Nm/kg	1.456	0.743	0.235

Discussion

In this study, maximal speed of movement and isometric strength of the knee extensors were identified as key components in everyday function. These parameters might be particularly useful to screen for physical frailty, since they explained nearly 50% of the variability in functionality of elderly women, as recorded by the mPPT. As hypothesized, this study identified threshold values below which (mild) physical frailty occurs, i.e. 350°/s for SoM and 1.46Nm/kg for $PT_{stat90°}$.

In accordance with previous research (14,25,26,36), muscle mass of the upper leg and force-velocity characteristics of the knee extensors were significantly correlated with physical frailty in elderly women. Results in Table 1 provide additional evidence that frail women have less muscle mass and strength than women without frailty. Muscle mass, however, was not an independent determinant of functional performance when included in the same regression model as muscle strength, suggesting that muscle mass primarily contributes to functional performance through its association with muscle strength (11,44).

Previous research emphasized the role of muscle power and speed of contraction in relation to physical frailty (13,16,40). Therefore, ballistic tests were added to the study protocol. During these tests, the subject extends the knee as fast as possible against a constant resistance (isotonic mode), relying on the ability to activate the fast-twitch muscle fibers. As many activities of daily living involve moving a specific object (weight) and include an acceleration component, ballistic tests seem most applicable to real-world situations. In this study, significantly higher correlations were found between functional performance and speed of movement when external loadings were lower and hence speed of movement higher. This finding is in line with a study by Cuoco et al. (16), where power at lower external resistance (40 % of 1RM) was found to be a better predictor of functional performance compared with power at high resistances (70% of 1RM). Additionally, other investigators pointed out that the velocity component of muscle power is a critical determinant in different functional tasks tasks (13,40). Consistently, in our study, maximal speed of movement (SoM) explained the majority of the variance in mPPT-score (45.4%). In other words, our analysis suggests that the maximal speed of movement may be the most important force-velocity characteristic related with functional performances.

The aim of this study was to identify individuals who are close to or just entering the early stages of physical frailty and in whom interventions are most likely to be effective. In our study sample, only 12% of the women had sarcopenia as identified by a skeletal muscle mass index below 5.67kg/m² (measured by DXA) (15). In contrast, 72% could already be classified as physically frail. Therefore, we chose to determine threshold values that optimally differentiated between women who were 'not frail' and those who were 'mildly frail'. For maximal speed of movement of the knee extensors, this threshold was set at 350°/s. Sensitivity analysis showed that the threshold correctly identified 77% of the subjects who were mildly frail, whereas specificity analysis showed that 71% of the women were correctly identified as not frail. To our knowledge, this is the first study to determine such a velocity-specific threshold value. This value can be interpreted as a first alarm signal for (future) physical frailty, rather than as an absolute cut-point.

Over the past several years, adults of different age groups have performed standardized knee strength tests on the Biodex Medical System 3 dynamometer at our research center. In one study on the effects of aging on force-velocity characteristics in women aged between 40 and 89 years, maximal speed of movement exponentially declined with age (data not published). When comparing this progressive age-related decline with our new threshold value, women are expected to reach the value of 350°/s from, on average, 74 years on.

In the current study, aside from maximal speed of movement, isometric muscle strength also contributed to functionality. A sufficient 'potential of the musculature to generate force' (strength) is a prerequisite for speed production and must also be considered as an essential factor in functional performance. With regard to relative isometric muscle strength, our threshold was set at 1.46Nm/kg. The sensitivity and specificity values in Table 4 indicate that this threshold correctly identified 74% of the mildly frail women and 77% of the not frail women, respectively. Several cross-sectional studies have identified cut-points for knee extensor strength in the onset of functional limitations. It is not always easy to compare these values with our data because of methodological differences (25,35). However, in a prospective cohort study in 1429 women, Manini and colleagues used a protocol very similar to our measurement of isokinetic knee extension strength at 60°/s. High and low risk for developing severe mobility limitations corresponded to less than 1.01Nm/kg and more than 1.34Nm/kg, respectively (32). In line with these results, women in our 'mildly frail' and 'not frail' categories scored on average 1.02Nm/kg and 1.29Nm/kg for dynamic knee extension strength, respectively. Likewise, a knee extension strength level at 60°/s, needed for independence in older adults, was identified by Cress et al. (14) as 2.5Nm/[kg.m^{-1}]. Adjusted for body height and weight, our females categorized as 'not frail' and

'mildly frail' scored on average 2.66Nm/[kg.m^{-1}] and 2.05Nm/[kg.m^{-1}], respectively, above and below this threshold.

As previously shown, muscle power declines with aging to a greater extent than strength, which highlights the importance of movement speed, coordination, and other neuromuscular factors in power generation (30,34). This line of reasoning is supported by our finding that, of all muscle parameters, maximal speed of movement was most connected to functional outcomes in daily life. Therefore, we suggest the use of this parameter to gain a better insight in the onset and the process of physical frailty.

Once persons at risk are detected, attention should be paid to preventive interventions. Progressive resistance training at 60 to 80% of 1RM, as recommended by international guidelines (3), has profound effects on muscle size and strength in older adults (24,43). However, the effectiveness of this traditional training approach for increasing muscle speed and power has been questioned, because this type of training tends to enhance maximal strength only at slow movement velocities (4). Even though there is some carryover of training effects, high-velocity exercises may be preferred to improve muscle power and functional performance (9,42). Nevertheless, it remains crucial to simultaneously train for strength to provide the basis for optimal power development (4). As indicated by our findings, both maximal speed of movement and isometric strength are important contributors to everyday function. Therefore, the design of an optimal exercise program for older adults, at risk for sarcopenia and physical frailty, should consist of both strength and velocity components.

From a practical perspective, it may be an option to combine the threshold of a speed of movement test and an isometric test to determine the most appropriate exercise intervention for the individual. If both threshold values are combined as a 'double check', the sensitivity to detect physical frailty increases up to 89%, indicating that more women are correctly detected as being mildly frail. However, the combination of both threshold values does also result in a decrease in specificity to 59%, indicating that there are a higher number of false positives.

Study Limitations

Some limitations of this study need to be considered. First, the stringent exclusion criteria for the knee extensor testing resulted in a sample of mainly 'not frail' (n = 34) and 'mildly frail' (n = 70) women. Only nineteen women were considered 'moderately frail', i.e. obviously limited in everyday function. It would have been beneficial if our frailty categories were similar in number of subjects. Second, only women were included in this study, resulting in a sex-specific velocity threshold that cannot be applied to men without further research.

Conclusions

These findings highlight the importance of force-velocity characteristics of the knee extensors in physical frailty. Both maximal speed of movement and isometric strength contribute significantly to the onset of physical frailty. For each of these parameters, a threshold value for physical frailty was identified. Crossing any of these thresholds should be considered as an alarm signal. If confirmed in different settings, our findings should allow exercise interventions that are more adapted to the needs of the individual: with a focus on speed, on strength or on both components. In this context, future research should focus on verification of results of this study in different groups of older women.

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Resistance exercise as countermeasure

against sarcopenia and functional decline

The impact of external resistance and maximal effort

on strength training-induced effects on muscle performance:

a proof of concept

Impact of external resistance and maximal effort on force-velocity characteristics of the knee extensors during strengthening exercise: a randomized controlled experiment

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Abstract

It remains controversial whether maximal effort attained by high external resistance is required to optimize muscle adaptation to strengthening exercise. Here, we compared different training protocols reaching maximal effort with either high resistance (HI_{max}, 80% of one repetition maximum (1RM)) or low resistance (LO_{max}, ≤ 40% 1RM). Thirty-six young volunteers were randomly assigned to 9 weeks leg extension training at either HI_{max} (one set of 10-12 repetitions at 80% 1RM), LO (one set of 10-12 repetitions at 40% 1RM, no maximal effort), or LO_{max} (one set of 10-12 repetitions at 40% 1RM, preceded (no rest) by 60 repetitions at 20-25% 1RM). Knee extension 1RM was measured pre and post intervention, and before the 7th, 13th, and 19th training session. Pre and post intervention, knee extensor static ($PT_{stat90°}$) and dynamic ($PT_{dyn60°/s}$) peak torque, maximal work (MW), and speed of movement at 20% (S_{20}), 40% (S_{40}) and 60% (S_{60}) of $PT_{stat90°}$ were recorded with a Biodex dynamometer. All groups showed a significant increase in 1RM, with a greater improvement in HI_{max} from the 13th session on ($P < 0.05$). HI_{max} was the only group that significantly increased $PT_{stat90°}$ (+7.4 ± 8.1%, $P = 0.01$). LO_{max} showed a significantly greater increase in S_{20} (+6.0 ± 3.2%), $PT_{dyn60°/s}$ (+9.8 ± 5.6%) and MW (+15.1 ± 10.6%) than both HI_{max} and LO ($P = 0.044$ for S_{20}, $P = 0.030$ for $PT_{dyn60°/s}$, $P = 0.025$ for MW), and was the only group that increased in S_{40} (+7.7 ± 9.7%, $P = 0.032$). In conclusion, significant differences between HI_{max} and LO_{max} on force-velocity characteristics of the knee extensors were found, although maximal effort was achieved in both training regimens. Thus, LO_{max} may not be considered as a replacement for HI_{max}, but rather as an alternative with different training-specific adaptations.

Keywords: resistance training; training load; muscle fatigue; muscle strength; muscle power

Introduction

Resistance training is widely recognized as an important component of health-related physical activity recommendations, with documented benefits like gains in muscle strength, muscle mass, muscle power, and muscle endurance (1,13). Although the exact mechanisms underlying strength adaptations remain elusive, a well-documented key issue is mechanical resistance, expressed as a percentage of one repetition maximum (1RM), at which training is performed (7,14,24). In order to maximize gains in muscle strength and mass, international guidelines currently recommend training at moderate to high external resistances (70-85% of 1RM) (1). While this recommendation has been extensively proven to be safe and effective (11,33), practitioners remain reluctant to prescribe high-resistance exercises in conditions such as injury rehabilitation,

chronic diseases or physical frailty. Exercises at a lower external resistance but with a higher number of repetitions might be a good alternative.

In fact, Carpinelli hypothesized that the external resistance used during exercise is of minor importance for neuromuscular adaptations, as long as maximal effort is achieved (5). Maximal effort is reached at the end of a series of repetitions when the subject is no longer able to perform an additional repetition. This approach is typically applied in traditional resistance training, in which the resistance is prescribed as a number of repetitions maximum (RM). For example, 12RM describes a set where the 12th repetition is a maximal effort, with the inability to execute a 13th repetition. Several studies found larger gains in strength and mass for training with maximal effort as opposed to training without maximal effort (15,28,32). Achieving maximal effort may be needed to maximize motor unit recruitment, which might be responsible for enhanced hypertrophic response (5,15).

The fact that maximal effort can also be attained when training with lower external resistances (< 70% of 1RM), is supported by results of resistance exercise with moderate vascular occlusion (34,37,38). During this training, blood flow to the exercising muscle is partially restricted, reducing metabolic clearance and, despite working at low resistance, reaching maximal effort at an earlier exercise phase (22,41). As the muscle has to perform at extreme conditions, there is a need for optimal activation of motor units to maintain muscle contraction. It is hypothesized that under these extreme conditions of blood flow restriction, type II motor units are activated and intramuscular synchronization is stimulated, which facilitates neuromuscular adaptations (26,38). However, resistance exercise with vascular occlusion is often associated with discomfort, and the overall safety continues to be clarified (41).

Endurance-type regimens, in which maximal effort is realized by performing a high number of repetitions with low resistances, might be an alternative for optimizing motor unit recruitment. In line with this assumption, previous research showed that in conditions in which a muscle is fatigued, motor unit activation is increased, leading to enhanced activation of the higher threshold motor units that innervate type II fibers (25,29). There is some evidence that these regimens can be very effective in inducing muscular hypertrophy and strength gains (4,19,35,36). Nevertheless, previous studies have shown that high-resistance exercise might be the preferred option to optimize gains (2,4,19). Takarada and Ishii suggested that, in endurance-type regimens, interset rest periods have to be short (~30 seconds) to reduce metabolic clearance and optimize training adaptations (36).

Furthermore, there is a lack of information about the effects of endurance-type strengthening exercise on force-velocity characteristics of the muscle. Previous research emphasized the role of

muscle power and speed of movement in activities of daily living, especially in sedentary and frail populations (6,10,31,40). This highlights the importance to focus on force-velocity characteristics in health-enhancing training regimens, instead of solely on strength and mass. Resistance training with the intention to develop the highest possible speed during exercise, is preferred to increase muscle power and speed of movement (12,13,30). However, the question rises whether resistance training at moderate speed with maximal effort, hypothesized to recruit higher-threshold motor units of type II fibers, can also improve velocity parameters, regardless of the external resistance used during the exercise.

As previously stated, low-resistance exercise might be preferred over high-resistance exercise in some chronic conditions. However, its beneficial effects remain to be elucidated. Therefore, in the present study, the purpose was to compare the effects of low-resistance training and traditional high-resistance training on muscle strength and force-velocity characteristics of the knee extensors. To further investigate the importance of maximal effort in training regimens, two low-resistance exercise protocols were created and compared with traditional high-resistance training (HI_{max}): one low-resistance protocol ending in maximal effort (LO_{max}), one low-resistance protocol without achieving maximal effort (LO). It was hypothesized on the one hand that both HI_{max} and LO_{max} would be similarly effective, because of the likely activation of type II fibers at the end of each training session. On the other hand, it was expected that HI_{max} and LO_{max} were more effective than LO.

Methods

Experimental approach to the problem

The primary purpose of this study (9-week intervention) was to compare gains in muscle strength and force-velocity characteristics for high- and low-resistance exercise, ending with or without maximal effort. All subjects participated in a supervised resistance training program that was conducted 3 times weekly. The leg extension was the exercise selected for all testing and training procedures. This exercise was chosen in order to create a similar movement pattern during training as during testing on a Biodex dynamometer, which has already been proven to be reliable for testing force-velocity characteristics of the knee extensors (isometric strength: ICC = 0.96, isokinetic strength: ICC = 0.91, speed of movement: ICC = 0.80). To examine the importance of both maximal effort and external resistance in training regimens, three training protocols were compared: traditional high-resistance training (10 to 12 repetitions, ending in maximal effort; HI_{max}), low-resistance training (10 to 12 repetitions, no maximal effort; LO) and low-resistance training, in which the muscle was first pre-exhausted (60 repetitions), immediately followed by

exercising at low resistance (10 to 12 repetitions, ending in maximal effort; LO_{max}). One RM was measured at baseline (pre, October 2010), before the 7th, 13th, and 19th training session, and post intervention (within one week after the intervention, December 2010). Pre and post intervention, force-velocity characteristics of the knee extensors were measured with a Biodex dynamometer.
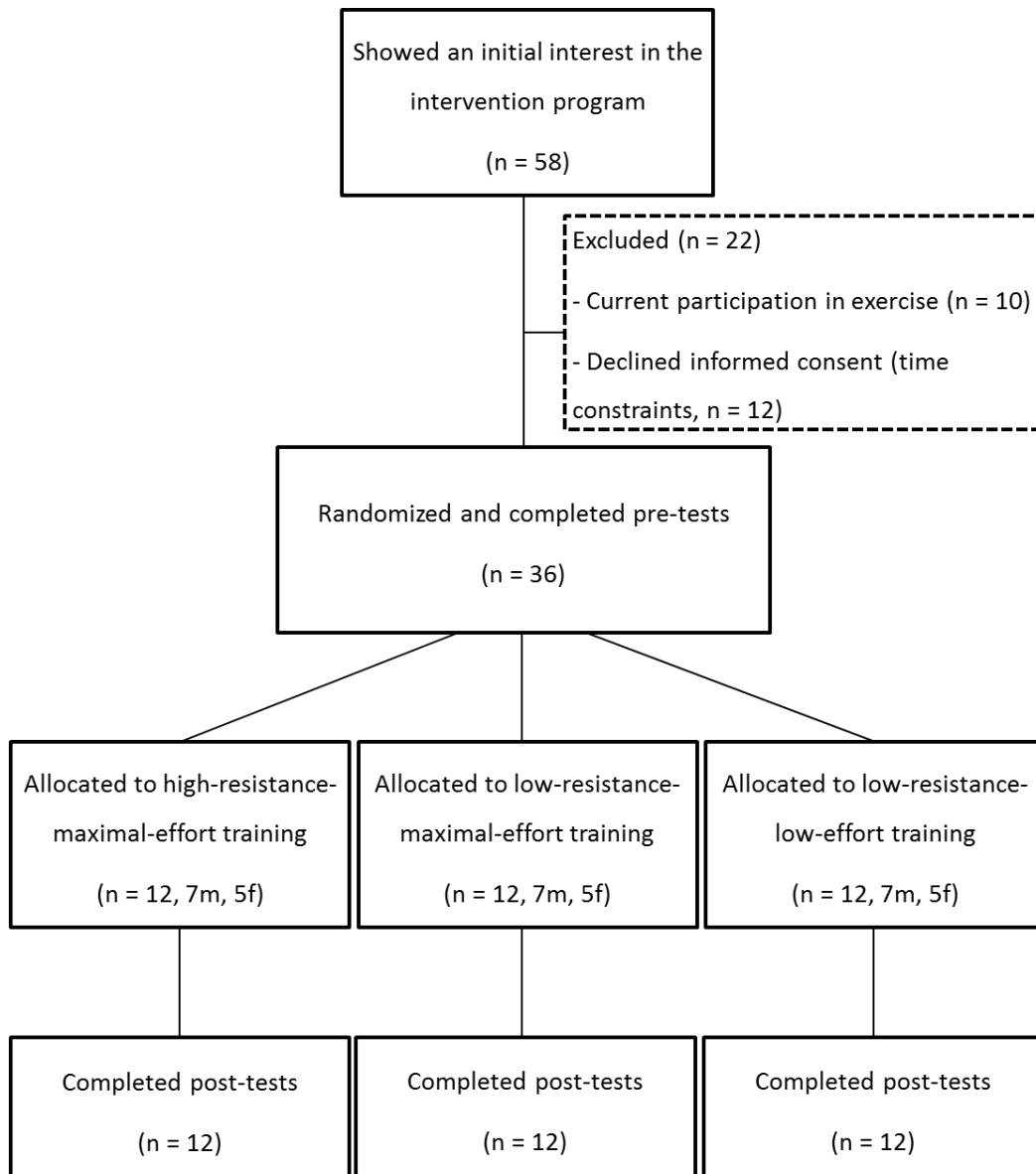
Figure 1. Flowchart of the study.

Subjects

A flowchart of the study is provided in Figure 1. Volunteers were locally recruited through advertisements and oral communications. All apparently healthy subjects aged 20-30 years willing to complete the 9-week training program were eligible to participate. All subjects were asked to

report their current level of physical activity and their previous participation in endurance or resistance training. Exclusion criteria were current participation in structured endurance and/or participation in resistance exercise in the last 6 months prior to the study, and knee pathologies. Thirty-six young men and women, aged between 20 and 28 years, participated in this study. They were randomly assigned to one of three training interventions: traditional high-resistance training with maximal effort (HI_{max}, n = 12), low-resistance training with low effort (LO, n = 12), or low-resistance training with maximal effort (LO_{max}, n = 12), respectively. Randomization was stratified for gender and baseline isometric knee extension strength. All subjects completed the study and were asked to report important changes in lifestyle as to physical activity, diet, or medication. The overall adherence (number of training sessions attended as a percentage of the total number of training sessions) to the training program was 93.5% for HI_{max}, 92.0% for LO, and 93.5% for LO_{max}, with no significant differences between groups. One person in LO_{max} suffered from persistent muscle cramps in the right calf during post testing on the Biodex dynamometer. The results of this measurement were excluded from analysis, because this person was not able to perform with maximal effort. Subject characteristics are presented in Table 1. The University's Human Ethics Committee approved all the procedures used, and all subjects provided written informed consent after being briefed on the risks and benefits of the research.

Table 1. Subjects' characteristics (mean ± SD)

	HI_{max} (n = 12: 7m, 5f)	LO_{max} (n = 12: 7m, 5f)	LO (n = 12: 7m, 5f)	P*
Age (y)	22.15 ± 2.68	21.39 ± 1.80	21.92 ± 1.69	0.66
Weight (kg)	70.55 ± 15.50	67.70 ± 9.56	69.71 ± 8.58	0.83
Height (m)	1.76 ± 0.10	1.76 ± 0.09	1.77 ± 0.08	0.87
BMI (kg/m²)	22.66 ± 4.15	21.92 ± 2.06	22.09 ± 1.58	0.80

HI_{max} = high-resistance training with maximal effort; LO_{max} = low-resistance training with maximal effort; LO = low-resistance training with low effort. *Results of one-way analysis of variance between baseline group means.

Procedures

Resistance training protocol. After an initial familiarization session, participants exercised 3 days a week on nonconsecutive days for 9 weeks (total of 27 sessions). A bilateral isotonic leg extension equipment (Life Fitness Optimal Series, Franklin Park, IL) was used. Each training session was preceded by a 5 min warm-up on a cycle ergometer (Technogym Bike Forma, Gambettola, Italy). Participants were instructed to perform each repetition on the leg extension at

a moderate speed of 1s for each concentric and 2s for each eccentric action. Training sessions were supervised by a qualified fitness instructor.

External resistance for HI_{max} was chosen based on international guidelines for resistance exercise (1), which prescribe 8 to 12 repetitions per set of exercise for a safe, effective and time-efficient strength training protocol. Based on Hoeger et al. (18), describing external resistance specifically for the leg extension exercise, the external resistance for HI_{max} was initially set at 80% of 1RM, and further adjusted if necessary. More into detail, HI_{max} completed one set of 10 to 12 repetitions at a resistance of about 80% of 1RM. Mean number of repetitions per set was 11.9 and mean resistance was 80.8%.

LO completed one set of 10 to 12 repetitions at a resistance of 40% of 1RM. After every 1RM test, resistance was calculated as 40% of 1RM. The first 3 training sessions consisted of one set of 10 repetitions, followed by 3 training sessions of one set of 12 repetitions.

LO_{max} completed one set of 10 to 12 repetitions at a resistance of about 40% of 1RM, similar to LO. This set was preceded by a fatiguing protocol of 60 repetitions at a resistance of 20-25% of 1RM. No rest was provided between the fatiguing protocol and the training set. Mean number of repetitions per set was 10.7 and mean resistance was 40.9% of 1RM.

In both HI_{max} and LO_{max}, participants were instructed to perform a maximal number of repetitions in every training session, resulting in maximal effort. If the number of successful repetitions (full ROM) exceeded 12, training resistance was adjusted for the next training session. In LO, participants performed the prescribed number of repetitions without achieving maximal effort.

Knee extension 1RM testing. 1RM was evaluated 5 times on the same equipment as the training sessions: at baseline (pre), before the 7th, 13th, and 19th training session, and post intervention, respectively. Before the first training session, two methods for estimating 1RM were compared on nonconsecutive days: a direct method (3) and an estimation method based on the Oddvar Holten diagram (17). The direct method starts with a warm-up set of 8 repetitions at approximately 50% of the estimated 1RM, followed by another set of 3 repetitions at 70% of the estimated 1RM. Subsequent lifts are single repetitions with progressively heavier resistances until the resistance exceeds the subject's ability. The heaviest successful lift is determined as 1RM.

Previous research has shown that the percentage of 1RM can be estimated from the maximal number of repetitions (nRM) that can be performed with a given resistance (9). In this study, the percentage of 1RM, and subsequently the 1RM, was estimated through a logarithmic regression formula based on the Oddvar Holten diagram: % 1RM = 101 - 9.6 x ln(nRM). This formula was introduced, because the Oddvar Holten diagram does not include the total range of possible repetitions and matching percentages of 1RM. The logarithmic regression, previously tested in

our lab, is a good representation of the Oddvar Holten diagram (R² = 0.98) and was shown to be appropriate for the leg extension exercise (data not published). In this 1RM testing procedure, the subject performs a maximum number of successful repetitions with a resistance selected by the supervisor. A range of 5 to 15 repetitions is targeted when selecting the resistance. By using the formula, the percentage of 1RM at which the test is performed, and subsequently the 1RM, can be estimated. The intraclass correlation coefficient between both 1RM testing methods was 0.99. Using Bland Altman analysis, 1RM obtained with the estimation method showed a small overestimation of on average 1.27kg or 1.5% compared with the direct method. Because of this high agreement, we chose to continue with the estimation method, which was considered less time consuming.

Measurement of force-velocity characteristics. Force-velocity characteristics of the knee extensors were evaluated using a Biodex Medical System 3® dynamometer (Biodex Medical Systems, Shirley, NY). Tests were performed unilaterally on the right side, in a seated position on a backward-inclined (5°) chair. Safety belts were used to stabilize the upper leg, the hips, and the shoulders. The rotational axis of the dynamometer was aligned with the transversal knee-joint axis and was connected to the distal end of the tibia with a length-adjustable rigid lever arm. The dimensional positions of the rotational axis, the position of the chair, and the length of the lever arm were identical at pre- and posttest. The force-velocity characteristics of the knee extensors were determined by three standardized tests: an isometric test, a speed of movement test, and an isokinetic test. The protocol was performed twice, and the best performance was used for further analysis.

First, isometric knee extension strength was obtained at a knee joint angle of 90°. Subjects were instructed to extend the leg as hard as possible over a 5-second period. Maximal voluntary isometric contractions were performed twice, separated by a 20-second rest interval. The static peak torque ($PT_{stat90°}$, Nm) was recorded as the maximal isometric strength performance.

Second, subjects performed three ballistic tests for the knee extensors to determine speed of movement. They were asked to extend the lower leg as quickly as possible from a knee joint angle of 90° to 160°. As it is the objective to measure actual gains in velocity, one should take into account the increases in maximal strength. In this study, pre and post measurements of speed of movement of the knee extensors were performed relative to the individual isometric strength. This means that, if a subject had gained in maximal strength post intervention, he or she had to accelerate higher resistances in the speed of movement test. Therefore, increased velocity during the speed of movement test reflects actual gains in velocity, independent of maximal strength increases. Consequently, the test was performed with controlled resistances on the lever arm:

20%, 40%, and 60% of the individual static peak torque, respectively. In each of these conditions, speed of movement (S, in °/s) was recorded twice. The maximum speed recorded at the loading of 20%, 40%, and 60% was reported as S_{20}, S_{40}, and S_{60}, respectively.

Third, subjects performed three times a maximal concentric action of the knee extensors, followed by a maximal concentric action of the knee flexors, at an angular velocity of 60°/s. ROM was set from a knee joint angle of 90° to 160°. Maximal isokinetic strength of the knee extensors was defined as the dynamic peak torque ($PT_{dyn60°/s}$, in Nm), irrespective of knee angle. The knee joint angle (in °) at $PT_{dyn60°/s}$ was also used for further analysis. As peak torque does not take into account ROM, maximal work (MW, in Joule, representing the ability to develop torque throughout the ROM) was additionally evaluated. Finally, to evaluate whether the different interventions were more effective in increasing either isokinetic or isometric strength, we calculated the isokinetic-isometric strength ratio as ($PT_{dyn60°/s}/PT_{stat90°}$) x 100.

Statistical analyses

Baseline between-group differences for subjects' characteristics and outcome variables (1RM, $PT_{stat90°}$, S_{20}, S_{40}, S_{60}, $PT_{dyn60°/s}$, Angle $PT_{dyn60°/s}$, MW and $PT_{dyn60°/s}/PT_{stat90°}$) were analyzed by one-way analysis of variance (ANOVA) with Bonferroni post hoc testing. Within-group changes from pre to post for all outcome variables were analyzed with paired T-test.

To assess between-group differences in changes over time for all outcome variables, linear mixed-model analysis with an unstructured covariance structure, time as repeated factor and group as fixed factor, was used. Post hoc analyses were conducted to determine differences in changes between groups, as it was hypothesized that HI_{max} and LO_{max} would be more effective than LO. All statistical tests were performed with SPSS software version 16.0 (SPSS Inc., Chicago, IL). Level of significance was set a priori at $P < 0.05$.

Results

Baseline measures

At baseline, no significant differences were found between the groups for age, height, weight, or BMI (all $P > 0.05$; Table 1). Also, there were no baseline differences among groups in any of the outcome variables, except for S_{40}. For this parameter, LO_{max} scored marginally lower than LO at baseline ($P = 0.044$).

Changes from baseline

Knee extension 1RM. Linear mixed-model analysis indicated a significant time effect from pre to post for knee extension 1RM. Although all groups showed a significant increase in 1RM, a time x group interaction effect was found (P = 0.004), with HI_{max} (+50.7 ± 25.1%) improving significantly more than both LO (+30.7 ± 10.1%, P = 0.002) and LO_{max} (+32.2 ± 12.3%, P = 0.008) (Table 2). More specifically, the greater improvement for HI_{max} was apparent from the 13th training session on (Figure 2).
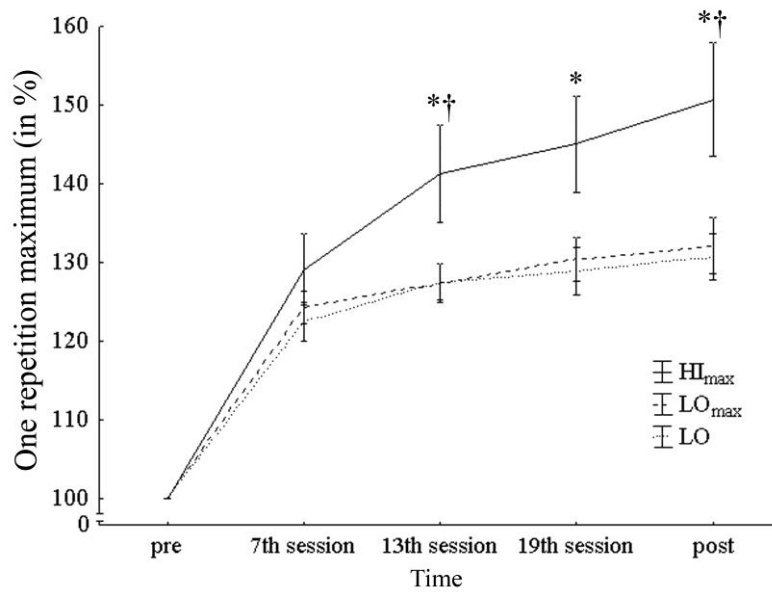
Figure 2. Knee extension one repetition maximum (mean ± standard error) for high-resistance-maximal-effort training group (HI_{max}), low-resistance-maximal-effort training group (LO_{max}), and low-resistance-low-effort training group (LO). 1RM was measured at baseline (pre), before the 7th, 13th, and 19th training session, and post intervention. Baseline 1RM was equated as 100%.
*Significant difference in change from previous measurement between HI_{max} and LO at P < 0.05.
†Significant difference in change from previous measurement between HI_{max} and LO_{max} at P < 0.05.

Table 2. Mean and SD for pre- and posttest and % change (±SD) for force-velocity characteristics of the knee extensors for the three intervention groups

		HI$_{max}$ (n = 12)			LO$_{max}$ (n = 12)			LO (n = 12)			P-values	
		Mean	SD	%	Mean	SD	%	Mean	SD	%	Time	Time x group
1RM (kg)	Pre	58.2	17.9		63.7	19.5		61.5	18.7			
	Post	84.8	20.7	50.7±25.1*†	82.9	22.0	32.2±12.3*‡	79.3	22.1	30.7±10.1*‡	< 0.001	0.004
PT$_{stat90°}$ (Nm)	Pre	234.2	74.4		237.6	79.6		232.5	68.1			
	Post	249.4	74.9	7.4±8.1*	242.8	83.9	4.9±9.6	235.3	65.9	2.1±10.1	0.004	0.259
S$_{20}$ (°/s)	Pre	417.9	38.7		400.2	48.8		442.1	36.9			
	Post	419.2	28.9	0.9±9.1	426.3	46.3	6.0±3.2*†‡	442.2	35.5	0.2±5.3	0.049	0.044
S$_{40}$ (°/s)	Pre	286.3	29.7		266.6	47.9		307.5	37.0			
	Post	283.5	30.8	-0.4±11.5	290.1	34.7	7.7±9.7*	309.1	27.6	1.5±12.0	0.196	0.134
S$_{60}$ (°/s)	Pre	187.5	44.8		168.4	52.8		208.6	49.6			
	Post	183.7	34.2	1.6±24.8	192.0	42.7	18.4±36.5	199.2	43.3	-2.5±17.8	0.675	0.274
PT$_{dyn60°/s}$ (Nm)	Pre	180.1	39.8		173.4	44.0		183.2	38.0			
	Post	186.2	42.1	3.3±6.3	187.6	47.0	9.8±5.6*†‡	186.1	39.2	2.0±8.9	< 0.001	0.030
Angle PT$_{dyn60°/s}$ (°)	Pre	110.3	4.4		107.9	2.4		109.7	4.7			
	Post	109.8	5.0	0.7±4.4	109.3	2.0	0.8±5.0	109.2	3.4	-1.6±4.4	0.773	0.264
MW (Joule)	Pre	140.8	31.1		130.4	33.3		151.1	31.9			
	Post	147.2	32.9	4.8±8.2	148.4	37.1	15.1±10.6*†‡	156.8	30.6	4.6±10.4	< 0.001	0.025
PT$_{dyn60°/s}$/PT$_{stat90°}$ (%)	Pre	80.6	15.4		75.1	9.0		81.6	13.8			
	Post	77.2	12.1	-3.4±8.2	79.8	10.0	5.2±8.5‡	81.2	11.2	0.3±8.4	0.937	0.048

P-values: Linear mixed-models analyses, significance level P < 0.05. HI$_{max}$ = high-resistance training with maximal effort; LO$_{max}$ = low-resistance training with maximal effort; LO = low-resistance training with low effort; 1RM = knee extension one repetition maximum; PT$_{stat90°}$ = static (isometric) peak torque; S$_x$ = speed of movement at x% of PT$_{stat90°}$; PT$_{dyn60°/s}$ = dynamic (isokinetic) peak torque; MW = maximal work.

* Significant change from pre to post; † Significant difference with LO; ‡ Significant difference with HI$_{max}$.

Force-velocity characteristics. For static peak torque, an overall time effect was found, but only HI_{max} showed a significant increase from pre to post (+7.4 ± 8.1%, P = 0.010). However, no time x group interaction effect was found for this parameter (Table 2).

Figure 3 clearly shows an upward shift of the force-velocity curve from pre to post in LO_{max} only. This finding indicates that LO_{max} was the only group that increased in speed of movement. This increase was significant for S_{20} (+6.0 ± 3.2%, P < 0.001) and S_{40} (+7.7 ± 9.7%, P = 0.032). Furthermore, a time x group interaction effect was found for S_{20}, with post hoc testing revealing a significantly greater gain in S_{20} for LO_{max} compared to HI_{max} (+0.9 ± 9.1%, P = 0.033) and to LO (+0.2 ± 5.3%, P = 0.026) (Table 2, Figure 3).

With regard to dynamic peak torque (Table 2), both a time effect and a time x group interaction effect were found. LO_{max} significantly improved dynamic peak torque (+9.8 ± 5.6%, P < 0.001) and demonstrated a greater gain in $PT_{dyn60°/s}$ than both HI_{max} (+3.3 ± 6.3%, P = 0.048) and LO (+2.0 ± 8.9%, P = 0.011). HI_{max} and LO did not show significant improvements in $PT_{dyn60°/s}$, although a trend was apparent for HI_{max} (*p* = 0.095) (Table 2). The angle of peak torque did not change after the intervention for any of the groups. A time effect (*p* < 0.001) and a time x group interaction effect (P = 0.025) were demonstrated for maximal work during isokinetic testing. This parameter showed a significantly greater increase in LO_{max} (+15.1 ± 10.6%) compared with both HI_{max} (+4.8 ± 8.2%, P = 0.020) and LO (+4.6 ± 10.4%, P = 0.015). LO_{max} was the only group that significantly improved MW (P = 0.001), while a trend was found for HI_{max} (P = 0.074) (Table 2).

Linear mixed-model analysis indicated an additional time x group effect for the isokinetic-isometric strength ratio, with post hoc testing revealing a significant difference between LO_{max} and HI_{max} (P = 0.015). LO_{max} showed a trend towards an increase (+5.2 ± 8.5%, P = 0.073), suggesting that isokinetic strength tended to improve more than isometric strength in this group (Table 2).
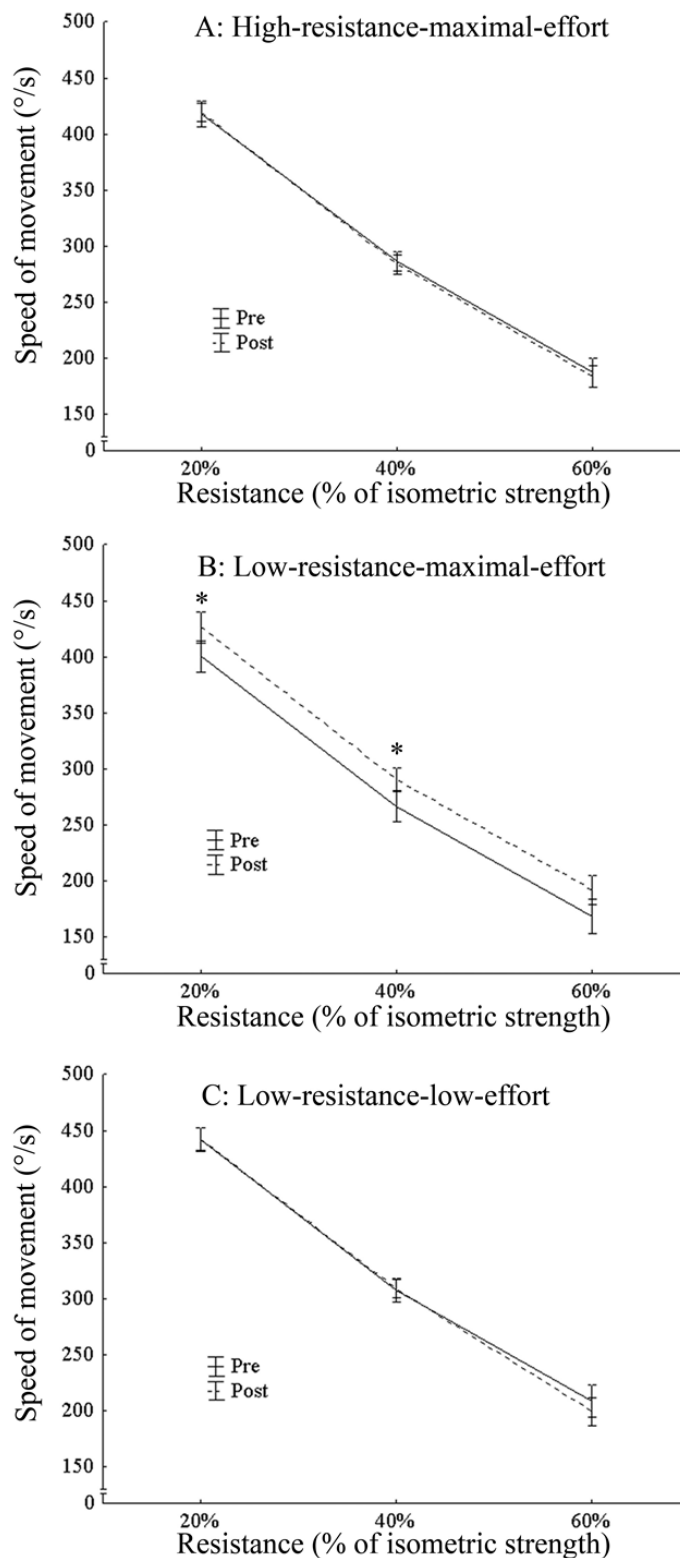
Figure 3. Speed of movement of knee extension (mean ± standard error) with an external resistance of 20%, 40%, and 60% of the individual isometric strength before (pre) and after 9 weeks of training (post). A: high-resistance-maximal-effort training group, B: low-resistance-maximal-effort training group, C: low-resistance-low-effort training group. * Posttest values are significantly higher than pretest values at $P < 0.05$.

Discussion

The primary findings of this study demonstrate that, when training at moderate speed, high-resistance exercise with maximal effort may be preferable to increase 1RM and isometric strength, whereas low-resistance exercise with maximal effort may be more effective in increasing isokinetic strength, maximal work, and speed of movement. Low-resistance exercise with low effort did not show any major effect on force-velocity characteristics of the knee extensors.

In the literature, high-resistance training has already been proven to be effective in increasing muscle strength and muscle volume (4,11,16,19,21,33,35). However, it remains controversial whether maximal effort is required to optimize muscle adaptation in the context of strengthening exercise. Low-resistance exercise has been considered as a potential alternative for high-resistance exercise, as long as maximal effort is achieved during training, but previous studies have been inconclusive (2,4,19,35). The findings in this study support the idea that training at maximal effort, resulting in optimal activation of the muscle, may be needed to optimize strength gains (15,28,29,32).

Mechanical stress has always been considered as an essential trigger for strength adaptations. It was even suggested that resistances below 65% of 1RM are insufficient to result in strength gain (24), a hypothesis contradicted by our findings and by several other studies (34,36-39). LO_{max} showed gains in isokinetic strength and both LO and LO_{max} significantly increased in 1RM strength, while the training load always remained below 45% of 1RM.

In this study, after 6 training sessions, the increases in 1RM were similar for HI_{max}, LO_{max}, and LO. This large initial improvement was probably due to coordinative and neural adaptations. However, from the 13th training session on, training at high resistance (80% of 1RM) was most effective for increasing 1RM strength. One might suggest that HI_{max} had an advantage over LO_{max} and LO for increasing 1RM, since testing and training procedure were identical for HI_{max}. However, a learning effect is probably not the sole explanation, since between-group differences were found only from the 13th session on. The findings of this study are therefore in line with Campos et al. showing that gains in 1RM are related to the resistance used during training, with higher resistances leading to greater gains (4). The gain in 1RM after 9 weeks in HI_{max} (+50.7%) was comparable to gains in other studies (4,14,21,39).

With respect to isometric strength, an overall time effect was found, with no differences between groups. However, HI_{max} was the only regimen that significantly increased $PT_{stat90°}$. This increase (+7.4%) was notably smaller than the gains found in previous research (14). Although it was emphasized in both HI_{max} and LO_{max} that training should be performed with maximal effort in

order to optimize motor unit recruitment, no significant improvement was found for $PT_{stat90°}$ in LO_{max}.

Thus, traditional high-resistance training seems to be the most effective training approach for increasing 1RM and isometric strength. The use of low resistances, with or without maximal effort, seems unable to maximize effects on these parameters. However, LO_{max} was found to be most effective in increasing isokinetic strength. The combination of maximal effort and a high number of repetitions seems to be beneficial for increasing dynamic strength when compared with traditional low-repetition high-resistance training. In LO_{max}, the training protocol was focused on repetitive movements, potentially leading to greater dynamic changes over the full ROM. Indeed, LO_{max} demonstrated a greater improvement on maximal work during isokinetic testing than HI_{max} or LO. In other words, LO_{max} was more able to develop torque throughout the ROM after the intervention. Moreover, LO_{max} tended to increase more on a dynamic (isokinetic) test in which peak torque is registered irrespective of the knee joint angle, than on an isometric test.

On the one hand, the disparity in gains between HI_{max} and LO_{max} can be explained from a mechanical point of view: in the isometric test, high forces were needed in a knee joint angle of 90°. In 1RM testing, the high external resistance more specifically requires a high force production at the start of the movement, i.e. in a knee joint angle of 90°, to overcome inertia. Therefore, although 1RM is a dynamic test, it closely resembles the isometric testing procedure. From the three training groups in our study, HI_{max} was mostly challenged in a knee joint angle of 90° because the muscle was exposed to high external resistances. Since adaptations are training-specific, it seems plausible that traditional high-resistance training demonstrates the greatest increases in 1RM and isometric strength at a knee angle of 90°.

On the other hand, the disparity in gains on isokinetic strength between LO_{max} and HI_{max} might be explained by the difference in training volume (23). In this study, three different exercise protocols were designed in order to obtain different combinations for levels of effort and external resistance within a similar number of repetitions (10 to 12): HI_{max} with high resistance and attaining maximal effort; LO_{max} with low resistance immediately after an intense fatiguing protocol also attaining maximal effort; and LO with the same low resistance as LO_{max}, but not attaining maximal effort. This approach inevitably led to a higher training volume for LO_{max}.

Although HI_{max} and LO_{max} clearly showed training-specific differences in neuromuscular adaptations, they both appeared to be effective in increasing muscle strength. However, gaining muscle strength should not be the sole focus of strength training regimens. In fact, muscle power, i.e. the product of force and velocity, might be of even greater importance in activities of daily life (ADL) (10). Therefore, in the current study, different levels of resistance and effort were used to

examine the effects of 9 weeks of resistance training at moderate speed on force-velocity characteristics of the knee extensors. It was hypothesized that both the training protocols HI_{max} and LO_{max}, in which maximal effort was attained, would be similarly more effective than low-resistance exercise that did not result in maximal effort (LO).

Contrary to our hypothesis, HI_{max} failed to increase speed of movement at any of the resistances. This finding is in line with a study of Roelants et al., in which moderate-to-high-resistance exercise at moderate speed did not improve speed of movement, even though a trend was found (27). It is possible that high-speed resistance training would attain greater gains in speed of movement (12,13,30). However, S_{20} and S_{40} significantly improved in LO_{max} in our study, while this group also trained at moderate speed. Although further research is needed to explain these results, it should be noted that previous studies also found increases in maximal strength at relatively high speeds after low-resistance exercise. The movement during the high-fatiguing protocol and subsequent training set may have resulted in ballistic actions because of the low resistance, hereby improving motor unit recruitment at high movement velocities (16,39). The finding that speed of movement can be increased with low-resistance training with maximal effort at moderate speed is of great importance in clinical practice, since speed of movement is a key component in everyday function, especially in frail elderly in whom high resistances are not always feasible (40).

Isokinetic testing procedures can also be used to examine velocity-related force production but this approach has been questioned, since isokinetic muscle actions do not simulate natural movement patterns (8). Activities of daily life include accelerations and decelerations, concentric and eccentric phases. An isoinertial assessment, in which a constant resistance is applied to the muscle and speed can vary during movement, closely resembles ADL and was therefore used in this study.

Some limitations of this study need to be considered. Although the findings suggest that adaptations following HI_{max} and LO_{max} are based on different mechanisms, most probably related to motor unit recruitment, intramuscular synchronization and/or activation of high threshold motor units, we were not able to measure any of these mechanisms within the scope of this study. Furthermore, the use of a single-set design over a short time period (9 weeks) resulted in rather small gains in isometric and isokinetic strength. A multiple-set design would most likely have been associated with greater strength gains (20,42), more clearly revealing differences between groups. Also, although all groups performed a similar number of repetitions per training set, LO_{max} additionally performed a fatiguing protocol of 60 repetitions, leading to differences in training volume.

Interestingly, and contrary to our expectations, significant differences between high- and low-resistance training on force-velocity characteristics of the knee extensors were found, despite the fact that maximal effort was achieved in both training regimens. Traditional high-resistance exercise was most effective in increasing 1RM and isometric strength. However, low-resistance exercise with a focus on repetitive movements resulting in maximal effort was substantially more effective in increasing dynamic strength and maximal work. Even more, this training protocol lead to an increase in speed of movement, irrespective of strength gains, although training was performed at moderate speed. Thus, low-resistance exercise with maximal effort should not be considered as a replacement for high-resistance training, but rather as an alternative with different training-specific adaptations.

Practical applications

In the attempt to unravel the dose-response relationships, research on the impact of low-resistance exercise on muscle characteristics has recently gained interest. The present results clearly demonstrated the effects of low-resistance exercise with maximal effort on dynamic strength, maximal work, and speed of movement. Although the precise mechanism for its effects remains unclear, the application of high-repetitive movements before training at low resistance may be useful in training programs aiming at improving speed-related parameters, even if a moderate speed of movement is used during exercise. Differences were found with traditional high-resistance exercise, in which gains in 1RM and isometric strength were more important. Thus, in designing a strength training program, both resistance and repetitions should be adjusted according to the desired training-specific outcomes. Rather than prescribing only one of both training regimens, it might also be interesting to consider a combined training approach, especially when aiming for increases in both 1RM and speed of movement.

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Subchapter 2.2

Strength training at high versus low external resistance in older adults

Strength training at high versus low external resistance in older adults:

effects on muscle volume, muscle strength,

and force-velocity characteristics

E. Van Roie, C. Delecluse, W. Coudyzer, S. Boonen, I. Bautmans

Abstract

Muscle adaptations can be induced by high-resistance exercise. Despite being potentially more suitable for older adults, low-resistance exercise protocols have been less investigated. We compared the effects of high- and low-resistance training on muscle volume, muscle strength, and force-velocity characteristics. Fifty-six older adults were randomly assigned to 12 weeks of leg press and leg extension training at either HIGH (2 x 10-15 repetitions at 80% of one repetition maximum (1RM)), LOW (1 x 80-100 repetitions at 20% of 1RM), or LOW+ (1 x 60 repetitions at 20% of 1RM, followed by 1 x 10-20 repetitions at 40% 1RM). All protocols ended with muscle failure. Leg press and leg extension 1RM were measured at baseline and post intervention, and before the first training session in week 5 and 9. At baseline and post intervention, muscle volume (MV) was measured by CT-scan. A Biodex dynamometer evaluated knee extensor static peak torque in different knee angles ($PT_{stat90°}$, $PT_{stat120°}$, $PT_{stat150°}$), dynamic peak torque at different speeds ($PT_{dyn60°/s}$, $PT_{dyn180°/s}$, $PT_{dyn240°/s}$), and speed of movement at 20% (S_{20}), 40% (S_{40}), and 60% (S_{60}) of $PT_{stat90°}$. HIGH and LOW+ resulted in greater improvements in 1RM strength than LOW ($P < 0.05$). These differences were already apparent at week 5. Similar gains were found between groups in MV, PT_{stat}, $PT_{dyn60°/s}$, and $PT_{dyn180°/s}$. No changes were reported in speed of movement. HIGH tended to improve $PT_{dyn240°/s}$ more than LOW or LOW+ ($P = 0.064$). In conclusion, high- and low- resistance exercise ending with muscle failure may be similarly effective for hypertrophy. High-resistance training led to a higher increase in 1RM strength than low-resistance training (20% of 1RM), but this difference disappeared when using a mixed low-resistance protocol in which the resistance was intensified within a single exercise set (40% of 1RM). Our findings support the need for more research on low-resistance programs in older age, in particular long-term training studies and studies focusing on residual effects after training cessation.

Keywords: muscle hypertrophy; resistance training; training load; muscle fatigue

Introduction

Human aging is characterized by a progressive decline in skeletal muscle mass, accompanied by marked decreases in muscle strength and muscular function. These losses can have a significant impact on a person's ability to independently perform activities of daily life (1,32). It is clear that effective interventions are needed to prevent or reverse these losses in older adults.

For optimal muscle growth, strengthening exercise at moderate to high external resistance (70-85% of the one repetition maximum (1RM)) is recommended (3). However, practitioners remain reluctant to prescribe exercises that challenge the musculoskeletal system of older adults at high

external resistances (2). Interestingly, numerous studies suggest that low-resistance exercise, with vascular occlusion, can induce gains in muscle volume and strength equivalent to those observed after training at higher resistances (23,30,49). In line with these and other (47,51,53) findings, Mitchell et al. provided evidence that lifting low resistances to the point of momentary muscle fatigue (failure) leads to hypertrophy and strength gains roughly equivalent to those achieved with conventional high-resistance training (36). This would suggest that the use of high external resistances may not be a necessity to elicit muscle hypertrophy.

Rather than having to be exposed to high external resistances, achieving maximal effort might be of greater importance for gains in muscle mass and strength (11,17,40,44). Maximal effort is typically reached when performing a series of repetitions to the point of momentary muscle fatigue. This maximal effort might be needed to maximize motor unit recruitment and thus to enhance the hypertrophic response (11,17).

In previous research, endurance-type strength training regimens have been compared to traditional high-resistance training. Effects on muscle mass and muscle strength, however, remain inconclusive (5,9,21,47). Remarkably, most endurance-type protocols restricted the number of repetitions per set to about 20 or 30. Takarada and Ishii suggested that, in these protocols, the interset rest period should be kept short (~ 30 s) to reduce metabolite clearance, which in turn creates the need for additional motor unit recruitment in subsequent sets (48). One can expect that high-repetition exercise protocols (≥ 60 repetitions) would also be effective to maximize motor unit recruitment. However, to date, virtually no studies have focused on the effects of such high-repetition protocols.

Another interesting approach to further optimize motor unit recruitment might be to vary training resistance. Training resistance can not only vary over the course of a training period (periodization), but also from set to set within a single training session (50). A previous study by Goto et al. suggested that adding a single set of exercise at 50% of 1RM to a strength-type regimen at 90% of 1RM may optimize strength adaptation (18). A recent study tested a strength training protocol in young adults, in which a highly fatiguing protocol of 60 repetitions at 20-25% of 1RM was immediately followed (no rest) by a set of 10 repetitions at 40% of 1RM. This mixed low-resistance exercise protocol showed interesting benefits on dynamic strength and speed of movement of the knee extensors (53). Especially in older adults, these muscle parameters are of major importance in activities of daily living (43,54).

In this study, the purpose was to compare the effects of low-resistance training at high repetitions with traditional high-resistance training at low repetitions (HIGH) on muscle volume, muscle strength, and force-velocity characteristics in older adults. To further investigate the beneficial

effect of varying training resistance within a single training session, two low-resistance exercise protocols were created: one high-repetition low-resistance protocol (LOW) in which external resistance was kept constant within one session, but also one mixed high-repetition low-resistance protocol (LOW+) in which resistance was increased after 60 repetitions. All training protocols were designed to end in maximal effort (i.e. muscle fatigue and failure to continue the exercise). If performing repetitions to the point of momentary muscle fatigue is sufficient to reach (near) maximal motor unit recruitment, and thus to activate type II muscle fibers, all exercise protocols would be expected to be effective in improving muscle volume, muscle strength, and force-velocity characteristics. However, it might be possible that, in addition to muscle fatigue, a mechanical stimulus is needed to activate type II muscle fibers, especially when training at very low external resistances (protocols with many repetitions). If that is the case, increasing the resistance in LOW+ at the end of a high-repetition protocol should allow this group to obtain better effects than LOW on muscle volume, muscle strength, and force-velocity characteristics.

Methods

Study participants

Community-dwelling adults aged 60 and older were locally recruited through advertisements and oral communications for inclusion in a 12-week resistance training program. Exclusion criteria were current participation in structured endurance exercise and/or participation in resistance exercise in the last 6 months prior to the study, knee or hip problems, unstable cardiovascular disease, neuromuscular disease, and acute hernia. A flowchart of the study is provided in Figure 1. Fifty-six older men and women were randomly assigned to one of three training interventions: traditional high-resistance training (HIGH), low-resistance training (LOW), or mixed low-resistance training (LOW+). Randomization was stratified for gender, age, and baseline isometric knee extension strength. The study was approved by the University's Human Ethics Committee in accordance with the declaration of Helsinki. All participants provided written informed consent.

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                    │   89 responded to advertisement  │
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Excluded (n = 33):

- Declined informed consent (n = 19)

- Current participation in exercise (n = 3)

- Unstable cardiovascular disease (n = 4)

- Acute hernia (n = 4)

- Hip (n = 1) and knee (n = 1) problems

- Planned surgery (n = 1)

Randomized and completed pretests

(n = 56)

Allocated to HIGH

(n = 18, 8m, 10f)

Allocated to LOW

(n = 19, 9m, 10f)

Allocated to LOW+

(n = 19, 9m, 10f)

Completed posttests

(n = 18)

Completed posttests

(n = 19)

Completed posttests

(n = 19)

Figure 1. Flowchart of the study.

Resistance training protocol

The exercise sessions were organized at a local fitness and health center over a period of 12 weeks. Baseline and post intervention measurements were performed from January to March 2012 and from April to June 2012, respectively. After an initial familiarization session, in which proper lifting technique was demonstrated and practiced for each of the exercises, participants exercised three times weekly on nonconsecutive days for 12 weeks (total of 36 sessions). Exercise

equipment included leg press and leg extension (Technogym, Gambettola, Italy). Training programs were inspired by previous research (53). Each training session started with a 10min warm-up on a cycle ergometer (Technogym Bike Excite, Gambettola, Italy) or on a treadmill (walking pace) (Technogym Run Excite, Gambettola, Italy). Participants were instructed to perform all exercises at a moderate speed, i.e. 2s for each concentric and 3s for each eccentric action. Between the exercises, a rest period of at least two minutes was provided. The IsoControl (Technogym, Gambettola, Italy) provided feedback on the number of repetitions, the movement speed, the rest period between sets, and the range of motion during exercise. All training sessions were closely supervised by a qualified fitness instructor, and participants were verbally encouraged to continue the exercises until failure (i.e. inability to perform more repetitions due to local muscle fatigue). Immediately after each individual exercise, participants graded their level of perceived exertion on the OMNI-Resistance Exercise Scale of perceived exertion (scale from 0 to 10) (39).

Exercise protocols were initially designed to be approximately equal in volume (% resistance x repetitions) (Figure 2). The protocol used in HIGH was based on ACSM's guidelines for resistance training (3). These guidelines recommend performing at least one set to the point of failure for healthy individuals. In HIGH, the external resistance was initially set at 80% of 1RM. To ensure that maximal effort would be reached at the end of each set, participants were instructed to perform at least 10 to 15 repetitions. Two sets were performed with one minute of rest between sets. In LOW, the external resistance was initially set at about 20% of 1RM. Participants were instructed to perform 1 set of 80 to 100 repetitions. In LOW+, participants were instructed to complete a fatiguing protocol of 60 repetitions at about 20% of 1RM. Immediately afterwards (no rest), external resistance was increased to about 40% of 1RM and participants were instructed to perform 10 to 20 additional repetitions.

In all groups, participants were encouraged to continue the exercise if maximal effort was not achieved after the prescribed number of repetitions. External resistance was adjusted if participants performed repetitions beyond the prescribed training zone, as well as if the rate of perceived exertion dropped below 6. This strategy was used to ensure that maximal effort was reached at the end of each exercise set, as this may be necessary to optimize muscular adaptations (17,40,44).
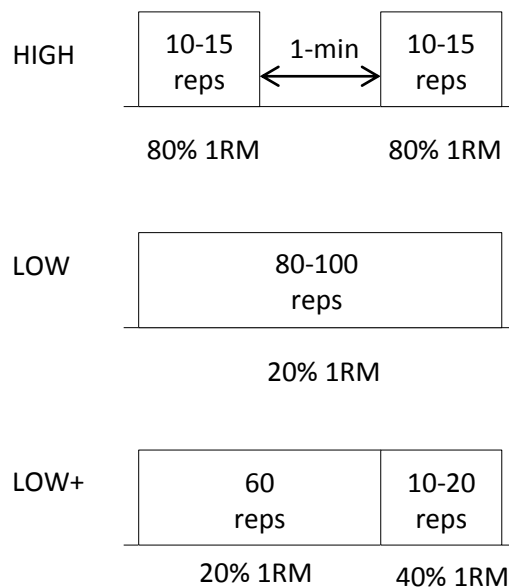
Figure 2. Protocols for exercise training on leg press and leg extension.

Average training volume per exercise session was calculated for each participant as:

$$\frac{\sum_{i=1}^{n}(\text{number of repetitions leg press} \times \%1RM)i + (\text{number of repetitions leg extension} \times \%1RM)i}{n}$$

with n = total number of exercise sessions performed during the 12-week training intervention. This equation used relative data on training resistance (training load as a percentage of 1RM) instead of absolute data (in kg), as the latter can be biased by a number of confounding factors. Amongst others, confounding factors that influence training load (kg) in individuals may be gender, body weight, strength level, and muscle volume.

Outcome measures

Muscle volume. At baseline and post intervention, four 2.5mm-thick axial slices were measured in the middle of the right upper leg was measured by a computed tomography scan (Siemens Somatom Definition Flash, Forchheim, Germany). The axial images were obtained at the midpoint of the distance between the medial edge of the greater trochanter and the intercondyloid fossa of the femur. The four slices were then put together as one 10mm-thick slice and the software program Volume (Siemens) calculated the overall muscle volume (in cm³) for this 10mm-thick slice. Standard Hounsfield Units ranges for skeletal muscle (0-100) were used to segment muscle tissue area. Corrections were made for bone marrow. All measurements were performed by one expert radiologist in the University Hospital.

One repetition maximum and local muscular endurance. One repetition maximum was evaluated every 4 weeks: at baseline (pre), before the first training session in week 5 and week 9, and after

12 weeks of training (post). Training volume on the test sessions in week 5 and week 9 was reduced to only the leg extension exercise. Local muscular endurance was assessed at baseline and post intervention.

The assessment of leg press 1RM started with a warm-up set of 8 repetitions at approximately 50% of the estimated 1RM, followed by another set of 3 repetitions at 70% of the estimated 1RM. Subsequent lifts (ranging from 3 to 5) were single repetitions with progressively heavier resistances until failure. A rest period of one to five minutes was allotted between each attempt to ensure recovery. The heaviest successful lift was determined as 1RM.

Leg extension 1RM was estimated through a logarithmic regression formula (53). In this testing procedure, participants had to complete a maximum number of repetitions at a resistance that was selected by the supervisor (5 to 15 repetitions were targeted). Using the formula, the percentage of 1RM was estimated based on the number of repetitions, and subsequently, the 1RM was derived. This method was chosen over a direct method, as it was considered less time consuming.

After determining leg extension 1RM, the local muscular endurance test was assessed, consisting of completing a maximum number of repetitions at 60% of 1RM (until failure) (9).

Force-velocity characteristics. Force-velocity characteristics of the knee extensors were measured on a Biodex Medical System 3® dynamometer (Biodex Medical Systems, Shirley, NY). Tests were performed unilaterally on the right side, unless there was a medical contraindication. Participants were seated on a backwardly-inclined (5°) chair and secured with safety belts across the upper leg of the test side, the hips, and the shoulders. The rotational axis of the dynamometer was aligned with the transversal knee-joint axis and was attached to the tibia with a length-adjustable lever arm. The position of the rotational axis and the chair, as well as the length of the lever arm were identical at pre- and posttest. The protocol consisted of three standardized tests: an isometric test, a speed of movement test, and an isokinetic test. These three tests, as described below, were consecutively performed with about 2 minutes of rest between tests. After a first completion of the three tests and a rest period of 5 minutes, the protocol was repeated for a second time. The best performance for each parameter was reported.

First, static knee extension strength was obtained at different knee joint angles: 120°, 90°, and 150°. Maximal voluntary isometric contractions over a 5-second period were performed twice at each angle, separated by a 15-second rest interval. The static peak torque (Nm) recorded at these knee joint angles was reported as $PT_{stat120°}$, $PT_{stat90°}$, and $PT_{stat150°}$, respectively.

Second, three ballistic speed of movement tests for the knee extensors were performed, separated by a 20-second rest interval. Participants extended the lower leg twice as quickly as

possible from a knee joint angle of 90° to 160°. Resistances were 20%, 40%, and 60% of the individual static peak torque (90°). The maximum speed (°/s) recorded at these resistances was reported as S_{20}, S_{40}, and S_{60}, respectively.

Third, three maximal isokinetic extension-flexion movements were performed at an angular velocity of 60°/s, followed by five movements at both 180°/s and 240°/s. A 20-second rest period was provided between the sequences. The dynamic peak torque (Nm) of the knee extensors, irrespective of knee angle, was recorded as $PT_{dyn60°/s}$, $PT_{dyn180°/s}$, and $PT_{dyn240°/s}$, respectively.

**Functional performance**. The modified Physical Performance Test (mPPT) (8) was executed at baseline in order to document the overall functional performance level of our study sample. The mPPT consists of nine functional items: (i) Romberg test for balance, (ii) chair sit-to-stand test, (iii) lifting a book from waist height to a shelf at shoulder level, (iv) putting on and taking off a coat, (v) picking up a penny from the floor, (vi) turning 360°, (vii) walking 15m, (viii) ascending one flight of stairs, and (ix) climbing four flights of stairs. The score of each item ranged from 0 (the inability to complete the task) to 4 (the highest level of performance), with a summary performance score (mPPT-score) of maximum 36 points.

To analyze the effects of the intervention on functional performance, the following tests were performed at baseline and post intervention: 6-minute walk test, maximal gait speed test, 30-second chair sit-to-stand test, 5-repetition chair sit-to-stand test, and timed up-and-go test.

The 6-minute walk test was performed over a walking course of 20m (4). Participants walked up and down the course at a fast but comfortable pace, and the 6-minute walk distance (in meters) was reported.

To measure maximal gait speed, participants were asked to walk 7.5m as quickly as possible without running. The test was performed twice, and the best result (in meters per second) was used.

The 5-repetition and 30-second chair sit-to-stand test were performed using a standard chair without arm rests (34). Participants crossed both arms against the chest, started from a seated position (upper back against seat), stood up to full extension and sat down again (upper back against seat). The time required (in seconds) to perform 5 chair stands, was evaluated in the 5-repetition chair sit-to-stand test. This test was performed twice, using the best result in further analyses. In the 30-second chair sit-to-stand test, the number of successful repetitions was counted over a 30-second period. Due to the exhausting nature of this test, it was performed only once.

In the timed up-and-go test, the time (in seconds) required for the participant to stand up from a standard armchair, walk a distance of 3m, turn, walk back and sit down again, was measured

(7,38). The test was performed as quickly as possible, however, without running. The best result from two trials was used.

Statistical analyses

Data were initially analyzed for normality with a Shapiro-Wilk test. The following variables were not normally distributed: muscle volume, leg press 1RM, static peak torque (at 90°), speed of movement (at 40% of $PT_{stat90°}$), dynamic peak torque (at 60°/s, 180°/s, 240°s), mPPT-score, and 5-repetition chair sit-to-stand test.

For all normally distributed variables, one-way analysis of variance with Bonferroni post hoc testing was used to test for baseline differences between groups. Within-group changes from baseline to post were analyzed with paired T-tests. To assess between-group differences in changes over time, linear mixed-model analysis with an unstructured covariance structure was used, with time as repeated factor and group as fixed factor. To account for differences in average training volume, this variable was introduced as a covariate in the mixed-model analyses. Post hoc analyses were conducted to determine differences in changes between groups.

For all non-normally distributed variables, Kruskal-Wallis tests were used to search for baseline differences between groups. Time-effects from baseline to post intervention were analyzed with Friedman tests, and within-group changes from baseline to post were analyzed with Wilcoxon-signed rank tests. Percent changes from baseline to post were calculated for each individual and were divided by the average training volume to account for differences in training volume. These variables were then used in Kruskal-Wallis tests to determine differences in changes between groups. Only when significance was revealed with the Kruskal-Wallis test, Mann-Whitney U tests were used as post hoc tests.

Pearson's correlation coefficient was determined to assess associations between percent changes in muscle parameters and percent changes in functional performance measures.

All statistical tests were executed with SPSS software version 19 (SPSS Inc., Chicago, IL). Level of significance was set at P < 0.05.

Results

Baseline characteristics and training adherence

No side effects of the intervention were reported in any of the groups. All subjects completed the study. However, two Biodex measurements (one baseline for HIGH, one post for LOW+) failed due to a lack of compliance of the participants with the test instructions, and were excluded from analysis. Overall adherence (number of training sessions attended as a percentage of the total

number of training sessions) to the training program was 95.7% in HIGH, 95.8% in LOW, and 95.3% in LOW+, with no significant differences between groups. Moreover, none of the participants' characteristics (Table 1) nor any of the outcome variables differed between groups at baseline (all $P > 0.05$). At baseline, the overall summary performance score on the mPPT was 35.34 ± 1.16.

Table 1. Participants' characteristics at baseline (mean ± SD)

	HIGH (n = 18: 8m, 10f)	LOW+ (n = 19: 9m, 10f)	LOW (n = 19: 9m, 10f)	P
Age (y)	67.72 ± 4.28	67.43 ± 5.90	68.76 ± 4.96	0.701[a]
Weight (kg)	71.58 ± 11.33	76.63 ± 12.10	75.58 ± 14.77	0.460[a]
Height (m)	1.67 ± 0.08	1.66 ± 0.08	1.65 ± 0.09	0.769[a]
BMI (kg/m²)	25.54 ± 2.82	27.57 ± 3.08	27.62 ± 4.12	0.117[a]
mPPT-score	35.61 ± 0.70	35.32 ± 1.06	35.11 ± 1.56	0.616[b]

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; mPPT = modified physical performance test.
[a]Results of one-way analysis of variance between baseline group means.
[b]Results of Kruskal-Wallis test.

Training volume

Training variables are listed in Table 2. The average training volume accomplished during each session was calculated for all groups. Although training programs were designed to be approximately equal in volume, the average training volume per session on the leg extension exercise revealed a significantly higher volume in LOW compared to HIGH and LOW+ ($P < 0.05$). Average training volume (leg press and leg extension summed) was therefore used as a covariate in the mixed-model analyses and in the Kruskal-Wallis tests.

Outcome measures

Muscle volume. Muscle volume of the upper leg increased significantly over time, with no difference between HIGH (+3.2 ± 3.7%, $P = 0.003$), LOW (+2.4 ± 2.7%, $P = 0.002$), and LOW+ (+2.6 ± 3.8%, $P = 0.016$) (Table 3 and Figure 3A).

Table 2. Training variables (mean ± SD)

		HIGH	LOW+	LOW
		(n=18: 8m, 10f)	(n=19: 9m, 10f)	(n=19: 9m, 10f)
Repetitions per set	Leg press set 1	16.1 ± 2.4	60.1 ± 0.1	91.6 ± 9.7
	Leg press set 2	15.1 ± 1.8	20.8 ± 7.1	-
	Leg extension set 1	13.6 ± 1.5	60.1 ± 0.3	87.8 ± 9.3
	Leg extension set 2	12.2 ± 1.1	16.6 ± 2.7	-
Resistance (% of 1RM)	Leg press set 1	87.2 ± 9.5	29.9 ± 5.0	35.5 ± 8.4
	Leg press set 2	87.0 ± 9.3	50.3 ± 7.2	-
	Leg extension set 1	76.2 ± 2.7	24.2 ± 5.2	30.0 ± 3.5
	Leg extension set 2	76.1 ± 2.6	45.0 ± 6.6	-
Training volume	Leg press	27.4 ± 5.8	28.6 ± 6.2	32.2 ± 6.7
	Leg extension	19.7 ± 2.3	22.1 ± 6.2	26.3 ± 5.3[*†]
	Leg press + leg extension	47.2 ± 6.9	50.8 ± 11.3	58.7 ± 9.0[*†]

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; 1RM = one repetition maximum.

Training volume = $\frac{\sum_{i=1}^{n}(\text{number of repetitions} \times \%1RM)i}{n}$, with n = total number of exercise sessions performed during the 12-week training intervention.

[*]Different from HIGH (p < 0.05, results of one-way analysis of variance with Bonferroni post hoc testing).

†Different from LOW+ (p < 0.05, results of one-way analysis of variance with Bonferroni post hoc testing).

Table 3. Mean and SD for baseline (pre-) and posttest and % change (±SD) for muscle volume, one repetition maximum, and force-velocity characteristics of the knee extensors for the three intervention groups

		HIGH (n=18)			LOW+ (n=19)			LOW (n=19)			p-values	
		Mean	SD	%	Mean	SD	%	Mean	SD	%	Time	Time x group
MV (cm³)	Pre	150.2	39.0		155.0	38.8		156.6	36.0			
	Post	154.5	38.1	3.2±3.7*	158.4	37.6	2.6±3.8*	160.3	36.8	2.4±2.7*	<0.001[b]	0.570[c]
1RMLP (kg)	Pre	99.8	56.4		96.2	40.7		110.0	56.3			
	Post	137.2	64.9	46.2±32.3*†	130.9	51.3	39.2±20.7*†	132.2	68.3	23.1±20.7*	<0.001[b]	0.002[c]
1RMLE (kg)	Pre	30.0	6.0		29.5	6.7		31.0	8.4			
	Post	38.8	7.5	30.0±11.5*†	37.5	6.5	29.7±19.8*†	36.9	10.2	19.2±5.3*	<0.001[a]	0.003[a]
END (reps)	Pre	16.4	3.8		16.6	4.7		17.1	3.3			
	Post	17.8	2.5	14.6±31.3	18.9	5.4	16.3±20.6*	19.8	3.8	19.8±29.8*	<0.001[a]	0.770[a]
PT$_{stat90°}$ (Nm)	Pre	162.5	55.0		158.3	54.0		158.7	56.5			
	Post	166.1	51.1	5.5±8.7	168.7	56.4	6.8±9.3*	164.1	59.5	3.3±5.7*	<0.001[b]	0.202[c]
PT$_{stat120°}$ (Nm)	Pre	143.5	39.9		140.2	40.0		138.0	44.3			
	Post	156.3	44.7	11.8±7.3*	154.4	42.6	10.1±9.2*	150.4	47.7	9.5±10.5*	<0.001[a]	0.749[a]
PT$_{stat150°}$ (Nm)	Pre	74.2	19.8		71.0	18.9		68.9	22.5			
	Post	79.0	22.0	8.6±9.8*	75.9	19.3	7.7±11.9*	76.9	27.2	11.4±14.8*	<0.001[a]	0.634[a]
S$_{20}$ (°/s)	Pre	370.0	52.0		367.8	48.3		360.5	49.3			
	Post	370.3	48.1	0.0±3.6	364.1	47.3	-0.6±5.5	366.7	45.3	2.2±8.3	0.751[a]	0.338[a]
S$_{40}$ (°/s)	Pre	260.7	33.1		264.8	42.4		254.3	40.7			
	Post	263.2	41.9	-0.5±6.6	258.8	45.2	-1.3±12.0	261.0	32.1	4.0±12.5	0.276[b]	0.326[c]
S$_{60}$ (°/s)	Pre	172.6	29.8		182.1	45.8		179.8	36.8			
	Post	183.6	34.0	5.1±12.3	180.8	53.4	1.0±30.2	189.9	31.5	9.1±28.3	0.229[a]	0.430[a]
PT$_{dyn60°/s}$ (Nm)	Pre	126.7	37.8		127.4	35.3		128.9	44.6			
	Post	131.4	37.9	5.7±11.8	130.1	37.8	1.9±9.5	134.3	45.7	4.8±9.1	0.074[b]	0.620[c]
PT$_{dyn180°/s}$ (Nm)	Pre	80.3	25.8		81.1	22.9		81.9	28.8			
	Post	83.3	26.1	6.1±7.9*	83.7	24.2	2.6±5.0	84.9	29.4	3.8±6.5*	<0.001[b]	0.319[c]
PT$_{dyn240°/s}$ (Nm)	Pre	71.2	21.7		73.7	21.4		72.2	24.5			
	Post	74.6	22.4	6.9±8.3*	75.4	22.6	1.4±6.4	74.2	25.9	2.5±6.0	0.006[b]	0.064[c]

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; MV = muscle volume; 1RMLP = leg press one repetition maximum; 1RMLE = leg extension one repetition maximum; END = muscular endurance (number of repetitions at 60% of 1RMLE); PT$_{statx}$ = static (isometric) peak torque at knee angle of x°; S$_x$ = speed of movement at x% of PT$_{stat90°}$; PT$_{dynx}$ = dynamic (isokinetic) peak torque at x°/s.
[a]Results of Linear Mixed-Models analyses, time x group effect corrected for average training volume; [b]Results of Friedman test; [c]Results of Kruskal-Wallis test corrected for average training volume; significance level P < 0.05. *Significant change from pre to post (P < 0.05); †Significant difference with LOW (P < 0.05).
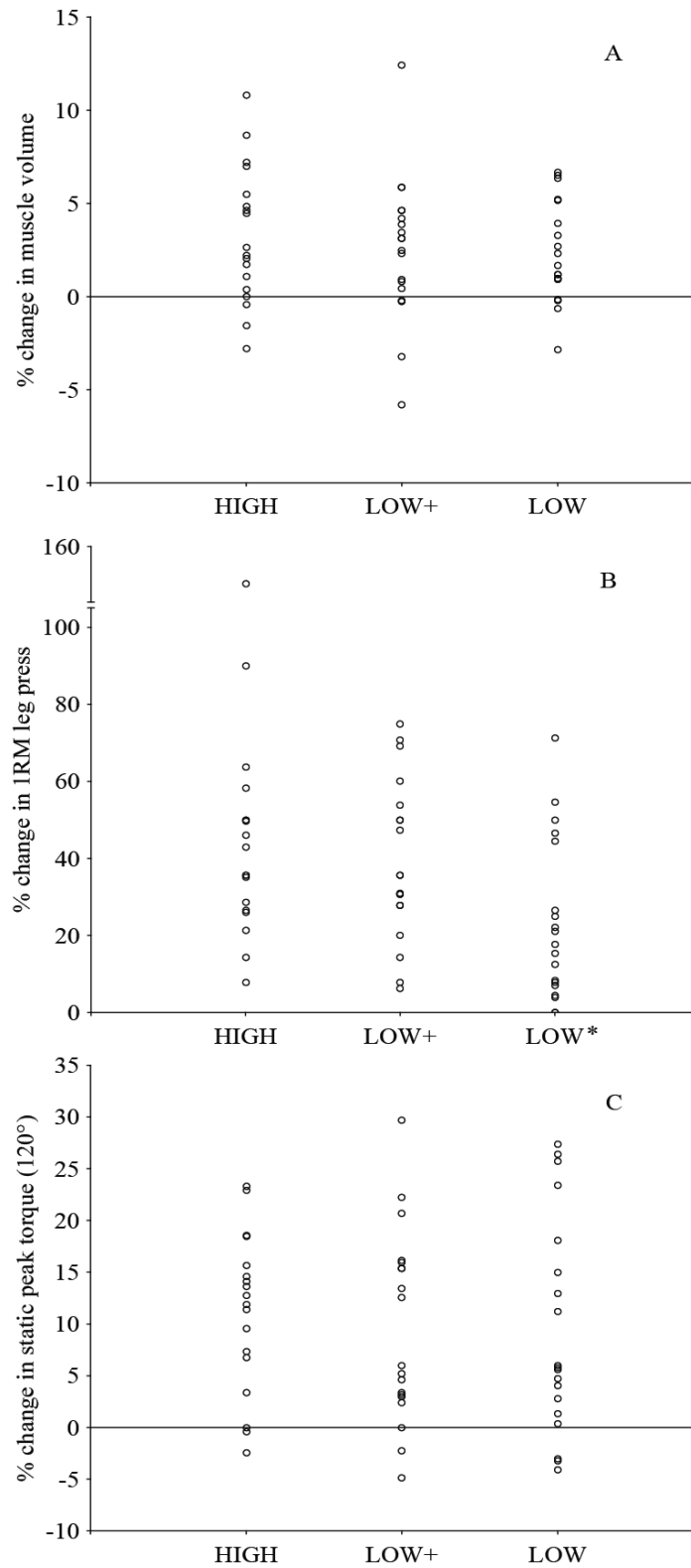
Figure 3. Plot of the individual percent changes (baseline to post) in muscle volume (A), 1RM leg press (B), and static peak torque (knee joint angle of 120°) (C) for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). *Significant difference with HIGH and LOW+ (P < 0.05).

One repetition maximum and local muscular endurance. All training groups showed a significant increase from baseline to post in both leg press 1RM and leg extension 1RM (all P < 0.05).

With regard to leg press 1RM, a significant time by group interaction effect was observed from baseline to post (P = 0.002), with post hoc tests revealing that both HIGH (+46.2% ± 32.3%) and LOW+ (+39.2 ± 20.7%) increased significantly more than LOW (+23.1% ± 20.7%) (P = 0.001 and P = 0.006, respectively) (Table 3 and Figure 3B). From baseline to week 5, a higher increase was found in HIGH (P < 0.001) and LOW+ (P = 0.002) compared to LOW (Figure 4).

For leg extension 1RM, linear mixed-model analysis revealed a time by group interaction effect from baseline to post (P = 0.003), with HIGH (+30.0 ± 11.5%) and LOW+ (+29.7 ± 19.8%) improving significantly more than LOW (+19.2 ± 5.3%) (P = 0.001 and P = 0.011, respectively) (Table 3). From baseline to week 5, LOW showed less of an increase than both LOW+ (P = 0.007) and HIGH (P = 0.040). From week 5 to week 9, HIGH tended to increase more than LOW (P = 0.067). From week 9 to post, HIGH increased more than both LOW (P = 0.011) and LOW+ (P = 0.045) (Figure 5).

Local muscular endurance increased significantly in LOW (+19.8 ± 29.8%, P = 0.021) and LOW+ (+16.3 ± 20.6%, P = 0.008). However, no time by group interaction effect was found for this variable (P = 0.770) (Table 3).
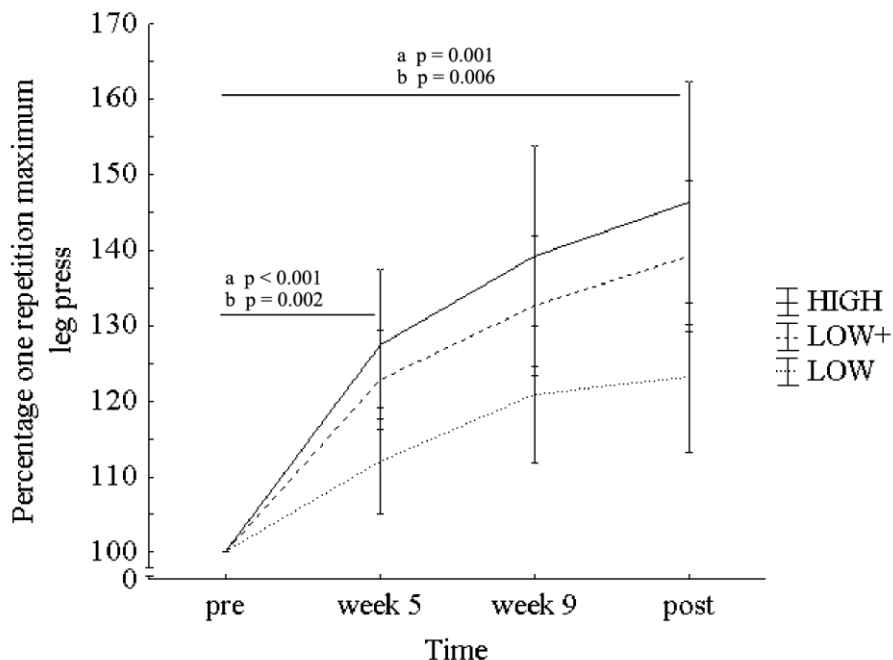
Figure 4. Leg press one repetition maximum (mean ± standard error) for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). 1RM was measured at baseline (pre), before the first training session at week 5 and 9, and post intervention. Baseline 1RM was equated as 100%. [a] Difference in change between HIGH and LOW (p < 0.05). [b] Difference in change between LOW+ and LOW (P < 0.05).
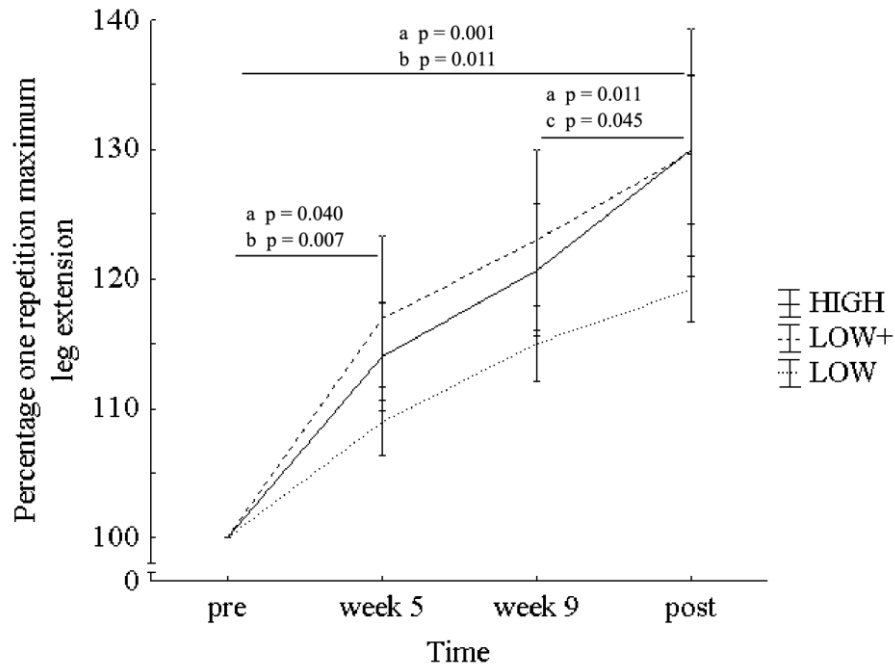
Figure 5. Leg extension one repetition maximum (mean ± standard error) for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). 1RM was measured at baseline (pre), before the first training session at week 5 and 9, and post intervention. Baseline 1RM was equated as 100%. [a] Difference in change between HIGH and LOW (P < 0.05). [b] Difference in change between LOW+ and LOW (P < 0.05). [c] Difference in change between HIGH and LOW+ (P < 0.05).
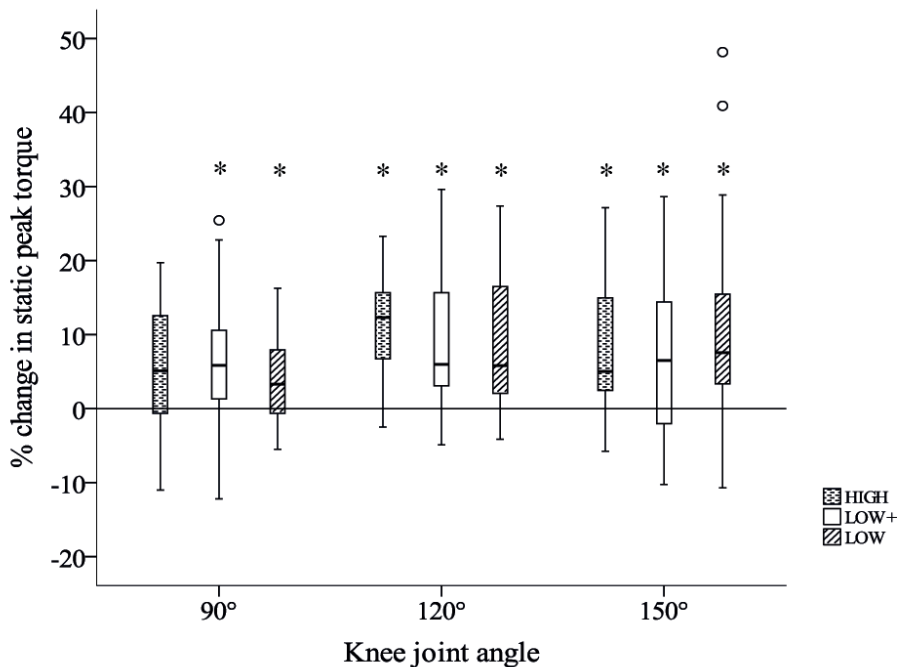
Figure 6. Box plot representing percent changes in static peak torque of the knee extensors at different knee joint angles for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). * Significant change (P < 0.05).

Force-velocity characteristics. No differences were observed between groups for changes in static peak torque (Figure 3C), speed of movement, or dynamic peak torque at 60°/s and at 180°/s (Table 3, all P > 0.05). Static peak torque at all knee joint angles increased significantly in all groups, although only a trend was found for $PT_{stat90°}$ in HIGH (P = 0.084) (Figure 6). Speed of movement (S_{20}, S_{40}, and S_{60}) did not change from baseline to post in any of the groups. Dynamic peak torque at 60°/s tended to increase in LOW only (P = 0.051). Dynamic peak torque at 180°/s increased significantly in HIGH (P = 0.011) and LOW (P = 0.018). At 240°/s, HIGH was the only group with a significant increase in dynamic peak torque, although LOW also tended to show an increase (P = 0.064). A trend towards a significant time by group interaction effect was found for dynamic peak torque at 240°/s (P = 0.064) (Table 3), with HIGH (+6.9 ± 8.3) improving more than LOW+ (+1.4 ± 6.4, P = 0.044) and LOW (+2.5 ± 6.0, P = 0.041).

Functional performance. A trend towards a time by group interaction effect was only observed for maximal gait speed (P = 0.051), with HIGH improving significantly more than LOW+ (P = 0.023) and tending to improve more than LOW (P = 0.051). However, for 6-minute walk distance, 30-second and 5-repetition chair sit-to-stand test, and timed up-and-go test, no time by group interaction effect was revealed (all P > 0.05) (Table 4). HIGH showed a significant improvement for 6-minute walk distance (P = 0.029), 30-second chair sit-to-stand test (P < 0.001), and 5-repetition chair sit-to-stand test (P = 0.001), and a trend to improvement for timed up-and-go test (P = 0.076). In LOW, a significant improvement was only seen for 5-repetition chair sit-to-stand test (P < 0.001), and a trend for improvement for 30-second chair sit-to-stand test (P = 0.050). LOW+ showed a significant improvement for 30-second chair sit-to-stand test (P < 0.001) and 5-repetition chair sit-to-stand test (P = 0.001), and a trend to improvement for 6-minute walk distance (P = 0.060) and timed up-and-go test (P = 0.063).

Most Pearson's correlation coefficients between percent changes in muscle parameters and changes in functional performance did not reach statistical significance. Only the change in $PT_{stat90°}$ was positively correlated with the change in 30-second chair sit-to-stand test (r = 0.30, P = 0.030) and negatively correlated with the change in timed up-and-go test (r = -0.41, P = 0.002).

Table 4. Mean and SD for baseline (pre-) and posttest and % change (±SD) for functional performance for the three intervention groups

		HIGH (n=18)			LOW+ (n=19)			LOW (n=19)			P-values	
		Mean	SD	%	Mean	SD	%	Mean	SD	%	Time	Time x group
6MWD (m)	Pre	595.6	65.8		564.1	92.5		553.0	71.3			
	Post	627.7	72.0	5.7 ± 9.7*	588.5	87.2	5.1 ± 11.4	570.2	70.0	3.5 ± 9.1	0.001[a]	0.871[a]
GS_{max} (ms^{-1})	Pre	1.83	0.29		1.82	0.33		1.93	0.29			
	Post	2.05	0.30	12.6 ± 11.9*	1.86	0.27	3.7 ± 12.4	1.97	0.39	2.0 ± 13.3	0.001[a]	0.051[a]
30-s STS (reps)	Pre	15.8	2.5		15.0	2.1		15.7	2.3			
	Post	17.1	2.5	8.6 ± 8.0*	16.3	1.8	9.1 ± 9.2*	16.4	2.1	5.0 ± 9.0	<0.001[a]	0.239[a]
5x STS (s)	Pre	9.1	1.7		9.5	1.1		9.5	1.8			
	Post	8.1	1.0	-10.0 ± 8.5*	8.4	0.9	-11.5 ± 10.0*	8.3	1.1	-10.6 ± 10.0*	<0.001[b]	0.756[c]
TUG (s)	Pre	5.8	0.8		6.3	0.8		6.0	1.1			
	Post	5.6	0.7	-2.9 ± 7.7	5.9	0.7	-4.9 ± 11.4	5.8	1.2	-3.2 ± 8.8	0.003[a]	0.570[a]

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; 6MWD = 6-minute walk distance; GS_{max} = maximal gait speed over 7.5m; 30-s STS = 30-second chair sit-to-stand test; 5x STS = 5-repetitions chair sit-to-stand test; TUG = timed up-and-go test.
[a]Results of Linear Mixed-Models analyses, time x group effect corrected for average training volume; [b]Results of Friedman test; [c]Results of Kruskal-Wallis test corrected for average training volume; significance level P < 0.05.
*Significant change from pre to post (P < 0.05).

Discussion

In this study, we investigated whether high-repetition low-resistance exercise protocols (LOW and LOW+) would be similarly effective in achieving gains in muscle volume, muscle strength, force-velocity characteristics, and functional performance as traditional high-resistance training (HIGH). This question is of great importance for older adults, as muscle volume and strength decline with aging and since practitioners remain skeptical about applying high-resistance exercise in this population. In one of the low-resistance exercise protocols used in this study (LOW+), external resistance was increased after a fatiguing protocol of 60 repetitions in order to examine the beneficial effect of intensifying the training resistance at the end of a single exercise set. Interestingly, despite doing a smaller volume of work compared to LOW, HIGH and LOW+ achieved the same or greater improvements on muscle volume, muscle strength, and functional performance.

In particular, all groups demonstrated similar gains in muscle volume (2.4 - 3.2%), irrespective of the resistance used during training. These results are in line with previous research showing that low-resistance exercise, as long as maximal effort is reached, can induce comparable hypertrophic responses as high-resistance exercise (36,47,49). Henneman's size principle of motor unit recruitment indicates that, when a submaximal contraction is sustained, initially recruited motor units will fatigue, creating the need to additionally activate larger motor units (20). When the exercise is repeated to the point of muscle failure, (near) maximal motor unit recruitment will occur, regardless of the external resistance used (11,20). Thus, activation of a similar amount of muscle fibers can be expected when training with either high or low resistances until muscle failure, clarifying the equivalent extent of hypertrophy found in our three training groups. However, it cannot be excluded that differences in central and peripheral fatigue might have occurred between the three protocols, leading to different levels of muscle fiber activation at the end of each exercise session. However, within the scope of this study we were not able to assess the contribution of central and peripheral factors in the occurrence of muscle failure in our participants.

Another training variable that needs to be taken into account when studying the hypertrophic response to resistance exercise is the volume of work (% resistance x repetitions) performed during training (27,33,36). In this study, exercise protocols were designed to be approximately equal in training volume. However, in LOW, the external resistance (35.5 ± 8.4% of 1RM for leg press and 30.0 ± 3.5% of 1RM for leg extension) used to reach muscle fatigue within the prescribed number of repetitions, was higher than the initially aimed resistance of about 20% of 1RM. It cannot be excluded that (improvements of) strength-endurance capacity of the muscle

might have played a role here. This phenomenon led to a higher average training volume for LOW than initially anticipated. On the leg extension, average training volume was significantly higher in LOW than in both HIGH and LOW+. This difference in training volume between groups was probably a consequence of the strategy used to adjust training resistance over the training period. Another strategy could have been to use a fixed number of repetitions at a predetermined resistance (% 1RM) in order to exactly match training volumes between groups. However, maximal effort would not have been reached in all participants when using the latter strategy. This could potentially lead to smaller muscular gains (17,40,44). To ascertain that this difference did not interfere with the exercise-induced effects, all analyses were corrected for average training volume as confounding factor.

Confirming our results on hypertrophy, basic strength gains obtained from the Biodex dynamometer, including static strength and dynamic strength at low speed (60°/s), did not differ between the three training groups. These training-induced gains, ranging from 3.3 to 11.8% and from 1.9 to 5.7% for static and dynamic strength parameters, respectively, were rather low compared to gains previously reported in older adults (10,22). Although none of the subjects had been participating in resistance exercise prior to the start of the intervention, they were all healthy, well-functioning and rather active older adults. Gains would probably have been greater if weaker and more sedentary older adults were included in the study.

As typically found in previous research, gains in 1RM strength exceeded gains obtained from the Biodex dynamometer, probably because of neuromuscular adaptations specific to the trained movement. These 1RM strength gains were comparable to gains in previous studies (10,22,29,42,45). It should be noted, however, that training resistance had an impact on 1RM strength. HIGH clearly demonstrated a larger gain in 1RM than LOW on both the leg press and leg extension exercise. Previous work on the impact of different external resistances focused on 1RM strength of the trained movement. These studies agree with our findings and suggest that the use of high external resistances is a prerequisite for maximizing gains in 1RM (5,9,21,36). Overall, our data support the "strength-endurance continuum" of DeLorme suggesting that low-repetition high-resistance training favors strength adaptations and high-repetition low-resistance training increases muscular endurance (14). However, a unique aspect of the current study was the design of a low-resistance exercise protocol, in which training resistance varied within a single set (LOW+). More specifically, after a fatiguing protocol of 60 repetitions, additional repetitions at a higher resistance were performed until failure. Importantly, training resistance always remained low (≤ 50 % of 1RM). Interestingly, no differences were found in 1RM gains between HIGH and LOW+. Nevertheless, differences in 1RM gains between LOW+ and LOW did occur. These

differences might be linked to the supplementary mechanical stimulus in LOW+, created by increasing resistance after a highly repetitive fatiguing exercise protocol. However, it might as well be the case that differences in voluntary muscle activation at fatigue between LOW and LOW+ account for the difference in 1RM gain. There are studies suggesting that sustained contractions at low resistance tend to cause more central fatigue, while protocols at higher resistances tend to induce more peripheral fatigue (or fatigue within the muscle itself) (37,56). However, these studies investigated sustained isometric contractions, contrary to repetitive dynamic contractions as in our training protocol. Kay et al. and Babault et al. already stated that neuromuscular fatigue appears to develop differently, depending on the muscular action modes (6,24). Thus, the underlying mechanism of this difference in 1RM gain remains poorly understood and should be investigated more into detail in further research. What we did find was that differences in 1RM gains between LOW and both HIGH and LOW+ were already apparent after 4 weeks of training. Therefore, they were probably due to coordinative and neuromuscular adaptations specific to the movement that was trained.

Regarding local muscular endurance, our results are in line with the "strength-endurance continuum" as well (14), since significant improvements were only found in LOW and LOW+. Although no significant increase was found in HIGH, linear mixed-model analysis did not reveal a time by group interaction effect. However, the training protocols in LOW and LOW+ used resistances that were notably lower than the resistance applied in the local muscular endurance test.

In addition to muscle volume, muscle strength, and muscular endurance, strength training regimens in older adults should focus on muscle power and speed of movement. Muscle power, i.e. the product of force and velocity, appears to be a key component in everyday function (12). A recent study in younger adults, in which a similar protocol was used as LOW+, showed promising results on speed of movement at different resistances, even though training was performed at a moderate speed (53). More specifically, gains in speed of movement were demonstrated after 9 weeks of mixed low-resistance exercise, whereas no gains were found after high-resistance exercise. The current study, however, failed to confirm these findings in older adults. No increases in speed of movement were found in any of the groups. Two possible explanations may have contributed to this disparity. First, speed of movement during training, although moderate in both studies, was different. The older subjects in this investigation trained at a moderate speed of 2s for each concentric and 3s for each eccentric action. As the range of motion on each exercise covers about 70°, concentric actions were performed at about 35°/s. In the study with young adults, concentric actions were performed in only 1s, and thus at about 70°/s, i.e. twice as fast as

in the study with older adults. It can be argued that a resistance training protocol using higher speeds is likely to attain greater gains in speed of movement (15,16,42). However, we chose a training speed that is more commonly used in practice because of its safety and effectiveness (13,22). It represents a similar speed as the one recommended by the visual feedback system of the training devices used in this study, which is often used in fitness centers (IsoControl, Technogym). Second, literature on age-related changes to central activation is mixed, with many studies indicating no effect of age (25,26,28,41). However, an article by Stevens and colleagues indicated that there may be a meaningful deficit in voluntary muscle activation in the knee extensors of older adults (46). Although further research is needed and no definite conclusions can be drawn, it seems possible that older adults might not be able to activate type II muscle fibers as easily as young adults. Combined with the fact that aging is accompanied by a selective atrophy and denervation of type II muscle fibers (31), it seems plausible that older adults show less effect on speed-related parameters. Noteworthy is that speed of movement tests were performed relative to the individual isometric strength. Thus, if a subject improved isometric strength, higher resistances were used in the speed of movement test. This method was chosen in order to measure actual gains in velocity, independent of increases in strength.

Velocity-related force production can also be measured using an isokinetic testing approach. Although this is a standardized procedure, it does not simulate natural body movements. However, to extend our data on force-velocity characteristics, we included isokinetic strength at high speeds (180°/s and 240°/s) in our testing protocol. A time effect was found, indicating that dynamic peak torque at high speeds increased after training, similarly as in dynamic peak torque at 60°/s. For increases in dynamic peak torque at 240°/s, HIGH did appear to be beneficial, but the underlying mechanism remains unclear. Older adults might experience some difficulty in activating type II muscle fibers, and the use of high resistances might facilitate the activation of these fibers, leading to better performances on high-speed strength tests.

Improvements in muscle volume and muscle strength do not automatically result in improved functional performance (35). In line with this concept, we found hardly any significant relationships between gains in muscle volume and strength and changes in functional performance. It should be noted that the older adults in this study were already well-functioning before the start of the intervention. Only two subjects were considered 'mildly frail' (mPPT-score of 31), while all other subjects could be categorized as 'not frail' (mPPT-score > 31) (8). Nevertheless, improvements in functional performance were demonstrated after 12 weeks of training. All groups performed better on both sit-to-stand tests after training, with no differences between groups. On the 6-minute walk test and the timed up-and-go test, only HIGH and LOW+

improved, even though not significantly different from LOW. Only for maximal gait speed, the gains in HIGH tended to exceed those in LOW and LOW+. So it seems that strengthening exercise at high- and low-resistances may be similarly effective in improving functional performance.

Some limitations of this study need to be considered. First, although our findings suggest that differences in 1RM gains following HIGH and LOW+ compared to LOW might be related to neuromuscular adaptations, assessment of these adaptations was not within the scope of this study. Second, our data lack information on the acute cardiovascular responses of these training protocols, another research area of interest. Third, the findings in this study point to the value of high-repetition low-resistance exercise protocols in older adults. It should be noted, however, that training sessions were closely supervised by a personal trainer, who motivated subjects to continue the exercise until muscle failure. Because of inter-individual differences in strength-endurance capacity, it is difficult to predict the optimal training resistance. High-repetition low-resistance exercise protocols might therefore ask for more guidance and fine-tuning in the starting phase. Fourth, dietary control and adequate consumption of energy and proteins are especially relevant when studying the older population. Delaying protein intake after a program of resistance exercise training can significantly impact training induced adaptations (19). However, food intake was not monitored during the intervention. An inadequate protein consumption could be part of the explanation for the modest improvements on muscle volume and on static and dynamic peak torques. Fifth, an estimate was used for measuring leg extension 1RM, as this method was considered less time consuming. Using this estimate might have led to an overestimation of the 1RM, and can thus be considered a limitation of the study. It can be argued that this estimate for leg extension 1RM seems to recapitulate local muscular endurance measured on the same equipment. However, the average number of repetitions performed during both tests significantly differed (10.7 for 1RM versus 16.7 for endurance; $P < 0.001$). In addition, no significant correlation was found between leg extension 1RM (kg) and local muscular endurance (number of repetitions) (baseline $r = -0.041$; post $r = 0.150$; $P > 0.05$). Likewise, no significant correlation was found between percent changes from baseline to post for 1RM and local muscular endurance ($r = -0.153$; $P = 0.260$). These data seem to suggest that the two leg extension tests measure different aspects of muscular performance.

In conclusion, this study showed that strengthening exercise at either high or low external resistance can be similarly effective in increasing muscle volume and basic strength, as long as maximal effort is achieved during training. The unique aspect of the current study was the design of a highly repetitive protocol using even lower resistances than in previous research (LOW) (22,52,55). Moreover, we designed a mixed low-resistance exercise protocol (LOW+) to

investigate the added value of intensifying the resistance at the end of such a high-repetition low-resistance exercise protocol. Differences that did appear between groups were specific to the trained movement. Confirming previous research, high-resistance training led to a higher increase in 1RM strength than low-resistance training. However, when using a mixed low-resistance protocol in which the resistance was increased after a fatiguing protocol of 60 repetitions, this difference in 1RM gain disappeared. Although the underlying mechanism remains poorly understood, it seems possible that neuromuscular adaptations, specific to the trained movement, are triggered by a mechanical stimulus. This mechanical stimulus can be created either by using high resistances or by increasing resistance after a highly repetitive fatiguing protocol. However, it remains unclear whether differences in muscle activation or in stress/strain occurred between the different protocols. Long-term training studies as well as studies focusing on residual effects after training cessation are needed to confirm the current findings and to further clarify differences between these training approaches. Further research should additionally investigate the underlying mechanisms accounting for variations in the effectiveness of high- and low-resistance training protocols.

Acknowledgements

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Paper 4

Strength training at high versus low external resistance in older adults: long-term muscular adaptations and exercise adherence

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Abstract

This study was designed as a 24-week follow-up of a 12-week resistance training intervention. Subjects were free to decide whether or not they continued resistance training at their own expense post-intervention. We compared the long-term muscular and functional adaptations and the exercise adherence after high- and low-resistance exercise. Fifty-six older adults were randomly assigned to HIGH (2 x 10-15 repetitions at 80% of one repetition maximum (1RM)), LOW (1 x 80-100 repetitions at 20% of 1RM), or LOW+ (1 x 60 repetitions at 20% of 1RM + 1 x 10-20 repetitions at 40% 1RM). The main outcome measures included muscle volume, muscle strength, and functional performance. At follow-up, muscle volume and isokinetic strength were no longer different from baseline (P > 0.05). Post-intervention isometric strength gains were partly preserved in all groups. For leg press 1RM, the gain from baseline to follow-up was lower in LOW (+12.6 ± 7.2%) than in both HIGH (+34.9 ± 35.1%, P = 0.005) and LOW+ (+26.4 ± 19.7%, P = 0.012). For leg extension 1RM, the gain from baseline to follow-up was lower in LOW (+11.6 ± 5.9%) than in LOW+ (+21.7 ± 15.8%, P = 0.002) and tended to be lower than in HIGH (+16.3 ± 9.0%, P = 0.064). Most functional performance tests exceeded baseline levels at follow-up, with no difference between groups. Few subjects continued strength training after the intervention: 16.7% in HIGH, 21.1% in LOW+ and 11.1% in LOW. These findings highlight the importance of further research on developing strategies to overcome barriers of older adults to adhere to resistance exercise. Interestingly, highly repetitive low-resistance exercise protocols seem to be as effective as traditional high-resistance exercise protocols for long-term neuromuscular and functional adaptations.

Keywords: sarcopenia; muscle hypertrophy; elderly; resistance exercise; training load

Introduction

Muscle atrophy and muscle weakness as a consequence of advancing age can have a deteriorating effect on functional performance (1,28). Resistance training has been proposed as a potential strategy for counteracting this muscle deterioration in older adults. Moderate to high external resistances (60-85% of the one repetition maximum (1RM)) are currently recommended for obtaining optimal effects (3). While high-resistance exercise is reported to be safe for elderly individuals (16), therapists often remain skeptical about the use of such high resistances in older adults (2). Alternative low-resistance exercise protocols have therefore been introduced in previous research (46,55). However, up till now, it remains unclear whether low-resistance

alternatives are as effective as traditional high-resistance training for long-term muscular and functional improvements.

The majority of studies comparing the short-term effects of high- and low-resistance exercise have focused on muscle function outcomes such as 1RM and relative muscular endurance (4,9). These studies underlined the benefit of training at high external resistances. However, there is considerable evidence that low-resistance exercise can elicit hypertrophy and isometric/isokinetic strength gains equivalent to gains achieved at higher resistances in young (33,35,51) and older adults (45,52). Rather than the necessity to be exposed to high external resistances, training to the point of muscle failure might be crucial to optimize muscular adaptations. Training to muscle failure is hypothesized to optimize muscle fiber recruitment, irrespective of the external resistance used (10,19,40,42).

A current limitation of most studies on alternative low-resistance exercise protocols in older adults is that only immediate post-intervention effects are reported and compared to those obtained by high-resistance exercise (23,46,50,53). As older adults might be more prone to training interruptions because of lack of motivation or health-related issues, more data are needed on longer-term training benefits after cessation of high- and low-resistance exercise interventions.

Only few studies have published data concerning the influence of training resistance on muscle strength (15,21,48) and muscle mass retention (48) following a detraining period in older adults. However, the results of these studies remain inconclusive. While Harris et al. (21) reported that training resistance had no effect on the magnitude of strength loss or retention after a period of detraining, Fatouros et al. (15) suggested that strength gains are maintained for a longer period of time after high-resistance exercise compared to low-resistance exercise. Tokmakidis et al. (48) found, despite greater declines in muscle strength, greater retention in muscle strength and mass after a detraining period following high-resistance exercise than following moderate-resistance exercise.

A typical aspect of the above-mentioned detraining studies is that participants were asked to quit resistance exercise as soon as the guided intervention had ended. However, by restricting participants to continue resistance exercise, the opportunity is lost to obtain valuable information on long-term exercise adherence. Psychological and motivational factors associated with high- and low-resistance exercise protocols might influence long-term exercise adherence among older adults.

According to the Self-Determination Theory (SDT), different types of motivation regulate an individual's behavior (12). These types of motivation can be located on a continuum, ranging from

controlled (i.e. external regulation and introjected regulation) to personally valued or autonomous motivation (i.e. identified regulation, integrated regulation and intrinsic motivation). The SDT hypothesizes that the more an individual's behavioral regulation is autonomous and thus self-determined, the more the behavior is likely to sustain in the long run (41). Next to the degree of autonomous motivation, the level of self-efficacy might influence long-term exercise adherence. Self-efficacy is defined as the belief of one's capability to perform a task when confronted with specific barriers (6). Regarding the comparison between high- and low-resistance exercise, it can be hypothesized that if older individuals are more autonomously motivated or have higher levels of self-efficacy when training at a certain degree of external resistance, their long-term adherence would increase, hereby limiting the detraining effects.

The current study focuses on a 24-week follow-up after a 12-week resistance training program in older adults. The post-intervention muscular and functional adaptations of traditional high-resistance training at low repetitions (HIGH) and low-resistance training at high repetitions are reported elsewhere (52). Two low-resistance exercise protocols were designed: 1) a low-resistance protocol (LOW) in which external resistance was kept constant within one session, and 2) a mixed low-resistance protocol (LOW+) in which resistance was increased after 60 repetitions. The rationale behind LOW+ was to investigate the benefits of an additional mechanical stimulus for optimizing muscular gains in protocols with low external resistance and many repetitions. As previously reported, the three interventions resulted in similar gains in muscle volume and in muscle strength, except for gains in 1RM, which were greater in both HIGH and LOW+ than in LOW (52).

The first objective of the present study was to compare the residual effects of HIGH, LOW and LOW+ on muscular and functional outcomes in older adults, 24 weeks after the intervention had ended. The second objective of the current study was to investigate how many participants continued strength training after cessation of the intervention and whether or not this number differed between HIGH, LOW, and LOW+. Motivation and self-efficacy were taken into account. In addition, the perceived barriers for continuing strength training were examined.

Methods

Study design

The current study was designed as a 24-week follow-up of a 12-week resistance training program in older adults (52). In the initial intervention study, subjects were randomly assigned to one of three training interventions: traditional high-resistance training (HIGH, n = 18), low-resistance training (LOW, n = 19), or mixed low-resistance training (LOW+, n = 19). Exercise sessions were

performed at a local fitness center. Baseline and post-intervention measurements were performed from January to March 2012 and from April to June 2012, respectively. After the intervention, all subjects were free to decide whether or not they continued resistance training at their own expense. If an individual decided to subscribe to a fitness center, qualified fitness instructors, who were completely independent of the researchers, designed an individualized training program, irrespective of the training intervention in the study. Thus, during follow-up, no strict detraining period was applied and fitness instructors were free to prescribe any form of exercise program. This study design was chosen because it expands or knowledge on long-term exercise adherence and brings added value to the comparison of high- and low-resistance exercise training. The investigators did not interfere in any way in training participation and training program designs so that the follow-up period would more closely resemble real-life situations. In September 2012, all subjects were invited to participate in follow-up measurements. These measurements were performed from October to December 2012. The study was approved by the University's Human Ethics Committee in accordance with the declaration of Helsinki. All subjects provided written informed consent.

Subjects

Fifty-six community-dwelling older adults between 60 and 80 years old were enrolled in the initial 12-week intervention study. The detailed exclusion criteria have been published previously (52). Briefly, volunteers with contraindications for maximal strength testing, with neuromuscular disorders, or with recent training experience were excluded.

Resistance training intervention

Training was performed on a leg press and leg extension device (Technogym, Gambettola, Italy). The seated row (Technogym, Gambettola, Italy) was added to the training program to provide a more complete workout for subjects. However, this study only focused on outcomes of the lower limb. Subjects exercised three times weekly on nonconsecutive days over a period of 12 weeks (total of 36 sessions). In the first session, the proper lifting technique and speed of movement (2s for each concentric and 3s for each eccentric action) were demonstrated and practiced. All sessions were supervised by a qualified fitness instructor. After a 10-minute warm-up on a cycle ergometer (Technogym Bike Excite, Gambettola, Italy) or on a treadmill (walking pace) (Technogym Run Excite, Gambettola, Italy), the two exercises were performed with at least two minutes of rest in between. HIGH performed two sets of 10 to 15 repetitions. Resistance was initially set at about 80% of one repetition maximum (1RM). One minute of rest was provided

between sets. LOW performed one set of 80 to 100 repetitions. Resistance was initially set at about 20% of 1RM. LOW+ performed a fatiguing protocol of 60 repetitions at an initial resistance of 20% of 1RM, immediately followed (no rest) by 10 to 20 at an initial resistance of 40% of 1RM. In all groups, subjects were encouraged to continue the exercise if maximal effort was not achieved after the prescribed number of repetitions. External resistance was adjusted if subjects performed repetitions beyond the prescribed training zone. Training protocols have previously been described in more detail (52).

Muscle volume and performance measures

All measurements were performed at baseline (pre), within 8 days after the intervention (post), and at follow-up 24 weeks after the intervention.

Muscle volume. A computed tomography scan (Siemens Somatom Definition Flash, Forchheim, Germany) was used to measure muscle volume of the right upper leg. Four 2.5mm-thick axial images were obtained at the midpoint of the distance between the medial edge of the greater trochanter and the intercondyloid fossa of the femur. Standard Hounsfield Units ranges for skeletal muscle (0-100) were used to segment muscle tissue area, and corrections were made for bone marrow. The four slices were put together as one 10mm-thick slice, and the software program Volume (Siemens) was used to calculate the total muscle volume (cm³) of the 10mm-thick slice. All measurements were performed in the University Hospital by one expert radiologist who was blinded to group allocation.

One repetition maximum and local muscular endurance. One repetition maximum was measured on both the leg press and the leg extension. Testing procedures have previously been described in more detail (52). After measuring leg extension 1RM, local muscular endurance was tested on this device by completing a maximum number of repetitions at 60% of 1RM.

Isometric and isokinetic muscle strength. Isometric and isokinetic strength as well as speed of movement of the knee extensors were unilaterally measured on a Biodex Medical System 3® dynamometer (Biodex Medical Systems, Shirley, NY). As no post-intervention effects were found on speed of movement in any of the groups in the initial intervention study (52), we decided not to report speed of movement in this follow-up study. Tests were performed on the right side, unless there was a medical contraindication. Subjects were seated on a backwardly-inclined (5°) chair. Their position was stabilized with safety belts across the upper leg of the test side, the hips, and the shoulders. The rotational axis of the dynamometer was aligned with the transversal knee-joint axis and was connected to the tibia with a length-adjustable lever arm. Range of motion was

set from a knee joint angle of 90° to 160°. All settings were identical at pre, post, and follow-up. The protocol, as described below, was performed twice and the best result was reported.

First, isometric or static strength of the knee extensors was determined as the highest peak torque (in Nm) produced during two maximal voluntary isometric contractions (5 second duration) at different knee joint angles: 120°, 90°, and 150° ($PT_{stat120°}$, $PT_{stat90°}$, and $PT_{stat150°}$, respectively). As the results were similar in all knee joint angles, only $PT_{stat120°}$ is reported here.

Second, isokinetic or dynamic strength of the knee extensors was measured by performing a series of three maximal concentric extension-flexion movements at a movement velocity of 60°/s, followed by five movements at both 180°/s and 240°/s. The dynamic peak torque (Nm) of the knee extensors, irrespective of knee angle, was recorded as $PT_{dyn60°/s}$, $PT_{dyn180°/s}$, and $PT_{dyn240°/s}$, respectively.

Functional performance. The following tests were performed: 6-minute walk test, maximal gait speed test over a distance of 7.5m, 30-second chair sit-to-stand test, 5-repetition chair sit-to-stand test, and timed up-and-go test. Tests have previously been described in detail (52).

Psychological processes

Behavioral regulation in exercise questionnaire-2. The degree of motivation was assessed using an adapted (Dutch) version of the behavioral regulation in exercise questionnaire-2 (BREQ-2) (29). In this questionnaire, subjects' motivation to participate in resistance exercise, instead of in physical activity in general, was measured. The relative autonomy index (RAI), i.e. a single score derived from the questionnaire's subscales (amotivation, external regulation, introjected regulation, identified regulation, intrinsic regulation) that gives an index of the degree to which respondents feel self-determined, was calculated. The Self-Determination Theory, which is a promising theoretical approach to facilitate behavioral change, assumes that a self-determined behavior is more likely to persist in the long term (41). The BREQ-2 was completed after two weeks of training (pre), post-intervention (within 8 days after the last training session) and at follow-up. Cronbach's alpha coefficients for pre-, post- and follow-up tests ranged from 0.764 to 0.852.

Multi-dimensional self-efficacy questionnaire. Self-efficacy (SE), i.e. the belief of one's capability to perform a task when confronted with specific barriers, was measured by means of an adapted version of the multi-dimensional self-efficacy questionnaire that focused on physical activity in general (36). This questionnaire was adapted so that subjects had to indicate their confidence level for performing resistance exercise instead of for being physically active in general. A five-point Likert scale, ranging from 'not at all confident' to 'very confident' was used. As this

questionnaire is only relevant when individuals are actually engaged in resistance exercise, it was only implemented after two weeks of training (pre) and post-intervention (within 8 days after the last training session). The internal consistency of the questionnaire was very high. At pre- and posttest, Cronbach's alpha coefficients were 0.933 and 0.944, respectively.

Feelings related to exercise. During the 12-week intervention, the following 5 questions were answered by the subjects on an 11-point item scale (ranging from 0 = 'not at all…' to 10 = 'very…'), immediately after the second training session each week (12 times in total): (1) How much did you enjoy the strengthening exercises while executing them? (2) How proud are you that you were able to complete these strengthening exercises? (3) How relieved are you that these strengthening exercises are finished? (4) How confident are you that you will be able to complete these strengthening exercises in the next training session? (5) How motivated are you to complete these strengthening exercises in the next training session?

The internal consistency was checked with Cronbach's alpha analysis. As item 3 represents negative feelings towards exercise, this item was inversely coded in the Cronbach's alpha analysis. Cronbach's alpha was 0.627 for the 5 items. However, when item 3 was deleted, Cronbach's alpha increased to an acceptable value of 0.758. It was therefore decided to calculate the mean of the four remaining items 1, 2, 4 and 5 into one global scale representing positive feelings related to the training exercise, while item 3 was analyzed representing negative feelings.

Participation in resistance exercise training. At follow-up, subjects were asked whether or not they continued resistance exercise at a fitness center after completion of the intervention. If the answer was yes, the weekly frequency, the time period and their latest exercise program were retrieved. If the answer was no, subjects had to indicate their reasons for quitting by rating their agreement with 16 possible barriers for resistance exercise on a 5-point Likert scale (ranging from 1 = 'strongly disagree' to 5 = 'strongly agree'). Subjects could add another barrier if they experienced a barrier that was not suggested by the questionnaire. Proposed barriers were inspired by previous research (5,30,32) and were categorized based on the Social-Ecological Model as a theoretical framework (31). In this model, behavior is viewed as being determined by the following: intrapersonal factors, interpersonal factors and community or environmental factors.

Subjects were additionally asked whether or not they were planning to participate in resistance exercise in the future (yes or no).

Statistical analyses

Data were initially analyzed for normality with a Shapiro-Wilk test. Of the muscular and functional outcome variables, the following were positively skewed: muscle volume, leg press 1RM, dynamic peak torque at 60°/s, 180°/s, and 240°/s, and 5-repetition chair sit-to-stand test. To meet the assumptions for the use of parametric analyses, positively-skewed data were normalized with base 10 log transformations. Non-parametric statistics were used for the psychological process variables, as they were measured on ordinal scales.

One-way analysis of variance (parametric analysis) and Kruskal-Wallis tests (non-parametric analysis) were used to assess between-group differences at baseline and to check for between-group differences on the feelings related to exercise scales, SE and RAI at all points in time. Only when significance was revealed with the Kruskal-Wallis test, Mann-Whitney U tests were used as post hoc test. Equivalence between subjects who completed all follow-up tests (compliers) and those who did not (non-compliers) was assessed using Mann-Whitney U tests. Chi-square tests or Fisher's exact tests (when >20% of cells have expected counts of less than 5) were used to determine if the number of non-compliers and the number of yes-no responses to the questions about participation in resistance exercise differed between groups.

For the muscle volume and performance tests, within-group changes from post to follow-up and from baseline to follow-up were analyzed with paired t-tests. To assess between-group differences in changes over time, linear mixed-model analysis with an unstructured covariance structure was used, with time as repeated factor and group as fixed factor. Post hoc analyses were conducted to determine which groups differed in changes. Average training volume per exercise session was calculated as follows:

$$\frac{\sum_{i=1}^{n}(\text{number of repetitions leg press} \times \%1RM)i + (\text{number of repetitions leg extension} \times \%1RM)i}{n}$$

with n = total number of exercise sessions performed during the 12-week training intervention. As previously published data already showed a higher average training volume in LOW compared to HIGH and LOW+ (52), this variable was introduced as a covariate in the mixed-model analyses.

All statistical tests were executed with SPSS software version 19 (SPSS Inc., Chicago, IL). Level of significance was set at $P < 0.05$.

Results

Training adherence, lost to follow-up and baseline characteristics

Figure 1 shows a detailed flow diagram of the study. Training adherence during the initial 12-week intervention was previously reported and did not differ between groups (52). None of the subjects' characteristics (Table 1) nor any of the outcome variables differed significantly between groups at baseline (all P > 0.05) (52).

Table 1. Means ± SD for subjects' characteristics at baseline

	HIGH (n = 18: 8m, 10f)	LOW+ (n = 19: 9m, 10f)	LOW (n = 19: 9m, 10f)	P
Age (yrs)	67.72 ± 4.28	67.43 ± 5.90	68.76 ± 4.96	0.701
Weight (kg)	71.58 ± 11.33	76.63 ± 12.10	75.58 ± 14.77	0.460
Height (m)	1.67 ± 0.08	1.66 ± 0.08	1.65 ± 0.09	0.769
BMI (kg/m²)	25.54 ± 2.82	27.57 ± 3.08	27.62 ± 4.12	0.117

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training
P-values: results of one-way analysis of variance between baseline group means.

Two Biodex measurements (one baseline for HIGH, one post for LOW+) failed due to a lack of compliance of the participants with the test instructions, and were excluded from analysis (52). Importantly, none of the subjects in HIGH, LOW or LOW+ dropped out during the 12-week intervention study. One subject in LOW refused to participate in any of the follow-up tests. Not all of the remaining subjects completed all follow-up tests. Reasons for non-compliance are reported in Figure 1. The female in HIGH who did not comply at follow-up because of knee problems already reported symptoms of osteoarthritis before the start of the intervention without aggravation of symptoms post-intervention. The males in HIGH with knee or hip problems at follow-up did not report joint problems pre- or post-intervention. No adverse effects of the intervention were reported in any of the groups (52). The number of non-compliers did not differ between groups (P > 0.05). Table 2 shows no difference between compliers and non-compliers at baseline, at post-intervention for motivation and self-efficacy or in percent changes from baseline to post for muscle volume and 1RM.
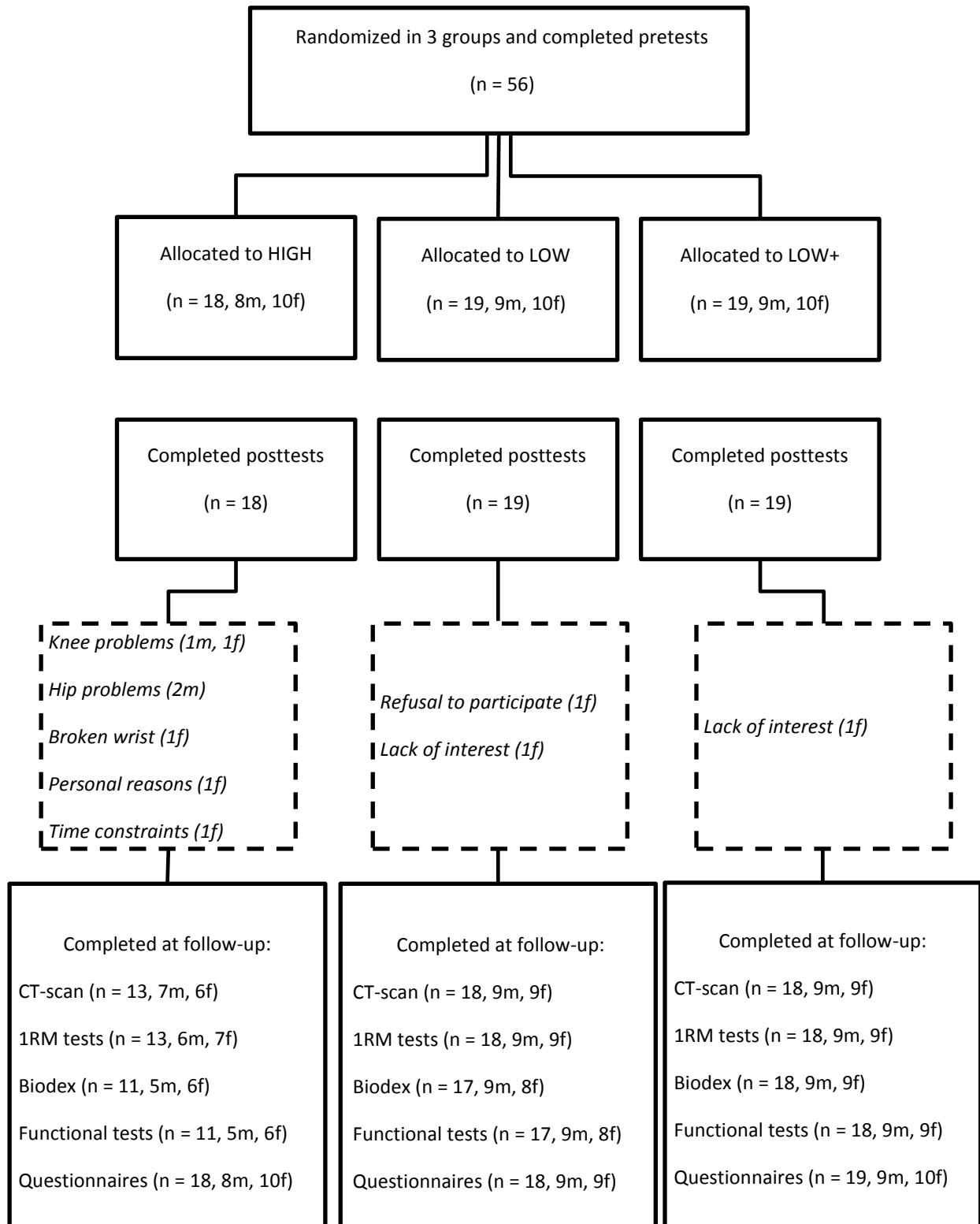
Figure 1. Flowchart of the study.

Table 2. Means ± SD for subjects' characteristics at baseline, for motivation and self-efficacy post-intervention and for percent changes from baseline to post for subjects who completed all follow-up measurements (compliers) and those who did not complete all follow-up measurements (non-compliers)

Variables	Compliers (*n*=46)	Non-compliers (*n*=10)	P
Age (y)	68.3 ± 4.8	66.3 ± 6.1	0.185
Weight (kg)	75.8 ± 13.1	69.3 ± 10.3	0.129
Muscle volume (cm³)	156.1 ± 38.4	144.4 ± 31.8	0.429
1RM leg press (kg)	105.0 ± 50.5	88.2 ± 53.6	0.214
1RM leg extension (kg)	30.7 ± 6.9	27.5 ± 7.3	0.239
Local muscular endurance (number of reps)	16.5 ± 4.0	17.5 ± 3.5	0.532
Isometric strength (120°) (Nm)	140.9 ± 42.0	138.2 ± 36.3	0.930
Isokinetic strength (60°/s) (Nm)	126.9 ± 40.1	131.2 ± 34.0	0.570
Isokinetic strength (180°/s) (Nm)	80.6 ± 25.7	83.6 ± 25.7	0.743
Isokinetic strength (240°/s) (Nm)	71.9 ± 22.6	75.0 ± 21.2	0.585
Relative autonomy index (post-intervention)	8.6 ± 4.6	10.1 ± 3.4	0.416
Self-efficacy (post-intervention)	3.5 ± 0.6	3.8 ± 0.5	0.292
Change in muscle volume (%)	2.6 ± 3.3	3.1 ± 3.7	0.732
Change in 1RM leg press (%)	35.0 ± 26.7	40.8 ± 26.0	0.341
Change in 1RM leg extension (%)	25.5 ± 15.0	29.7 ± 11.0	0.140

P-values: Mann-Whitney U test, significance level P < 0.05.

Muscle volume and performance measurements

All post-intervention results were previously reported (52) and were therefore not repeated in the current study. However, the level of significance was added for the changes from pre to post in Tables 3-4 and in Figures 2-4.

Muscle volume. Muscle volume of the upper leg changed significantly over time (P < 0.001), with no differences between groups (P = 0.225). After a post-intervention increase, muscle volume returned to baseline values in all groups during the 24 weeks after the end of the intervention (Table 3, Figure 2).
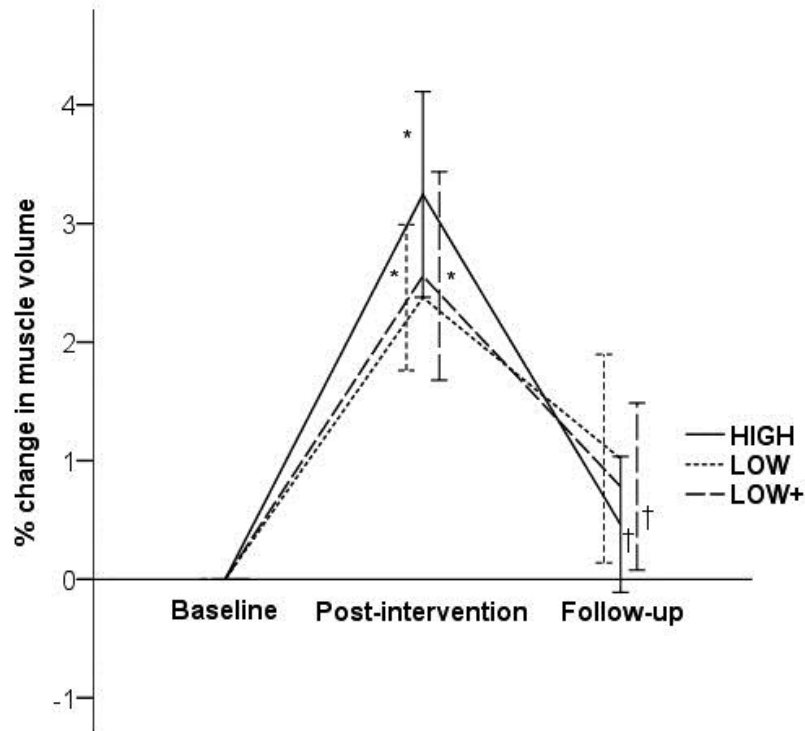
Figure 2. Percent changes over time with respect to baseline values in muscle volume for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). *Significant change from baseline to post. †Significant change from post to follow-up. Error bars: ± 1SE.

One repetition maximum and local muscular endurance. Results from linear mixed-model analyses indicated a significant effect of time for 1RM (P < 0.001). Despite statistically significant declines in 1RM from post to follow-up, substantial strength retention above baseline values was demonstrated in all groups (all P < 0.05). A group-by-time interaction effect was found for leg press 1RM (P = 0.032) and leg extension 1RM (P < 0.001). On leg press 1RM, LOW+ declined more from post to follow-up than LOW (P = 0.019). Interestingly, the residual gain from baseline to follow-up for leg press 1RM was still significantly lower in LOW (+12.6 ± 7.2%) than in both LOW+ (+26.4 ± 19.7%, P = 0.012) and HIGH (+34.9 ± 35.1%, P = 0.005) (Table 3, Figure 3a). On leg extension 1RM, HIGH lost more of the initial gain than LOW+ (P = 0.001) and LOW (P = 0.003), whereas LOW declined more than LOW+ (P = 0.011). When compared to LOW (+11.6 ± 5.9%), the residual gain from baseline to follow-up for leg extension 1RM was higher in LOW+ (+21.7 ± 15.8%, P = 0.002) and tended to be higher in HIGH (+16.3 ± 9.0%, P = 0.064) (Table 3, Figure 3b). Local muscular endurance changed significantly over time (P < 0.001), but the group-by-time interaction was not significant (P = 0.255) (Table 3). At follow-up, muscular endurance did not remain above baseline values in any of the training groups (all P > 0.05).
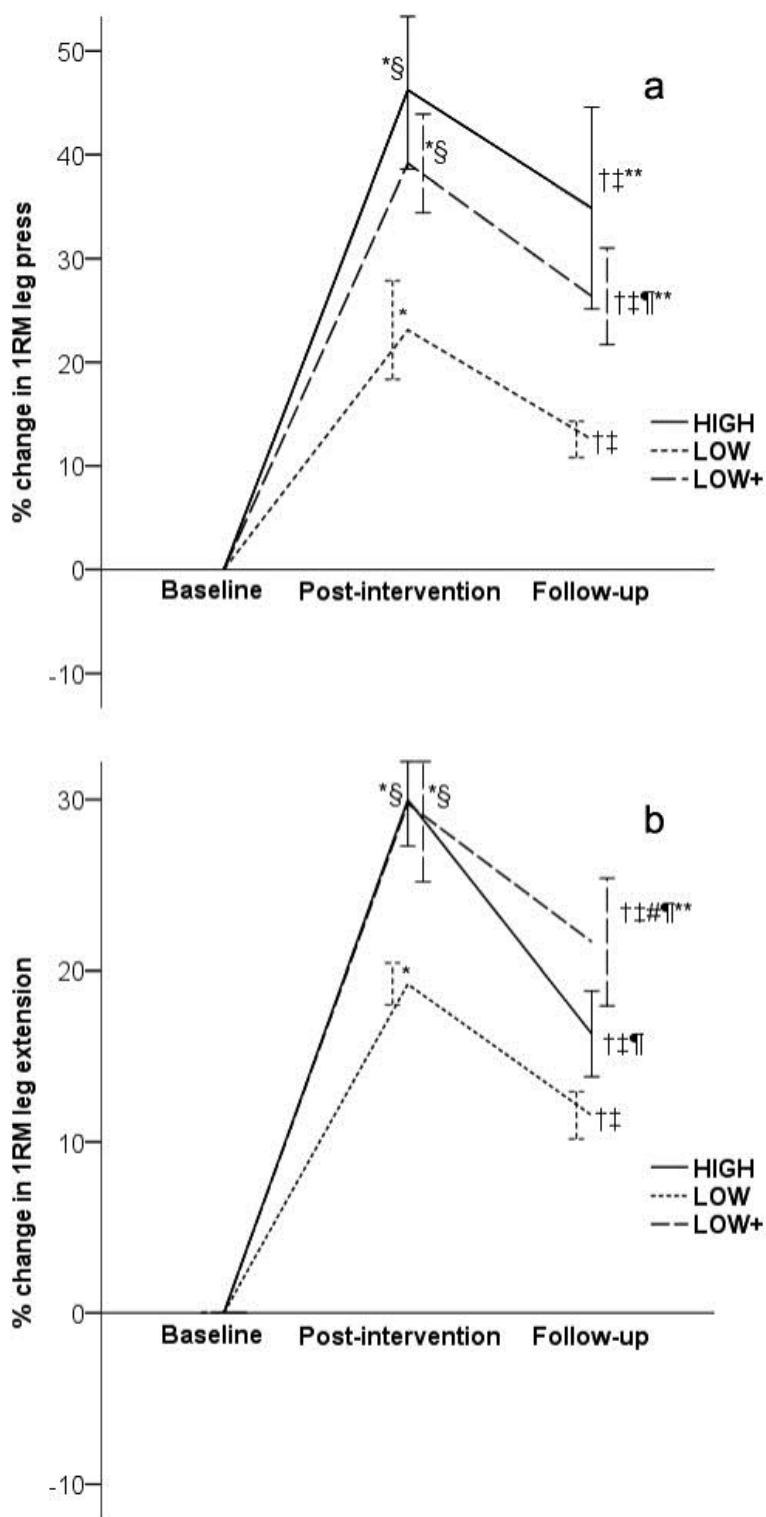
Figure 3. Percent changes over time with respect to baseline values in leg press (a) and leg extension (b) one repetition maximum for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). *Significant change from baseline to post. †Significant change from post to follow-up. ‡Significant change from baseline to follow-up. §Significant difference with LOW from baseline to post. ¶Significant difference with LOW from post to follow-up. #Significant difference with HIGH from post to follow-up. **Significant difference with LOW from baseline to follow-up. Error bars: ± 1SE.

Isometric and isokinetic muscle strength. For isometric strength, a time-effect was found (P < 0.001), whereas no group-by-time effect was revealed (P = 0.907). After an initial post-intervention gain, no significant decreases in isometric strength were found from post to follow-up (all P > 0.05). At follow-up, isometric strength exceeded baseline values in HIGH (+8.5 ± 11.4%, P = 0.028) and LOW+ (+6.0 ± 10.0%, P = 0.024) and tended to exceed baseline values in LOW (+5.9 ± 11.6%, P = 0.063) (Figure 4a).

Results also revealed a significant time-effect for isokinetic strength at 60°/s (P = 0.034) and at 180°/s (P < 0.001), with no group-by-time effect (P = 0.351 for $PT_{dyn60°/s}$ and P = 0.589 for $PT_{dyn180°/s}$). At follow-up, no residual effects on isokinetic strength at 60°/s and at 180°/s were found in any of the groups (all P > 0.05) (Table 3). Isokinetic strength at a high speed of 240°/s changed over time (P = 0.002) and this change differed between groups (P = 0.023). After a greater post-intervention gain in HIGH compared to LOW and LOW+ (52), HIGH decreased more from post to follow-up than LOW+ (P = 0.003) and LOW (P = 0.022). Similar to isokinetic strength at lower speeds, no strength retention above baseline levels was shown for isokinetic strength at high speed in any of the groups (all P > 0.05) (Figure 4b) (Table 3).

Functional performance. An overall time effect was found for all functional performance tests (all P < 0.05), indicating training-induced improvements (52). Except for the timed up-and-go test, performances at follow-up significantly exceeded baseline levels in all groups (all P < 0.05). Only for the maximal gait speed test, a significant group-by-time effect was found (P = 0.037). From baseline to follow-up, HIGH showed a greater improvement than LOW (P = 0.021), whereas the difference between HIGH and LOW+ did not reach significance (P = 0.163).
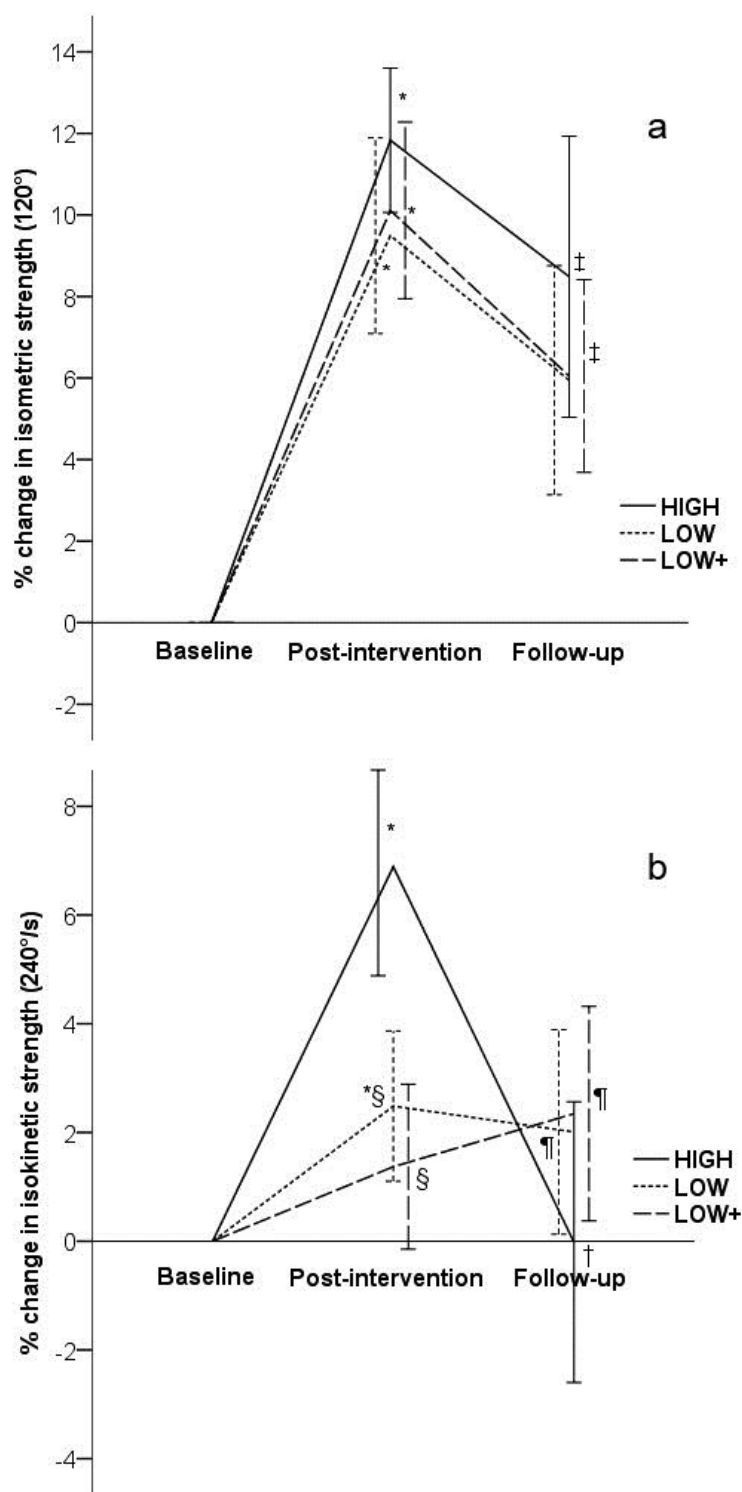
Figure 4. Percent changes over time with respect to baseline values in isometric (a) and isokinetic (b) strength for high-resistance training group (HIGH), low-resistance training group (LOW), and mixed low-resistance training group (LOW+). *Significant change from baseline to post. †Significant change from post to follow-up. ‡Significant change from baseline to follow-up. §Significant difference with HIGH from baseline to post. ¶Significant difference with HIGH from post to follow-up. Error bars: ± 1SE.

Table 3. Means ± SD at baseline and percent changes compared to baseline at post and follow-up for muscle volume and muscle strength in the three intervention groups

Outcome measures	Baseline	% Changes from baseline to post	% Changes from baseline to follow-up
Muscle volume (cm³)			
HIGH	150.2 ± 39.0	+3.2 ± 3.7*	+0.5 ± 2.1†
LOW+	155.0 ± 38.8	+2.6 ± 3.8*	+0.8 ± 3.0†
LOW	156.6 ± 36.0	+2.4 ± 2.7*	+1.0 ± 3.7
1RM leg press (kg)			
HIGH	99.8 ± 56.4	+46.2 ± 32.3*§	+34.9 ± 35.1†‡††
LOW+	96.2 ± 40.7	+39.2 ± 20.7*§	+26.4 ± 19.7†‡#††
LOW	110.0 ± 56.3	+23.1 ± 20.7*	+12.6 ± 7.2†‡
1RM leg extension (kg)			
HIGH	30.0 ± 6.0	+30.0 ± 11.5*§	+16.3 ± 9.0†‡#
LOW+	29.5 ± 6.7	+29.7 ± 19.8*§	+21.7 ± 15.8†‡#**††
LOW	31.0 ± 8.4	+19.2 ± 5.3*	+11.6 ± 5.8†‡
Local muscular endurance (number of reps)			
HIGH	16.4 ± 3.8	+14.6 ± 31.3	+7.0 ± 30.4
LOW+	16.6 ± 4.7	+16.3 ± 20.6*	+9.9 ± 30.7
LOW	17.1 ± 3.3	+19.8 ± 29.8*	-0.9 ± 23.6†
Isometric muscle strength (120°) (Nm)			
HIGH	143.5 ± 39.9	+11.8 ± 7.3*	+8.5 ± 11.4‡
LOW+	140.2 ± 40.0	+10.1 ± 9.2*	+6.0 ± 10.0‡
LOW	138.0 ± 44.3	+9.5 ± 10.5*	+5.9 ± 11.6
Isokinetic muscle strength (60°/s) (Nm)			
HIGH	126.7 ± 37.8	+5.7 ± 11.8	+3.0 ± 10.9
LOW+	127.4 ± 35.3	+1.9 ± 9.5	+3.0 ± 9.4
LOW	128.9 ± 44.6	+4.8 ± 9.1	+2.8 ± 8.4
Isokinetic muscle strength (180°/s) (Nm)			
HIGH	80.3 ± 25.8	+6.1 ± 7.9*	+5.6 ± 11.3
LOW+	81.1 ± 22.9	+2.6 ± 5.0	+3.4 ± 7.4
LOW	81.9 ± 28.8	+3.8 ± 6.5*	+2.5 ± 7.0
Isokinetic muscle strength (240°/s) (Nm)			
HIGH	71.2 ± 21.7	+6.9 ± 8.3*	-0.0 ± 8.2†
LOW+	73.7 ± 21.4	+1.4 ± 6.4¶	+2.4 ± 8.4**
LOW	72.2 ± 24.5	+2.5 ± 6.0*¶	+2.0 ± 7.8**

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; *Significant change from baseline to post (P < 0.05); †Significant change from post to follow-up (P < 0.05); ‡Significant change from baseline to follow-up (P < 0.05); §Significant difference with LOW from baseline to post (P < 0.05); ¶Significant difference with HIGH from baseline to post (P < 0.05); #Significant difference with LOW from post to follow-up (P<0.05); **Significant difference with HIGH from post to follow-up (P < 0.05); ††Significant difference with LOW from baseline to follow-up (P < 0.05)

Table 4. Means ± SD at baseline and percent changes compared to baseline at post and follow-up for functional performance in the three intervention groups

Outcome measures	Baseline	% Changes from baseline to post	% Changes from baseline to follow-up
6-minute walk distance (m)			
HIGH	595.6 ± 65.8	+5.7 ± 9.7*	+4.7 ± 4.3‡
LOW+	564.1 ± 92.5	+5.1 ± 11.4	+4.8 ± 8.6‡
LOW	553.0 ± 71.3	+3.5 ± 9.1	+5.0 ± 8.4‡
Maximal gait speed (m/s)			
HIGH	1.83 ± 0.29	+12.6 ± 11.9*	+15.0 ± 11.1‡
LOW+	1.82 ± 0.33	+3.7 ± 12.4§	+9.5 ± 11.6†‡
LOW	1.92 ± 0.29	+2.0 ± 13.3	+3.7 ± 6.8¶
30-second chair sit-to-stand (number of reps)			
HIGH	15.8 ± 2.5	+8.6 ± 8.0*	+9.6 ± 6.9‡
LOW+	15.0 ± 2.1	+9.1 ± 9.2*	+9.3 ± 8.8‡
LOW	15.7 ± 2.3	+5.0 ± 9.0	+8.3 ± 11.8‡
5-repetition chair sit-to-stand (s)			
HIGH	9.1 ± 1.7	-10.0 ± 8.5*	-10.7 ± 11.7‡
LOW+	9.5 ± 1.1	-11.5 ± 10.0*	-11.1 ± 10.3‡
LOW	9.5 ± 1.8	-10.6 ± 10.0*	-14.7 ± 11.2†‡
Timed up-and-go (s)			
HIGH	5.8 ± 0.8	-2.9 ± 7.7	+0.0 ± 8.9
LOW+	6.3 ± 0.8	-4.9 ± 11.4	-4.6 ± 9.6
LOW	6.0 ± 1.1	-3.2 ± 8.8	-3.5 ± 11.2

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training; *Significant change from baseline to post (P < 0.05); †Significant change from post to follow-up (P < 0.05); ‡Significant change from baseline to follow-up (P < 0.05); §Significant difference with HIGH from baseline to post (P < 0.05); ¶Significant interaction effect (time x group) with HIGH from baseline to follow-up (P < 0.05)

Psychological processes

Table 5 shows the scores on the questionnaire variables at different time points. The scale measuring subjects' positive feelings related to exercise revealed no significant differences between groups at any of the 12 time points (means of week 1 and week 12 reported in Table 5) (all P > 0.05). In addition, no differences emerged between groups for SE and RAI at any of the time points (all P > 0.05, Table 5). The scale referring to negative feelings related to exercise did show a difference between LOW and both HIGH and LOW+, but only in week 12 (Table 5). In this week, LOW demonstrated more negative feelings towards the exercise program than HIGH and LOW+.

Table 5. Means ± SD for questionnaire variables in the three intervention groups

Variables	HIGH	LOW+	LOW	P
Positive feelings related to exercise				
Week 1	8.3 ± 1.1	8.5 ± 1.0	8.5 ± 1.1	0.788
Week 12	8.2 ± 1.1	8.7 ± 1.1	8.4 ± 0.9	0.317
Negative feelings related to exercise				
Week 1	4.8 ± 2.0	4.8 ± 2.2	5.5 ± 2.2	0.548
Week 12	5.2 ± 2.5*	5.5 ± 2.0*	6.6 ± 2.8	0.042
Self-efficacy				
After 2 weeks of training	3.7 ± 0.6	3.3 ± 0.7	3.8 ± 0.7	0.105
Post-intervention	3.6 ± 0.6	3.5 ± 0.5	3.6 ± 0.6	0.806
Relative autonomy index				
After 2 weeks of training	10.2 ± 4.8	11.0 ± 4.1	9.8 ± 5.1	0.787
Post-intervention	8.9 ± 5.3	8.6 ± 4.4	9.0 ± 3.5	0.907
At follow-up	8.3 ± 4.3	9.4 ± 4.5	10.0 ± 4.2	0.434

HIGH = high-resistance training; LOW+ = mixed low-resistance training; LOW = low-resistance training
P-values: results of Kruskal-Wallis test
*Significant difference with LOW (Mann-Whitney U test, P < 0.05)

Only a minority of subjects continued strengthening exercises after cessation of the intervention: 3 out of 18 subjects in HIGH (16.7%), 4 out of 19 subjects in LOW+ (21.1%), and 2 out of 18 subjects in LOW (11.1%). Fisher's exact tests did not reveal significant differences in adherers between groups (P > 0.05). Subjects who continued strength training completed on average 18.6 exercise sessions (range 7 to 35) over a period of on average 14.4 weeks (range of 7 to 22). One of

these subjects had already quit exercising before follow-up measurements. Subjects received an individualized training program, prescribed by qualified fitness instructors and irrespective of the training program during the intervention. In their most recent training program of the follow-up period, five subjects still trained on the leg press, on which they performed on average 2 sets of 17 repetitions at a resistance of 38% of 1RM measured at follow-up. Also, five subjects continued exercising on the leg extension, on which they performed on average 2 sets of 16 repetitions at 41% of 1RM measured at follow-up. Although most participants quit strengthening exercises after the intervention, many of them indicated that they were still planning to participate in strength training at a fitness center in the future: 6 out of 17 participants in HIGH (35.3%), 12 out of 19 in LOW+ (63.2%), and 11 out of 18 in LOW (61.1%). Chi-square test did not reveal a significant difference in frequencies between groups (P = 0.183).

Table 6 shows medians and interquartile ranges for values reported on a 5-point Likert scale for the reasons to quit strengthening exercise. On average, 49.8%, 31.2% and 19.0% of the barriers reported by an individual (score of 4 or 5) were classified as intrapersonal, environmental and interpersonal factors, respectively. The most frequently reported barriers were perceived lack of time (45.7%, intrapersonal), seasonal reasons (40.0%, environmental), being more interested in other physical activities (40.0%, intrapersonal) and financial cost of subscription to the fitness center (28.3%, environmental) (Table 6).

Discussion

The objective of the present study was to compare the long-term effects of high- and low-resistance exercise on muscular and functional outcomes and on exercise adherence in older adults. The findings show that, 24 weeks after cessation of a 12-week resistance exercise intervention, muscle volume gains induced by training were lost, whereas strength and functional performance gains were partly preserved. Despite the fact that gains in 1RM remained higher in HIGH and LOW+ compared to LOW, no clear advantage was found for high-resistance training compared to low-resistance training for improving muscle characteristics and functional performance in the long-term. The present study also revealed that the degree of external resistance used during the intervention did not influence long-term resistance exercise adherence, which was limited in all exercise groups.

Table 6. Perceived barriers for continuation of strength training after cessation of the supervised intervention. Barriers were rated on a 5-point Likert scale (ranging from 1 = 'strongly disagree' to 5 = 'strongly agree')

Perceived barriers	Median (Interquartile range)	Percentage of subjects grading 4 or 5
Intrapersonal factors		
Lack of interest in resistance exercise	3.0 (2.0 – 3.0)	15.6%
Health-related issues	1.0 (1.0 – 2.0)	15.6%
More interested in other physical activities	3.0 (2.0 – 4.0)	40.0%
Resistance exercise is too strenuous	2.0 (1.0 – 2.0)	4.4%
Low outcome expectations	1.0 (1.0 – 2.0)	0.0%
Perceived lack of time	3.0 (2.0 – 4.3)	45.7%
Planned vacation/travel	1.0 (1.0 – 3.0)	20.0%
Interpersonal factors		
Lack of social support	1.0 (1.0 – 2.0)	2.3%
Exercise companion quitted	1.0 (1.0 – 2.0)	6.7%
Care of siblings/others	2.0 (1.0 – 3.0)	17.4%
No continuation of instructor's supervision	2.0 (1.0 – 3.0)	20.0%
Environmental factors		
Financial cost	2.5 (1.0 – 4.0)	28.3%
Seasonal reasons	3.0 (1.0 – 4.0)	40.0%
Lack of access to a fitness center	1.0 (1.0 – 2.0)	8.9%
Fitness centers are too busy	1.0 (1.0 – 2.0)	6.7%
Uncomfortable feeling in fitness center	1.0 (1.0 – 2.0)	6.7%

An important question that had not yet received sufficient attention in previous literature is whether or not older adults are more or less motivated to engage in either high- or low-resistance exercise. Differences in motivation could lead to differences in longer-term exercise adherence, and this should be taken into account when determining the effectiveness of resistance exercise protocols in counteracting age-related muscular and functional declines. Our study differs from previous detraining studies (15,21,48) that compare strength exercise protocols at different resistances, because here the subjects were allowed to continue strength training after the end of the guided intervention. This approach more closely resembles real-life situations with (un)planned training disruptions and provides us with valuable information on long-term exercise adherence.

In the current study, the older adults appeared to be highly motivated before, during, and after the training intervention, with no difference between groups. One might expect that older adults would be less motivated or less willing to engage in high- compared to low-resistance exercise, but the findings in the current study do not support this expectation. For the weekly positive feelings related to exercise, very high scores were reported in all groups. The relative autonomy index derived from the scores on the BREQ-2 indicated a high degree of self-determination. Moreover, the multi-dimensional self-efficacy questionnaire pointed out that subjects were moderately to highly confident that they would perform resistance exercise when confronted with barriers. The high scores on autonomous motivation and self-efficacy might be biased as a consequence of participants' self-selection. As training research is dependent on subjects who volunteer to participate, it is clear that only motivated people engage in interventions. In addition, we cannot exclude that a potential ceiling effect in motivation might have masked group differences.

Contradictory to the expectations that a high degree of self-determination and self-efficacy for participation in resistance exercise would result in the long-term persistence of exercise behavior (41), only few continued strength exercising after cessation of the intervention: 16.7% in HIGH, 21.1% in LOW+, and 11.1% in LOW. This low long-term resistance exercise adherence did not differ between groups. This finding corresponds with the experience in previous intervention studies, in which most participants quit exercising as soon as the structured and guided intervention ends, even though they appear to enjoy exercise participation (25,37). The discrepancy between the high degree of motivation and the low long-term adherence stresses the importance to focus on the barriers for maintaining resistance exercise behavior, a research area that has not yet received sufficient attention in literature.

In the current study, subjects most commonly reported intrapersonal factors as barriers for the maintenance of resistance exercise behavior after the end of the supervised intervention. Of these intrapersonal barriers, perceived lack of time (45.7% of subjects) and being more interested in other physical activities (40.0% of subjects) were most frequently cited. These main constraints to continue resistance exercise seem to represent motivational problems, which again seem contradictious to the high degrees of self-reported autonomous motivation and self-efficacy at post-intervention. Given that participation in exercise is a socially desirable behavior (34), social desirability might have led to an over-reporting of the motivation and self-efficacy for participation in resistance exercise. This may be part of the explanation for this discrepancy between the high degree of motivation and the low long-term adherence.

The reported barrier of perceived lack of time also suggests that subjects were not able to incorporate resistance exercise in their weekly schedule without professional assistance. In this regard, the abrupt ending of the provided structure and guidance during the intervention seems to be an important issue. Future research should focus on strategies to facilitate the incorporation of resistance exercise behavior in the real-life situation.

The barrier of being more interested in physical activities other than resistance exercise was frequently reported by older adults in our study. This highlights the need for increasing the knowledge and understanding of the detrimental effects of sarcopenia on functional performance and of the benefits of resistance exercise in older adults. Nowadays, the majority of older adults believes that the maintenance of a physically active lifestyle, without systematic training, is sufficient to prevent functional dependence as a consequence of aging. However, research contradicts this common believe (7) and points out the necessity of participation in resistance exercise (18,26,54). Increasing the awareness of sarcopenia might influence an older adult's motives to engage in resistance exercise. Physicians might play a key role in promoting resistance exercise behavior among older adults, because older adults generally respect their physician's advice (43).

Next to intrapersonal barriers, some environmental factors need to be considered. First, the supervised intervention ended in springtime, near the start of summer (April to June). The changes in weather, i.e. more hours of sun, might have stimulated the engagement in outside activities instead of in resistance exercise sessions at a fitness center. Indeed, 40.0% of subjects reported seasonal reasons as one of the barriers for continuing resistance exercise. Second, the financial cost of subscription to the fitness center was pointed out as an important barrier by 28.3% of subjects. This is in agreement with a study of Kruger et al. (27), which indicated that U.S. adults commonly perceive subscription fees as a barrier to access fitness facilities.

Although no differences in motivation and long-term exercise adherence were found between high- and low-resistance exercise, it should be noted that HIGH counted more non-compliers at follow-up than LOW and LOW+ (7 versus 2 and 1, respectively). Even though no adverse effects were reported during the intervention and the reasons for non-compliance could not be clearly linked to the high resistances used during the intervention, future research should investigate this finding more into detail. In addition, fewer participants in HIGH than in LOW and LOW+ indicated that they were planning to participate in strength training at a fitness center in the future, though not significantly different. This simple question represents an intention rather than an actual behavior. Considering that the actual long-term adherence did not differ between high- and low-

resistance exercise, it cannot be claimed that low-resistance exercise is preferred over high-resistance exercise. However, these results do provide interesting issues for future research.

A second objective of the current study was to report and compare the long-term effects of different resistance exercise protocols on muscular and functional outcomes. Whether these long-term effects are caused by the initial training stimulus of the exercise protocol or by the continuation of some sort of exercise after the intervention is of minor importance in our study approach. All subjects received the incentive of an exercise protocol, and if this incentive has led to a change in exercise behavior, we wanted to integrate this finding in our evaluation of the long-term effectiveness of the protocols.

With regard to muscle volume, a reversal in muscle hypertrophy occurred at follow-up. This finding is consistent with previous research, in which muscle volume returned to pre-training values 24 to 31 weeks after cessation of a resistance exercise intervention (20,24,49). Even after a shorter detraining period of 12 weeks, Correa and coworkers reported a complete loss of the initial training-induced gain in muscle volume (11).

In the current study, the loss in muscle volume and the level of muscle volume 24 weeks after the intervention had ended were irrespective of prior training resistance. This result is in contrast with the findings of Tokmakidis et al. (48). After a short detraining period, their study showed a slightly greater decline but still greater retention in mid-thigh cross-sectional area after high-resistance exercise (80% of 1RM) compared to moderate-resistance exercise (60% of 1RM). However, they also found greater post-intervention hypertrophy, probably because exercise protocols were not designed to reach muscular failure. If exercises are not performed until failure, high external resistances are preferred for activation of the type II fibers, which are known to be more responsive to hypertrophy (47).

Although a reversal in hypertrophy occurred in the current study, muscle strength gains were partly preserved in all groups. In other words, with the same amount of muscle volume subjects were able to generate higher levels of strength at follow-up compared to baseline. These results are consistent with former research showing that exercise-induced adaptations in muscle strength are maintained longer than muscle hypertrophy after training cessation (8,11,20,22,24,25,49).

All groups experienced losses in 1RM strength 24 weeks after cessation of the intervention. The decline rate in HIGH was -11.4 ± 7.7% for leg press 1RM and -10.7 ± 5.2% for leg extension 1RM, which is in agreement with the -10.8% decline in 1RM reported in older adults by Trappe and coworkers (2002). Interestingly, the residual gain from baseline to follow-up was greater for leg press 1RM in HIGH (+34.4% ± 35.1%) compared to LOW (+12.6% ± 7.2%) and tended to be greater

for leg extension 1RM in HIGH (+16.3 ± 9.0%) compared to LOW (+11.6 ± 5.9%). As training protocols were designed to be approximately similar in training volume, our data seem to suggest that higher external resistances might be more effective for longer-term 1RM gains. By contrast, a previous detraining study of Harris et al., in which strength exercise protocols at different resistances but with equivalent volume were compared, yielded no effect of prior training resistance on strength retention (21). However, large differences in training resistances between the two studies complicate the comparison. For example, Harris et al. (21) used resistances of 6RM, 9RM and 15RM, whereas in our study, the highest resistance was 10-15RM and much lower resistances of 80-100RM were applied in LOW. It could be argued that such low resistances might not be able to maximize 1RM, both immediately post-intervention as in the longer term.

A unique aspect of the current study was the design of a low-resistance exercise protocol, in which training resistance was increased after a highly repetitive fatiguing protocol (LOW+). This mixed-low resistance exercise protocol was designed in order to investigate whether an extra mechanical stimulus is needed in addition to muscle fatigue to maximize muscular adaptations. This question seems especially relevant when training at very low external resistances (protocols with many repetitions). Results on 1RM seem to suggest that LOW+ is preferred over LOW for gains in 1RM. Not only did LOW+ tend to show greater post-intervention gains in 1RM than LOW, but also greater residual gains from baseline to follow-up. On the contrary, LOW+ and HIGH were equally effective for longer-term 1RM strength gains.

In addition to 1RM strength tests, the current study also included standardized isometric and isokinetic tests measured by a motor-driven dynamometer. These strength measurements are considered the golden standard in both clinical and research settings (13,38) and might add valuable information to the comparison of high- and low-resistance exercise. With respect to isometric strength, all groups showed similar post-intervention increases (52). Interestingly, isometric strength values at follow-up still exceeded baseline values, hereby confirming previous research (25,49). None of the resistance exercise protocols was advantageous over another for improving isometric strength in the longer term. Likewise, isokinetic strength at 60°/s and at 180°/s did not reveal differences between groups. Only modest post-intervention improvements were found (52), with no residual effects at follow-up. With regard to isokinetic strength at 240°/s, HIGH seemed beneficial for immediate post-intervention gains (52). The underlying mechanism for this result remains unclear. The use of high resistances might facilitate the activation of type II muscle fibers, leading to better performances on high-speed strength tests. However, it should also be noted that HIGH demonstrated a higher rate of decrease in high-speed isokinetic strength during the follow-up period as compared to LOW and LOW+, with no

preventive effect on velocity-dependent strength in the longer term. For optimal effects on isokinetic strength at high-speed, it might be interesting to include higher-speed resistance exercises in future training programs for older adults. Higher-speed resistance exercise might also be beneficial for improving functional performance in the longer term (56).

In the current study, functional performance levels at follow-up exceeded baseline values in all groups, even though our subjects were already well-functioning before the start of the intervention. Only for maximal gait speed, HIGH demonstrated higher long-term improvements than LOW. This benefit of HIGH over LOW was not confirmed by other functional performance tests, so it seems that high- and low-resistance exercise at moderate speed is similarly effective for longer-term functional improvements. It should be noted that potential ceiling or floor effects might have masked group differences in functional performance. However, previous meta-analyses already stated that high external resistances are not necessarily superior to low external resistances for improving functional performance (39,44).

As reported earlier, only a minority of older adults continued strength exercising after cessation of the intervention (9 out of 56 participants). Those who did continue (or restart) resistance exercise after cessation of the intervention, reduced their training frequency to on average 1.3 sessions per week (range from 0.9 to 2.7). Trappe and coworkers (2002) already stated that resistance training one day a week can be sufficient to maintain muscle strength and volume in older men after a 12-week progressive resistance training program. In the current study, participants who still trained on the leg press or leg extension in their latest training program performed on average 2 sets of 17 repetitions at 38% of 1RM and 2 sets of 16 repetitions at 41% of 1RM respectively. These training intensities are markedly lower than the intensities in the initial training intervention (52). On the one hand, the lower intensities might be caused by the prudence of fitness instructors to not overburden the musculoskeletal system of older adults. On the other hand, older adults might have self-selected their resistances for performing a fixed number of repetitions. The resistances were indeed very similar to the self-selected resistance (42% of 1RM) for performing 10 to 15 repetitions by apparently healthy older women in previous investigations (14,17). Although a self-selection strategy can enhance intrinsic motivation because of a greater perception of autonomy (14), lack of progress because of inappropriate intensity selection may also undermine an individual's motivation (17). Hence, it is crucial for fitness instructors to closely supervise training intensity and individual's perceived effort.

One limitation of this study is that food intake was not monitored during both training and detraining periods. Inadequate protein consumption could have influenced muscle hypertrophy

and degradation. Additionally, the limited sample size in this study makes it susceptible to type II error.

In conclusion, this study was a first attempt to examine whether older adults were more motivated to engage in low- as compared to high-resistance exercise, which could lead to differences in long-term exercise adherence. To date, research lacked information on this topic, even though it is especially relevant when determining the long-term effectiveness of different resistance exercise protocols in older adults. Contrary to our expectations, our data suggest no difference in long-term maintenance of resistance exercise behavior after the end of a supervised resistance exercise intervention at high or (mixed) low external resistances. Long-term resistance exercise adherence was limited, suggesting the importance of further research on developing strategies to overcome barriers of older adults to engage in resistance exercise. The results also indicate that various aspects of muscle strength and functional performance remain elevated for several months even after the end of a supervised training intervention. Interestingly, if training is performed until muscle failure and results are corrected for training volumes, highly repetitive low-resistance exercise protocols appear to be as effective as traditional high-resistance exercise protocols for long-term neuromuscular and functional adaptations. The only clear long-term difference between LOW and both LOW+ and HIGH was demonstrated on the 1RM tests and was therefore very specific to the trained movements. These findings underline the value of low-resistance exercise protocols in older age as a potential alternative to high-resistance exercise or as variation in training approaches.

Acknowledgements

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PART 3

SUMMARY AND GENERAL DISCUSSION

The aim of this doctoral thesis was twofold. The first objective was to increase our understanding on the relative contribution of muscle mass, muscle strength and force-velocity components to functional performance in elderly individuals (**Chapter 1, *paper 1***). The second and main objective was to examine whether low-resistance exercise is as effective as high-resistance exercise for inducing muscular and functional adaptations in older adults (**Chapter 2**). In order to meet this objective, we first tested the feasibility of a newly designed high-repetition low-resistance exercise protocol in young adults (**Subchapter 2.1, *paper 2***). This allowed us to fine-tune the exercise protocol before applying it to older adults in **Subchapter 2.2**. In this subchapter, both the immediate post-intervention effects of low- and high-resistance exercise (***paper 3***) as well as the persistence of muscular and functional adaptations 24 weeks after cessation of the intervention (***paper 4***) were investigated. In addition, long-term resistance exercise adherence was examined in ***paper 4***.

In the following paragraphs, the main findings of the four research papers will be summarized and interpreted. In addition, practical implications will be pointed out, followed by a discussion of some methodological considerations of the studies and suggestions for future research.

1. Summary of main findings

1.1. Chapter 1: Relationship between force-velocity characteristics of the knee extensors and functional performance

Paper 1 focused on the relationship of different muscle parameters and functional performance in elderly women. Functional performance was measured with the modified Physical Performance Test (mPPT), an objective and well-validated assessment of the degree of functional limitations (19). One hundred twenty-three elderly women ($\geq$ 70 years of age) participated in this study.

The mPPT-score showed moderate to high correlations with muscle mass (r = 0.41, P < 0.05), muscle strength (r varied between 0.57 and 0.61, P < 0.05) and speed of movement tests (r varied between 0.31 and 0.68, P < 0.05). With regard to speed of movement during ballistic tests, these correlations became stronger when external loadings decreased and thus when speed of movement increased. Importantly, maximal speed of movement (SoM) showed the highest correlation with functional performance (r = 0.68, P < 0.05). In a forward stepwise regression model, only maximal speed of movement (SoM) and isometric strength ($PT_{stat90°}$) remained independently associated with mPPT (R² = 0.49), with SoM accounting for the majority of the variance (R² = 0.46). We were able to identify threshold values that optimally differentiated between women with mild (mPPT-score of 25 to 31) or without (mPPT-score $\geq$ 32) functional

limitations, i.e. 350°/s for SoM and 1.46Nm/kg for $PT_{stat90°}$. The area under the curve, 0.765 for SoM and 0.786 for $PT_{stat90°}$, reflected a fair to good discriminating power of the tests. Sensitivity and specificity were 77% and 70% for SoM and 74% and 77% for $PT_{stat90°}$, respectively.

In conclusion, the results of **paper 1** emphasize the role of the dynamic aspect of knee extensor performance, especially speed of movement, in everyday function of elderly women. Muscle mass, however, was not an independent determinant of functional performance when included in the same regression model as muscle strength, suggesting that muscle mass primarily contributes to functional performance through its association with muscle strength. This highlights the importance to focus on several aspects of muscle function in addition to muscle mass when designing exercise interventions to prevent functional decline.

1.2. Chapter 2: Resistance exercise as countermeasure against sarcopenia and functional decline

Low-resistance exercise might potentially be more suitable for older adults than high-resistance exercise. However, there is currently no agreement in literature as to whether low-resistance exercise can be as effective as high-resistance exercise for increasing muscle strength and mass. As **paper 1** suggested that speed of movement might be crucial in functional performance, we added force-velocity characteristics to the outcome variables in our intervention studies (**papers 2, 3 and 4**). However, exercise protocols were designed to improve muscle strength and mass as a prerequisite for speed production, hereby following the rules of proper periodization design in resistance exercise programs.

The purpose of **Subchapter 2.1** (**paper 2**) was to explore the feasibility of an experimental high-repetition low-resistance exercise protocol and to investigate the impact of external resistance and maximal effort in strength training programs on muscle strength and force-velocity characteristics in young adults (N = 36). Two low-resistance exercise protocols were created and compared to high-resistance exercise (HI_{max}): one low-resistance protocol ending in maximal effort (LO_{max}), one low-resistance protocol without achieving maximal effort (LO). After 9 weeks of training, HI_{max} appeared most effective in increasing 1RM and isometric strength, whereas LO_{max} was found to be most effective in increasing isokinetic strength, maximal work and speed of movement. LO was not able to achieve equivalent gains as HI_{max} and LO_{max}.

In conclusion, the findings in **paper 2** support the idea that training until maximal effort, probably resulting in optimal activation of the muscle, may be needed to optimize strength gains in low-resistance exercise protocols. Furthermore, low-resistance exercise until muscle failure might not be considered as a replacement for high-resistance training, but rather as an alternative with

different training-specific adaptations. Interestingly and unexpectedly, the experimental high-repetition low-resistance exercise protocol (LO_{max}) showed promising and advantageous results on dynamic strength and speed of movement.

In **Subchapter 2.2**, the experimental high-repetition low-resistance exercise protocol is applied in healthy older adults (N = 56). The LO_{max} protocol, here defined as LOW+, was compared to a high-repetition low-resistance exercise protocol at constant resistance (LOW) and to high-resistance exercise (HIGH). Exercise protocols were designed to be equal in training volume and ended in maximal effort in each training session. The aim of this subchapter was to compare the effects of HIGH, LOW and LOW+ on muscular and functional outcomes, both immediately post-intervention (*paper 3*) as well as 24-weeks after the end of the 12-week training intervention (*paper 4*). *Paper 4* additionally investigated if HIGH, LOW and LOW+ resulted in differences in motivation and self-efficacy beliefs, leading to differences in long-term exercise adherence.

Subchapter 2.2 demonstrated comparable improvements on most of the outcome variables between 12 weeks of training either at HIGH, LOW, or LOW+. All groups demonstrated similar gains in muscle volume, isometric strength and most functional performance tests, and small equivalent increases in isokinetic strength at 60°/s and 180°/s. None of the groups showed effects on speed of movement. HIGH appeared most effective in increasing isokinetic strength at a high speed of 240°/s. Moreover, HIGH and LOW+ were more effective than LOW for increasing 1RM. From baseline to follow-up, the only significant difference between LOW and both HIGH and LOW+ was the improvement in 1RM, which was lower in LOW.

Our study sample of older adults in **Subchapter 2.2** appeared to be highly motivated for resistance exercise training before, during and after the end of the intervention. However, only few continued strengthening exercise after cessation of the intervention: 16.7% in HIGH, 21.1% in LOW+, and 11.1% in LOW, with no difference between groups.

In conclusion, our findings support the idea that both high- and low-resistance exercise until muscle failure can be effective to prevent or counteract age-related declines in muscle strength, muscle mass and functional performance. The only clear long-term difference between LOW and both LOW+ and HIGH was demonstrated on the 1RM tests and was therefore very specific to the trained movements. As this benefit of HIGH and LOW+ over LOW could not be translated into a higher maximal strength capacity, greater muscle hypertrophy or greater functional improvements, its relevance can be questioned. It should be noted that long-term adherence to resistance exercise remains a challenge in older adults.

2. General discussion

2.1. Discussion of the findings and practical implications

2.1.1. Determinants of functional performance in elderly

Paper 1 investigated the relative contribution of muscle mass and force-velocity components to functional performance in elderly women. We focused on force-velocity characteristics of the knee extensor muscles because of their importance in a variety of functional tasks (74,117). Consequently, we also recorded muscle mass of the upper leg muscles by means of computed tomography (CT). Computed tomography is considered as one of the golden standards for body composition analysis (97).

In agreement with previous research, we showed that muscle mass was significantly correlated with functional performance in elderly women (8,79-81,100). However, muscle mass did not remain an independent predictor of functional performance when included in the same regression model as muscle strength and force-velocity characteristics of the knee extensors. Our findings support previous research by suggesting that muscle mass contributes to functional performance mainly because of its association with muscle strength (99,149). Indeed, muscle mass demonstrated a significant correlation with isometric strength (r = 0.70), isokinetic strength at 60°/s (r = 0.64) and maximal speed of movement (r = 0.43) in *paper 1* (all P < 0.001). Despite these moderate-to-high correlation coefficients, 51% to 59% of the variance in muscle strength and even 82% of the variance in maximal speed of movement of the knee extensors, which is identified as a key component in functional performance (*paper 1*), cannot be explained by muscle mass of the upper leg. This emphasizes the impact of neural factors and muscular factors that are not related to muscle size on force and speed production. However, one should also recognize the limitation of the method of muscle mass determination in *paper 1*, given that only one particular portion of the mid-thigh was imaged by CT and muscle mass might be non-uniformly distributed along the belly of the muscles and even between the individual components of muscle groups (62,155).

The following paragraphs will briefly discuss the interpretation of the correlation coefficients and coefficients of determination in *paper 1*. Correlation analysis is widely used in research to determine the magnitude of the relation between two variables. However, the correlation coefficient is difficult to interpret. A correlation coefficient that is statistically significant is not necessarily relevant. To give more meaning to correlations, it is common to use the square of the

correlation coefficient, i.e. the coefficient of determination. This index is defined as the percentage of variance in one variable that is predicted or explained by the other (114,140).

To the best of our knowledge, there are no specific rules for interpreting the relevance of such percentage values. Interpretation also differs on whether or not the independent and dependent variables are expected to be highly correlated. For example, muscle mass of the upper leg muscles is expected to be highly correlated with the maximal strength generating capacity of the knee extensors (i.e. isometric strength). An explained variance of 49%, as calculated based on data in *paper 1*, is lower than expected and points out the importance of neuromuscular factors other than muscle size in muscle function. However, in *paper 1*, stepwise regression analysis demonstrated that nearly 50% of the variance in the mPPT-score can be accounted for by maximal speed of movement and isometric strength of the knee extensors. The mPPT is a test battery that consists of 9 functional items with several items also involving upper body performance (lifting a book, putting on and taking off a coat, picking up a penny). In this case, the coefficient of determination can be considered relevant and clearly points out the importance of knee extensor function, especially speed of movement, in functional performance.

2.1.1.1. Functionally relevant cutpoints for knee extensor function

Knee extensor function is suggested as one of the most important factors limiting the ability to perform many functional tests (74,117). Functionally relevant cutpoints for strength and speed of movement could be useful for targeting individuals for early interventions to prevent disability. In addition, they could be used to guide strength training programs in the older population.

To date, isokinetic dynamometry is considered the golden standard for measuring muscle strength in both clinical and research settings. The different modes (i.e. isometric, isokinetic and isotonic) of a dynamometer offer the opportunity to evaluate different aspects of muscle function while only requiring one reliable assessment tool. To the best of our knowledge, *paper 1* of this doctoral thesis was the first to identify a functionally relevant cutpoint for knee extensor speed of movement in addition to strength in elderly women. If confirmed in different settings, the use of both cutpoints should allow exercise interventions that are more adapted to the needs of the individual, with a focus on strength, speed or both components.However, these values should not be considered as absolute cutpoints, but rather as alarm signals for (future) functional limitations. The counterpoint of isokinetic dynamometry is that its large-scale applicability remains limited. Alternative methods for measuring knee extensor function that allow for a quick and simple evaluation may be necessary (88).

2.1.1.2. Implications for resistance exercise prescription

The findings of *paper 1* support the growing body of evidence that knee-extensor muscle power, with specific attention to the contribution of velocity, is a critical component in functional performance of elderly individuals (10,11,31,36,49,118,133). These results have important implications for preventive and rehabilitation programs targeting functional adaptations in older adults. Instead of solely focusing on muscle strength gains and hypertrophy, improvements in speed of movement and power should additionally be aimed for.

Power training typically performed at moderate resistances and high speeds is preferred to improve muscle power and has an advantage over traditional strength training for functional outcomes in older adults (145). It seems to be a feasible training method for older persons who are still relatively fit. However, to date, research appears to be unable to draw strong conclusions about the safety of power training in older and frail persons (145). The nature of power training requires a high level of control over body movements and might therefore be inappropriate as first introduction to resistance exercise in untrained individuals.

To provide a strong basis for optimal power development, training cycles should first target basic gains in muscle size and strength at lower speeds. After this first training period designed to strengthen and to gradually adapt the tissues to resistance exercise, exercises at higher speeds should be included in older adults. In the case of frail elderly, functionally-based exercise interventions (56) might more feasible instead of power training.

To conclude, the results of *paper 1* emphasize the role of the dynamic aspect of knee extensor performance, especially maximal speed of movement, in everyday function of elderly. This highlights the importance to focus on several aspects of muscle function in addition to muscle mass when designing exercise interventions to prevent functional decline. In order to facilitate transfer to functional performance, an optimal training program for older adults and elderly should aim for improving muscle power in addition to muscle strength and mass. However, as already mentioned in chapter 2.2.3 of the introduction, proper periodization is warranted. Therefore, our intervention studies were designed to target hypertrophy and muscle strength as prerequisites for speed and power production. Power training or functionally-based exercise interventions should be considered the next phase in program designs for older adults.

2.1.2. Effects of high- and low-resistance exercise

2.1.2.1. Adaptations to the exercise protocols after paper 2

As mentioned earlier, our intention in **paper 2** was to test the feasibility of an experimental high-repetition low-resistance exercise protocol in young adults. This would allow us to fine-tune the protocol before applying it to older adults. As we did not intend to compare the effects of high- and low-resistance exercise between young and older adults, we optimized the program design after **paper 2** by means of the following adjustments:

(1) Training duration (from 9 weeks to 12 weeks) and training volume (additional exercise for lower-body by including leg press) were increased to optimize adaptations.

(2) Training volume was matched between exercise protocols.

(3) All exercise protocols were designed to end in maximal effort.

(4) Movement speed during training was changed from 1s to 2s for each concentric and from 2s to 3s for each eccentric muscle action. In **paper 2**, we experienced some difficulty in standardizing movement speed during training. Therefore, we searched for a tool to control movement speed in the study with older adults. The visual feedback system IsoControl (Technogym) was found suitable as it provides feedback not only on the movement speed, but also on the rest period between sets and the range of motion during exercise. In addition, it counts the number of repetitions performed per set, which is convenient in high-repetition protocols. Consequently, we adapted movement speed during training so that it would match with the speed indicated by the IsoControl.

These adjustments to the program design consequently complicate any comparisons between the training-induced effects of young versus older adults. The following paragraphs of this general discussion will mainly focus on the effects of high- and low-resistance in older adults, as they were the target population of this thesis. However, some differences in findings between **papers 2 and 3** should not be left unnoticed.

First, the mixed low-resistance exercise protocols, LO_{max} and LOW+, were similarly designed. Participants started with a fatiguing protocol of 60 repetitions at about 20% of 1RM, after which the external resistance was increased to about 40% of 1RM and a maximal number of repetitions were performed. Remarkably, although the mean resistance at which the 60 repetitions were performed on the leg extension was equal between young (23% of 1RM) and older adults (24% of 1RM) (P = 0.426), older adults performed on average more repetitions (16.6 versus 10.7, P = 0.001) and at higher resistance (45% versus 41%, P = 0.032) in part 2 of the protocol. This finding might partially be explained by the possibility of an underestimation of 1RM in older adults

compared to young adults (91) and by the fact that 1RM was more frequently evaluated in young (every 2 weeks) than in older adults (every 4 weeks). Especially in the first weeks of training, 1RM gains tend to be large. As % of 1RM was calculated based on the most recent 1RM measurement, a more frequent evaluation of 1RM might have led to lower % of 1RM.

Nevertheless, it remains remarkable that older adults appeared to be more fatigue resistant in this protocol, especially because one would expect that the slower movement speed during training would lead to a decrease in maximum repetitions instead of an increase (130). In line with this finding, a meta-analysis of Christie et al. concluded that older muscles develop less fatigue than young muscles during isometric contractions (30). In contrast, the age-related fatigue resistance seemed less obvious in dynamic contraction protocols, probably because of the greater requirement for power production during the task (22,30). As already mentioned in the introduction (chapter 1.2.2), power production declines prominently with aging (77,96,122). Our moderate-speed low-resistance exercise protocol might not rely that much on power production, hereby retaining the age-related fatigue resistance that is apparent in isometric contractions.
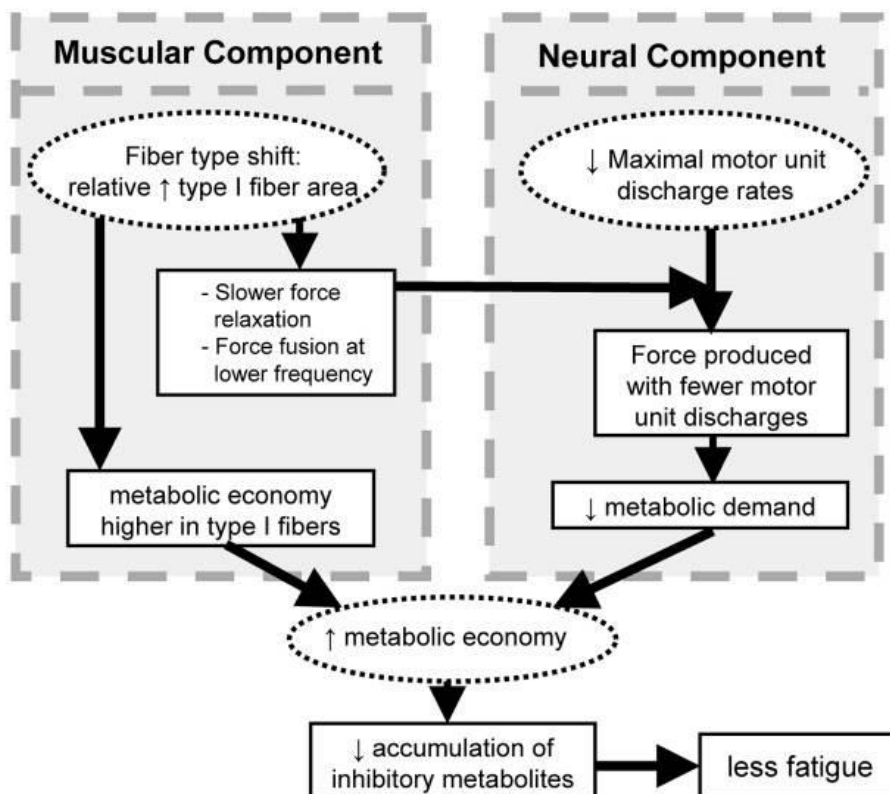
Figure 1. Hypothesis on a higher metabolic economy in older skeletal muscle that might lead to an age-related advantage in fatigue resistance, adapted from Kent-Braun (89).

As a potential mechanism of fatigue resistance in older adults, authors have proposed the greater proportion of type I muscle fibers in older muscles (see chapter 1.2.1 in the introduction) (30,39,107). However, the exact mechanisms remain to be elucidated (30). Kent-Braun suggested a hypothesis to explain this age-related fatigue resistance, which is illustrated in Figure 1. She hypothesized that higher metabolic economy might be a mechanism of enhanced fatigue resistance in older age, which is caused by both muscular and neural changes in the aging muscle (89).

A second notable difference between our intervention studies of young versus older adults is the training-induced effect on speed of movement. Surprisingly, gains in speed of movement were demonstrated after 9 weeks of mixed low-resistance exercise in young adults. ***Paper 3***, however, failed to confirm these findings in older adults. Two possible explanations may have contributed to this disparity. The primary reason is probably linked to the speed of movement during training. The young adults in ***paper 2*** were instructed to perform each concentric action at a speed of 1s. The movement during the high-fatiguing protocol and subsequent training set (LO_{max}) may have resulted in ballistic actions because of the low resistance, hereby improving motor unit recruitment at high movement velocities (57,139). The older adults in ***paper 3*** performed each concentric action at a speed of 2s, i.e. markedly slower than the young adults. We adapted the speed so that it would be similar to the visual feedback system of the training devices (IsoControl, Technogym). The IsoControl helps the participants to keep pace during each contraction through visual cues over the full range of motion. Consequently, it prevents participants from performing ballistic actions at the start of the movement. It can be argued that a resistance training protocol using higher speeds is likely to attain greater gains in speed of movement (45,47,132). A secondary explanation for the discrepancy of the effects on speed of movement might be linked to age-related changes in voluntary muscle activation. There are currently contradicting reports in the literature on whether advancing age reduces the capacity of maximal voluntary muscle activation (99). A review by Klass and colleagues concluded that there may be a meaningful deficit in voluntary muscle activation of proximal muscles in the lower limbs of older adults (90). In addition, Häkkinen et al. reported lower EMG activity in older adults compared to young adults during fast isometric contractions of the knee extensors (60). Although further research is needed and no definite conclusions can be drawn, it seems possible that older adults might not be able to activate type II muscle fibers as easily as young adults. Combined with the fact that aging is accompanied by a selective atrophy and denervation of type II muscle fibers (95), it seems plausible that older adults show less effect on speed-related parameters.

A third difference between our intervention studies of young versus older adults is related to the 1RM strength gain. In young adults, high-resistance exercise showed a greater increase in 1RM than mixed low-resistance exercise, whereas in older adults, gains in 1RM were similar between high- and mixed low-resistance exercise. The exact underlying mechanisms for this difference remain unclear and one should bear in mind the abovementioned differences in program designs. It seems that in young adults, the use of high resistances is a prerequisite for optimizing gains in 1RM, which is extensively reported in previous research (3,23,71,101,105,138). Nevertheless, the necessity of high resistances for optimizing 1RM gains in older adults is questioned based on **paper 3**. Although very low resistances (±30-35% of 1RM; LOW) seem insufficient, a combination of very low (±25-30% of 1RM) and low resistances (±45-50% of 1RM; LOW+) appears to be an adequate stimulus for optimizing 1RM gains. In line with these findings, previous research reported that resistance exercise at low resistances of 40-65% of 1RM equally increased 1RM as resistance exercise at high resistances of 75-85% of 1RM (72,120,146,148).

2.1.2.2. Muscular and functional adaptations to high- and low-resistance exercise in older adults

In our intervention study in older adults, we investigated whether 12 weeks of high-repetition low-resistance exercise (LOW and LOW+) would be similarly effective in achieving gains in muscle volume, muscle strength, force-velocity characteristics, and functional performance as traditional high-resistance exercise (HIGH). This question is highly relevant as lower-resistance exercise might be more suitable for older adults (see chapter 2.3 of the introduction).

All training groups demonstrated similar and significant gains in muscle volume (2.4-3.2%), irrespective of the resistance used during training. These results are in line with previous research in young adults showing that low-resistance exercise, as long as maximal effort is reached, can induce comparable hypertrophic responses as high-resistance exercise (101,111). Thus, muscle hypertrophy can occur without high resistance and the focus on external resistance as a crucial factor in muscle hypertrophy is too simplistic and inappropriate (111).

As typically found in previous research, gains in muscle strength exceeded gains in muscle volume in all groups. This finding stresses the importance of neural mechanisms underlying strength adaptations. Training-induced gains on 1RM and local muscular endurance, tests performed on the same equipment as the training sessions, seem to support the 'repetition maximum continuum' (see chapter 2.2.1 in the introduction) (108) by suggesting that low-repetition high-resistance training (HIGH) favors strength adaptations and high-repetition low-resistance training (LOW) increases muscular endurance. The uniquely designed mixed low-resistance exercise

protocol (LOW+) seems to offer the best out of both worlds by demonstrating a 1RM gain equivalent to HIGH and by increasing local muscular endurance. Importantly, without having to train at high external resistances.

One repetition maximum strength gains are highly specific to the trained movement. If these gains do not result in a higher maximal strength generating capacity of the muscle outside of the trained movement or in functional performance improvements, their relevance can be questioned. Our study underscores the value of our exercise protocols in healthy, well-functioning older adults by additionally showing increases in isometric and isokinetic strength and in functional performance. Interestingly, all exercise protocols seemed equally effective on these parameters, hereby putting into perspective the lower 1RM gain in LOW. Only on isokinetic strength at high speed (240°/s) and on maximal gait speed, HIGH appeared to be beneficial over LOW and LOW+.

A meta-analysis of Peterson et al. on resistance exercise for muscular strength in older adults (116) reported pooled estimates of mean 1RM gains from baseline to post-intervention for leg press (32 studies) and leg extension (28 studies). These pooled estimates were 31.63kg (29%) for leg press and 12.08kg (33%) for leg extension. The percent changes on 1RM in HIGH and LOW+ (*paper 3*) were comparable to these estimates for leg extension (30.0% and 29.7% respectively) and even higher than these estimates for leg press (46.2% and 39.2% respectively). Aside from 1RM strength gains, training-induced gains, ranging from 2.4 to 3.2% for muscle volume, from 3.3 to 11.8% for isometric strength and from 1.9 to 5.7% for isokinetic strength at low speed, appeared rather low compared to gains previously reported in older adults (24,44,53,72,75). Based on the 1RM gains, it seems that the training stimulus of our exercise protocols was sufficiently high and it is not clear why the effect on muscle volume and isometric and isokinetic strength was limited, even though it was significant. Inadequate protein consumption might be part of the explanation (see chapter 2.2.3.4 of the discussion).

Even though gains were limited, when comparing these gains to the annual age-related losses in muscle mass (±1%) (38,95,102) and muscle strength (±2-4%) (37,102), we can conclude that, in a training period as short as 12 weeks, our exercise protocols are capable of compensating for an age-related loss of about 1 to 3 years. It should be noted that initial improvements during the first months of resistance training in previously untrained older adults tend to be large probably due to neural adaptations, but that they level off as training continues over several months (103,126).

In conclusion, high- and low-resistance exercise protocols until muscle failure are equally able to counteract the age-related declines in muscle mass, basic muscle strength (isometric and isokinetic strength at low speed) and functional performance in older adults. Our study points out that it is time to re-think or at least nuance the high-resistance training philosophy that has gone unchallenged for decades. It is clear that there are different ways to achieve the desired training goal. However, it should be recognized that high-resistance exercise appears to be beneficial over low-resistance exercise for improving isokinetic strength at high speeds.

2.1.2.3. Underlying mechanisms of adaptations

Hypertrophic adaptations and its underlying mechanisms

As a muscle is overloaded from increased mechanical work during resistance exercise, muscle protein synthesis is increased in the post-exercise recovery period. Over time, this net positive balance between muscle protein synthesis and muscle protein breakdown leads to skeletal muscle hypertrophy (94,157).

Type II muscle fibers are known to be more responsive to hypertrophy than type I muscle fibers (142). As muscle fibers will only adapt to exercise if they are activated during exercise, training to muscular failure is theoretically more beneficial simply because doing so would ensure recruitment of as many motor units and muscle fibers as possible (46). A common misconception has always been that high external resistances are necessary in order to recruit and fatigue the larger motor units that innervate type II muscle fibers (26). However, evidence shows that smaller motor units (type I fibers) are recruited first, and when these motor units are fatigued, the larger motor units (type II fibers) are recruited (see Henneman's size principle, chapter 2.4 of the introduction) (46,66). To activate as much motor units as possible within a muscle group, and thus to recruit all the available muscle fibers to stimulate them to adapt to training, it is not the external resistance that is the primary factor but rather the requirement to train until muscular failure (26,46). Previous investigators already suggested that the extent of muscle protein synthesis after resistance exercise is not entirely dependent on the external resistance, but appears to be related to training volume and most likely to the extent of type II fiber recruitment (20).

Based on this abovementioned theory, we hypothesized that training with either high or low resistances until muscular failure would result in the activation of a similar amount of muscle fibers, hereby leading to an equivalent extent of hypertrophy. The results of *paper 3* support our hypothesis and most of the research to date (101,111), showing that high- and low-resistance

exercise induces equivalent hypertrophy when training is performed until muscular failure and training volumes are matched.

However, we acknowledge that we can only assume the activation of a similar amount of muscle fibers based on our study. It is very difficult to experimentally verify motor unit recruitment strategies during voluntary dynamic contractions (101). We cannot exclude that differences in voluntary muscle activation at fatigue occurred between our training protocols. Some studies suggested that sustained contractions at low resistance tend to cause more central fatigue, while protocols at higher resistances tend to induce more peripheral fatigue (or fatigue within the muscle itself) (109,156). However, these studies investigated sustained isometric contractions, contrary to repetitive dynamic contractions as in our training protocol. Kay et al. and Babault et al. already stated that neuromuscular fatigue appears to develop differently, depending on the muscular action modes (4,85). Our findings as well as those of Mitchell et al. (101) do show similar hypertrophic gains of the whole muscle and of type I and II fibers with high (80% of 1RM) or low (30% of 1RM) resistances, which is at least suggestive of the recruitment of an equivalent extent of both fiber types.

Neural mechanisms underlying muscle function adaptations

Despite evidence that suggests a significant role for neural mechanisms in the adaptations associated with strength training, there has been less progress on identifying the specific mechanisms responsible for these adaptations (40). The increases in muscle function following resistance exercise in **paper 3** are proposed to be caused by neural in addition to morphological adaptations in the muscle. First, **paper 3** showed disproportionately larger increases in muscle strength than size. Second, while equivalent hypertrophy was found in all training groups, some differences between groups did occur on muscle function gains. Third, the increases in 1RM were much greater than the increase in isometric or isokinetic strength, suggesting neural adaptations that are specific to the task.

In contrast with morphological adaptations, considerable debate exists about the nature of the neural changes that accompany strength training. Enhanced agonist muscle activation after strength training is often reported to be due to increased motor unit recruitment or firing frequency, decreased co-contraction of antagonists and increased motor unit synchronization. Although strength training seems to improve synchronization, it is not yet clear how motor unit synchronization contributes to muscular strength enhancement (40,50,55).

Early increases in muscle strength at the onset of strength training are possibly caused by increased motor unit firing rates (55,84). Thus, in **paper 3**, the significant gains in 1RM after 4

weeks of training might be, at least partially, due to increased motor unit firing rates. Previous research also showed that the neural mechanism producing the early increase in motor unit firing rate is moderated as other adaptations begin. Reductions in antagonist co-activation might be a possible mechanism for changes seen after initial adaptations (25,55). During more complex multi-joint movements, the level of antagonist activation may be greater, perhaps providing more opportunity for a reduction in co-activation with training (50). This may be part of the explanation of the greater increases in leg press 1RM than in leg extension 1RM. In addition, an improved coordination between agonist muscles may also contribute to the greater gain in leg press 1RM. In *paper 3*, the gain in 1RM was higher in both HIGH and LOW+ as compared to LOW. The use of high resistances (HIGH) or the increase in resistance after a fatiguing protocol at low-resistance (LOW+) may have resulted in a greater extent of the abovementioned neural adaptations, though very specific to the trained movement, than low-resistance exercise (LOW).

At the onset of rapid muscle contractions, discharge doublets (interspike interval < 10ms) may be observed in the firing pattern of single motor units (1,147). It is possible that the firing of discharge doublets serves to enhance the rate of force development, which in turn plays an important role in the ability to reach a higher force during fast movements (1). An elevated incidence of discharge doublets in the firing pattern of motor units may represent a mechanism responsible for the beneficial gains in isokinetic strength at high speed and concomitant in maximal gait speed after high-resistance exercise (HIGH) compared to low-resistance exercise (LOW or LOW+). A decrease in antagonist co-activation at pre-movement-time might also pose a potential mechanism for this benefit of HIGH at high speed. Previous research indicated that elderly demonstrate higher antagonist muscle co-activation than young adults at pre-movement-time during a simple reaction time test. This early phase antagonist co-activation is assumed to increase the time necessary to complete the movement task (9). It might thus contribute to the age-related slowing of human motor performance and a decrease in antagonist co-activation might lead to better performances on high-speed strength tests.

To conclude, it is clear that neural adaptations significantly contribute to the muscle function gains observed in *paper 3*. Although hypertrophic adaptations appear to be similar after high- and low-resistance exercise until muscular failure, it seems that some neural adaptations are in favor of high-resistance exercise. However, as neural adaptations were not measured in our study, the exact neural mechanisms underlying muscle function adaptations remain highly speculative.

2.1.2.4. Long-term exercise adherence and residual muscular and functional adaptations at follow-up

Long-term exercise adherence

In order to determine the effectiveness of high- and low-resistance exercise protocols in counteracting age-related muscular and functional declines, it is important to explore the long-term exercise adherence among older adults. Taking into account the psychological and motivational factors associated with high- and low-resistance exercise protocols might increase our understanding of long-term exercise adherence. It can be hypothesized that if older persons experience more pleasure when training at a certain degree of external resistance, their long-term adherence would increase, hereby limiting detraining effects.

Although we might expect that older adults would be less motivated or less willing to engage in high- compared to low-resistance exercise, the findings of *paper 4* do not support this expectation. Participants appeared to be highly motivated before, during, and after the training intervention, with no difference between training groups. The high scores on autonomous motivation and self-efficacy might have been influenced by a selection bias (see chapter 2.2.2.1 of the discussion). In addition, a potential ceiling effect in motivation might have masked group differences.

Contradictory to the expectations that a high degree of self-determination and self-efficacy for participation in resistance exercise would result in the long-term persistence of exercise behavior (129), only a minority continued strength exercising after cessation of the intervention: 16.7% in HIGH, 21.1% in LOW+, and 11.1% in LOW (no difference between groups). This finding corresponds with the experience in previous intervention studies, in which most participants quit exercising as soon as the structured and guided intervention ends, even though they appear to enjoy exercise participation (86,112). This discrepancy between the high degree of motivation and the low long-term adherence might be partly explained by an over-reporting of the motivation and self-efficacy for participation in exercise, as people tend to be give socially desirable answers to questionnaires (106). However, it also stresses the importance to focus on older adults' perceived barriers for continuation of resistance exercise after cessation of an intervention.

The following obstacles were most frequently given in our study: perceived lack of time, seasonal reasons, being more interested in other physical activities and financial cost of subscription to the fitness center. The reported barrier of perceived lack of time suggests that subjects were not able to incorporate resistance exercise in their weekly schedule without professional assistance. In our resistance exercise intervention, all exercise sessions were closely supervised by a qualified fitness instructor in order to strictly control the external resistance, the number of repetitions, the

movement speed and the movement techniques. This high degree of supervision and guidance was necessary to control for confounding factors in the initial comparison between high- and low-resistance exercise training, but it did not at all stimulate autonomy in our participants. The abrupt ending of the provided structure and guidance might have negatively influenced long-term adherence. Suddenly, participants had to take the first step to prolonged resistance training by subscribing to a fitness center, which would also provide supervision, but on a less intensive level. It might be interesting in future resistance exercise interventions to consider an approach in which supervision gradually evolves from 'fitness instruction' to 'fitness coaching'. More in specific, a high degree of instructor's supervision is necessary to ensure safety, to adjust movement techniques and to monitor training intensity during the first month of resistance exercise participation. After this initial phase, individuals might need less intensive guidance during exercise than provided our study, meaning that instructors do not need to control every movement at each session. Of course, regular face-to-face contact with instructors remains important to progressively adapt training programs according to the desired training goals. However, individuals should also be coached to monitor and plan their own training sessions and to overcome possible barriers for adherence. This might stimulate autonomy, making individuals less dependent on the fitness instructor. It can be hypothesized that such an approach would positively influence long-term adherence.

In **paper 4**, HIGH counted more non-compliers at follow-up tests than LOW and LOW+ (7 versus 2 and 1, respectively), although no differences in motivation and long-term exercise adherence were found between groups. Even though no adverse events were reported during the intervention and the reasons for non-compliance could not be clearly linked to the high resistances used during the intervention, future research should investigate this finding more into detail. In addition, fewer participants in HIGH than in LOW and LOW+ indicated that they were planning to participate in strength training at a fitness center in the future, though not significantly different. This simple question represents an intention rather than an actual behavior. Considering that the actual long-term adherence did not differ after high- or low-resistance exercise, it cannot be claimed that low-resistance exercise is preferred over high-resistance exercise. However, these results do provide interesting issues for future research.

Residual muscular and functional adaptations at follow-up

To evaluate and compare the long-term effectiveness of a short-term high- and low-resistance exercise intervention on muscular and functional adaptations, we decided not to apply a strict detraining period after the intervention. If one of the exercise protocols would result in a higher

number of exercise adherers hereby limiting detraining effects, we wanted to integrate this finding in our evaluation instead of controlling for it as a confounding factor.

It is widely reported that resistance exercise adaptations are reversed with cessation of training. Our data are consistent with previous research investigating the effects of detraining on muscle volume and strength in older adults. At follow-up, initial hypertrophic gains were no longer significant in our study. In line with these findings, the majority of studies that have applied a detraining period of approximately the same duration as the current study (24 to 31 weeks) found muscle volume to return to pre-training values (61,76,144). In *paper 4*, the loss of muscle volume 24 weeks after the intervention had ended, was irrespective of prior training resistance. This result contradicts Tokmakidis et al. (143), who found greater loss but also greater retention in mid-thigh cross-sectional area after high- (80% of 1RM) as compared to moderate-resistance exercise (60% of 1RM). However, they also found greater post-intervention hypertrophy, probably because exercise protocols were not designed to reach muscular failure. If exercises are not performed until failure, high external resistances are preferred for activation of the type II fibers, which are known to be more responsive to hypertrophy (142).

Although a reversal in hypertrophy occurred in the current study, muscle strength gains were partly preserved in all groups. In other words, with the same amount of muscle volume subjects were able to generate higher levels of strength at follow-up compared to baseline. These results are consistent with former research showing that exercise-induced adaptations in muscle strength are maintained longer than muscle hypertrophy after training cessation (14,32,61,67,76,86,144). The discrepancy between declines in muscle mass and strength again points out the importance of neural mechanisms in the development of muscle force.

With regard to declines in muscle strength, a distinction should be made between exercise-specific muscle strength (1RM), isometric strength, isokinetic strength at low speed and isokinetic strength at high speed. First, gains in isometric strength were longer preserved after cessation of the intervention than gains in isokinetic strength at low or high speed. In agreement with previous research, this finding indicates a more rapid decline in the ability to develop force quickly than in the ability to develop maximum force once the resistance exercise intervention had ended (98). The beneficial neural adaptations of high- over low-resistance exercise with regard to high-speed strength seemed no longer apparent at follow-up. Second, differences in initial 1RM gains between LOW and both HIGH and LOW+ were still preserved at follow-up. In the longer-term, high-resistance exercise and mixed low-resistance exercise are similarly more effective than low-resistance exercise for improving exercise-specific muscle strength. This longer-term benefit of HIGH and LOW+ over LOW was very specific to the trained movements and it did not coincide

with a higher maximal strength generating capacity, greater hypertrophy or greater functional improvements.

As reported earlier, only a minority of older adults continued strength exercising after cessation of the intervention (9 out of 56 participants). Those who did continue (or restart) resistance exercise after cessation of the intervention, reduced their training frequency to on average 1.3 sessions per week (range from 0.9 to 2.7). Trappe and coworkers already stated that resistance training one day a week can be sufficient to maintain muscle strength and volume in older men after a 12-week progressive resistance training program (144). In the current study, participants who still trained on the leg press or leg extension in their latest training program performed on average 2 sets of 17 repetitions at 38% of 1RM and 2 sets of 16 repetitions at 41% of 1RM respectively. These training intensities are markedly lower than the intensities in the initial training intervention in *paper 3*. On the one hand, the lower intensities might be caused by the prudence of fitness instructors to not overburden the musculoskeletal system of older adults. On the other hand, older adults might have self-selected their resistances for performing a fixed number of repetitions. The resistances were indeed very similar to the self-selected resistance (42% of 1RM) for performing 10 to 15 repetitions by apparently healthy older women in previous investigations (41,48). Although a self-selection strategy can enhance intrinsic motivation because of a greater perception of autonomy (41), lack of progress because of inappropriate intensity selection may also undermine an individual's motivation (48). Hence, it is crucial for fitness instructors to closely supervise training intensity and individual's perceived effort.

Although the average training frequency and intensity was low compared to the initial resistance exercise intervention, it appeared sufficient to retain (at least part of) the hypertrophic gains (from baseline to follow-up: + 1.7%, P = 0.032), the isometric strength gain (from baseline to follow-up: +12.7%, P = 0.001) and the isokinetic strength gain at 60°/s (from baseline to follow-up: +7.0%, P = 0.072) for at least 24 weeks after the end of the intervention. However, in the overall analyses of *paper 4*, participants who continued and those who ceased strengthening exercise were combined. Even though analyses did also include long-term exercise adherers, detraining effects were comparable to previous research and did not reveal differences between groups, probably because of the limited number of exercise adherers.

In conclusion, our data suggest the importance of long-term maintenance of resistance exercise behavior for increasing or maintaining muscle mass and muscle function, but indicate that various aspects of muscle strength and functional performance remain elevated for several months after the end of a supervised training intervention. When compared at follow-up, low-resistance exercise until muscle failure appears to be as effective as high-resistance exercise for maintaining training-induced neuromuscular and functional adaptations. These findings underline the value of low-resistance exercise protocols in older age as a potential alternative to high-resistance exercise or as variation in training approaches. However, long-term maintenance of resistance exercise behavior remains a challenge among older adults.

2.1.2.5. Practical recommendations for resistance exercise in older adults

Facilitating initial involvement in resistance exercise

Although the benefits of resistance exercise in older adults are well-documented (54), 87% of older adults have at least one barrier to prohibit exercise participation (110). To overcome barriers for resistance exercise participation in older adults, the following domains should receive attention (135).

(1) *Knowledge and the role of healthcare professionals*. The lack of knowledge and understanding of the detrimental effects of sarcopenia on functional performance and of the potential benefits of resistance exercise is a relevant barrier in older adults. Nowadays, the majority of older adults believes that the maintenance of a physically active lifestyle, without systematic training, is sufficient to prevent functional dependence as a consequence of aging. However, research contradicts this common believe (5) and points out the necessity of participation in resistance exercise (51,87,150). Increasing the awareness of sarcopenia might influence an older adult's motives to engage in resistance exercise. A first step in increasing the awareness is reaching a consensus definition of sarcopenia. This would allow for healthcare systems to acknowledge sarcopenia as a treat to functional independence of older adults. In the context of preventive medicine, healthcare systems should provide a framework for financial support for older adults at risk for sarcopenia who subscribe to a fitness center. In addition, physicians play a key role in promoting exercise behavior among older adults, because older adults generally respect their physician's advice.

(2) *Exercise facilities and supervision*. Nowadays, fitness facilities become more and more accessible to older adults. However, older adults lived through a time period when resistance exercise was not valued for health-related purposes, so they are still rather

reserved with entering a fitness center. There is an urgent need for the design of resistance exercise programs adapted to older adults, which are supervised by qualified fitness instructors. Implementing low-resistance strengthening exercise may be an important step towards resistance exercise that is more accessible to older adults. Also, it is important to keep in mind that social support might be crucial in this age-group. It might be an interesting approach to consider resistance exercise group sessions for older adults.

Proper periodization design and variation in training approaches to stimulate long-term adherence in older adults

Different training periodization plans have been suggested in literature. There is currently no evidence that one periodized plan or workout schedule is necessarily most favorable. What appears to be most important is the physical and mental readiness for each workout (46).

As generally accepted for novice trainees of any age, prescription of resistance exercise should include a '*familiarization*' period of about 4 weeks, in which training intensity is kept rather low with exercise sessions performed 2 times a week (115). This 'familiarization' period allows for a gradual adaptation of the contractile tissues, prepares the body for more intense strength training stimuli and enhances self-perceived competence. The need for competence is, next to the need for relatedness and for autonomy, one of three basic psychological needs that are essential for an individual's growth, integrity and well-being (129). Perceiving satisfactory levels of these needs may be necessary to increase an individual's intrinsic motivation to exercise behavior and may enhance long-term maintenance of exercise behavior.

In the familiarization period, training intensity should be gradually increased so that the body and mind are prepared for the next training cycle targeting *hypertrophy and strength gains*. In this training cycle, resistance exercise should be planned 2-3 times a week and should be performed until muscular failure, which is hypothesized to optimize motor unit recruitment and the hypertrophic response (see chapter 2.4 of the introduction and chapter 2.1.2.3 of the discussion). With proper supervision, both high- and low-resistance exercise protocols appear to be safe and feasible in older adults and effective for inducing hypertrophy. High-repetition low-resistance protocols as alternative to high-resistance exercise were suggested in ***paper 3***. Of course, these protocols need some fine-tuning depending on the type of exercise or muscle groups used.

It is clear that there are different ways to achieve hypertrophy, but the question is when to use high or (mixed) low resistances in strengthening exercise. A first consideration is whether or not an older adult suffers from contra-indications for the use of high external resistances. To date, it is

not clear what these contraindications are and further research in this domain is necessary. A higher dropout rate due to severe knee pain has been reported in high-resistance exercise as compared to low-resistance exercise in patients with knee osteoarthritis (78). The use of high resistances might also be contraindicated in the immediate rehabilitation phase following surgery or in persons with tendinopathy. In these cases, low-resistance exercise is recommended. If no contra-indications are reported, it might be interesting from a motivational point of view to let the older adults choose for themselves between high-resistance low-repetition and low-resistance high-repetition exercise. This would increase feelings of autonomy and would likely result in more pleasure during exercise, hereby facilitating maintenance of exercise behavior. To further increase pleasure during exercise, another interesting strategy may be to vary training resistances over time. For fitness instructors, it might be interesting to keep in mind that mixed low-resistance exercise is superior to low-resistance exercise for 1RM strength gains and that it might be beneficial over high-resistance exercise for improving muscular endurance. Although training to failure does appear beneficial for hypertrophic gains, its use should be limited in time to avoid overtraining and psychological burnout (134). A hypertrophy-oriented training period of 12 to 16 weeks may be sufficient in older adults.

Even though hypertrophy-oriented protocols appear to benefit functional performance in older adults, high-speed *power* training has been shown to favor functional adaptations (145). Once the muscles have been toughened and prepared for the added stress of power training, it might be interesting to include exercises at moderate resistances and high speeds, especially for the knee extensors. Power training is considered less exhaustive than hypertrophy-oriented training (131), but requires a high level of control over body movements. Therefore, the overall safety has yet to be determined in older adults (145). In this regard, gradually including more *functionally-based* exercises in a strength training protocol might be an alternative when power training is not feasible.

Paper 4 suggests the importance of long-term maintenance of resistance exercise behavior for increasing or maintaining muscle mass and muscle function in older adults. The World Health Organization recommends muscle-strengthening activities on 2 or more days a week in adults aged 65 and older (154). Although a year-round resistance exercise training frequency of 2-3 times weekly might be ideal, it might also be interesting to alternate a period of more intense resistance exercise, such as a 6-month training cycle of *familiarization – hypertrophy and strength gains – power and functionally-based exercises*, with a less intense period aiming at maintaining training adaptations. The minimum required dose of resistance exercise still needs to be investigated more into detail. However, it has already been shown that resistance exercise one

day a week for 24 weeks or 32 weeks can be sufficient to maintain hypertrophy and muscle strength gains after a 12-week or 16-week resistance training program (14,144).

At this point, it might also be worthwhile to investigate the role of aerobic exercise in maintaining these training adaptations. Especially since the older adults who quit strengthening exercise after the end of the intervention in *paper 4* mentioned that they were more interested in other types of physical activities. Systematic aerobic exercise might delay age-related declines in muscle mass and function (33,51). It has even been shown to improve muscle function (63) and to acutely (136) and chronically (137) stimulate protein synthesis in older adults, which is favorable for skeletal muscle growth. However, resistance exercise is a far more powerful stimulus for muscle hypertrophy and strength gain than aerobic exercise (17). Several reviews on sarcopenia agree that resistance exercise training remains the cornerstone of management for sarcopenia (2,21,128). However, to maintain what has already been trained in resistance exercise, systematic aerobic exercise might be valuable.

2.2. Methodological considerations and suggestions for future research

2.2.1. Study design

A limitation of *paper 1* is the cross-sectional study design. Because muscle mass, muscle strength and force-velocity characteristics were measured at the same time as functional performance, causal relationships could not be determined. In other words, we cannot conclude based on our findings that low muscle function causes functional limitations. However, Rantanen et al. already showed that, in middle-aged men, handgrip strength was highly predictive of functional limitations and disability 25 years later (124). In addition, findings of the Women's Health and Aging Study demonstrated that older women were more likely to develop new walking disability over a 3-year course if they suffered from low knee extension strength at baseline (123). Supporting these findings, Hicks et al. reported that older adults with low muscle strength or low muscle power were more likely to develop mobility disability (69). Although our cross-sectional study design was unable to determine causation, longitudinal research already confirmed the temporal sequence of the cause-and-effect relationship between muscle function and functional performance.

A limitation of *paper 2* is the short duration of the intervention (9 weeks). The choice for 9 weeks was mainly a practical one, but may have contributed to the small post-intervention improvements on some aspects of muscle strength. However, it is generally accepted that neuromuscular gains already occur in an early phase of a strength training program, even after

(less than) 4 weeks of training (24,47). The 9-week duration of the intervention was sufficient to induce and compare early gains in muscle strength and force-velocity characteristics.

In our resistance exercise intervention in older adults (***papers 3 and 4***), no strict detraining period was applied between post-intervention and follow-up measurements. This study design was chosen because it expands our knowledge on long-term exercise adherence and brings added value to the comparison of high- and low-resistance exercise training. We did not interfere in any way in training participation and training program designs so that the follow-up period would more closely resemble real-life situations. A minor disadvantage of this approach is that we were only able to retrieve limited information on exercise participation at follow-up. More specifically, we were able to trace which participants subscribed to a fitness center and when they had entered the fitness center for training purposes. However, we were not able to retrieve detailed information on program variables, such as choice of exercise, order of exercise, training intensity, training volume and rest periods between sets and exercises. Only the overview of their latest exercise program, including choice of resistance exercises, the number of repetitions, and the loads (in kg), was retrieved. Because of this lack of in-depth information on exercise participation during follow-up, we only compared whether the number of participants who continued resistance exercise after posttests differed between HIGH, LOW and LOW+.

2.2.2. Study population

2.2.2.1. Sample representativeness

The main objective of this doctoral thesis was to examine whether low-resistance exercise is similarly effective as high-resistance exercise for inducing muscular and functional adaptations in older adults. As it is imperative to implement exercise interventions before functional limitations and disability occur, we chose to focus on healthy community-dwelling older adults in ***papers 3 and 4***. After all, every human being is exposed to the age-related phenomenon of sarcopenia (27). Before implementing interventions, we first wanted to increase our understanding on the relative contribution of muscle mass, muscle strength and force-velocity components to functional performance in elderly individuals. To be able to identify cutpoints below which functional limitations started to occur, we needed to recruit individuals who were close to or just entering the early stages of functional limitations (***paper 1***). That is why we decided to recruit institutionalized elderly, but also elderly individuals in assisted living facilities and cloistered communities. This recruitment strategy resulted in a heterogeneous sample of older individuals across a broad range of the functional performance spectrum, in line with our study aim. It should

be noted that only women were included in ***paper 1***. Results cannot be applied to men without further research. However, although earlier studies suggest that sex differences might exist in the relationship between muscle characteristics and functional performance, they do point out the importance of velocity in addition to strength in both sexes (11,36,133).

An inevitable limitation in research studies is that participation always relies on voluntarism of individuals. Individuals who were willing to participate in resistance exercise programs (***paper 2-4***) or in muscle strength and functional performance measurements (***paper 1***) were probably highly motivated to improve muscle mass and function or at least very interested to know their current level of performance. Combined with the stringent exclusion criteria for maximal strength testing, voluntary participation might have resulted in a relatively healthy, active and motivated study sample. Baseline motivation and self-efficacy to engage in resistance exercise were indeed high in ***paper 4***. This favorable motivational profile of the participants might have contributed to the finding that no dropout was reported during the resistance exercise interventions in either young or older adults. Although we should recognize that voluntary participation and the exclusion criteria might have resulted in a study sample that is not representative for the overall population, the study sample of ***papers 3 and 4*** can be considered representative for an older population who is willing and able to engage in our resistance exercise protocols. It would be unethical to force individuals to participate in scientific research or to ignore contraindications for participation.

According to the National Institute of Statistics (43), 53.7% of the Flemish population aged 60-80 years and 49.8% of the Flemish population aged 20-30 years is female. The gender distribution in ***papers 3 and 4***, with 53.6% of participants being female, was thus very similar to the overall Flemish population aged 60-80 years. In ***paper 2***, women (41.7%) were underrepresented. This might be due to the probability that young men are more motivated to engage in resistance exercise to strengthen or build upper leg muscles than young women.

As a final point, it should be noted that the study sample in ***paper 2*** was limited to students or young researchers of KU Leuven due to practical reasons. Thus, the educational level of this sample was rather high.

2.2.2.2. Sample size

As ***paper 3*** reported no differences in gains on most outcome variables between HIGH, LOW and LOW+, one might question whether the sample size was sufficiently large to detect differences between groups. Therefore, we investigated the possibility of a type II error. This seems especially

relevant for evaluating the hypertrophic gains in our study, given that high-resistance exercise is claimed to maximize muscle hypertrophy (see chapter 2.2.2 in the introduction).

Previous research that evaluated the effects of high-resistance exercise over a similar duration with similar training volumes as HIGH reported gains in thigh cross-sectional area of 10-11% for the total muscles and 6-9% for the quadriceps muscle (24,53,83,152). Based on these data, we expected a hypertrophic gain of at least 6% in HIGH. We wanted to detect an effect size of 0.50 between HIGH and LOW as statistically significant. This means that if LOW would demonstrate a gain of about 4.5% compared to the expected gain of 6% in HIGH (SD for percent changes in muscle volume = 2.7, see *paper 3*), it should be marked as significantly different. In *paper 3*, the effect size between HIGH and LOW for percent changes in muscle volume was 0.30, and thus lower than the effect size that we wanted to detect as statistically significant. Therefore, we can rule out the possibility of a type II error. In addition, our sample size was comparable to or even higher as sample sizes in previous research comparing post-intervention effects of different resistance exercise protocols in older adults (12,65,72,146,148).

2.2.3. Methodology

2.2.3.1. Outcome measurements

Muscle volume

In *papers 1, 3 and 4*, muscle volume of the upper leg was measured by means of *computed tomography*. Like magnetic resonance imaging, CT is considered a criterion method for measuring body composition. It is capable of detecting small changes in soft tissue composition and is stated to be an ideal method for quantifying skeletal muscle composition in both cross-sectional and longitudinal studies (97). The CT-scan procedure and equipment used in *paper 1* were the same as the ones used in previous research in older adults (16). In a group of 12 older men (60-80 years), a high intraclass correlation coefficient (ICC) of 0.99 was found between test and retest (16). For *paper 3 and 4*, the newest CT-scanner of the University Hospital, a Siemens Somatom Definition Flash, and updated medical imaging software were used. This new procedure had the following benefits over the procedure used in *paper 1*. First, determination of the femur length and the anatomical midpoint of the femur as well as delineation of slices were fully computer-controlled in the new procedure, excluding all human delineation errors. When comparing femur lengths at pre- and posttest, a high ICC of 0.997 and only a small mean difference of 0.7mm was found. Second, the new equipment allowed for a greater thickness of slices (3 x 3mm in *paper 1* versus 1 x 10mm in *papers 3 and 4*). The computer-controlled delineation and the greater thickness of the

slices optimize the chances of overlap between slices in subsequent tests and consequently increase test-retest reliability. Due to financial limitations, we were not able to collect test-retest data of this new procedure. However, we re-analyzed baseline muscle volume data of 10 participants (5 men, 5 women) by re-running the baseline images through the computerized software. All values were exactly the same (in cm³, accurate to 8 decimals). At least, we can rule out that the computer interprets the same images differently on separate occasions. Possible errors that we were not able to capture in this re-analysis are related to the positioning of the legs of the participants and to the influence of fluid shifts on muscle volume (13). To limit these errors to a minimum, leg positioning and leg compression were standardized.

Muscle strength and force-velocity characteristics

Isokinetic dynamometry is considered the golden standard for measuring muscle strength in both clinical and research settings (88). Therefore, the *Biodex Medical System 3® dynamometer* was used in all four papers. The protocol consisted of knee-extension measurements in the isometric, isokinetic and isoinertial (isotonic) mode. Intra-observer reliability of the protocol was tested in 19 community-dwelling older adults aged 65 years and above (88). Intraclass correlation coefficients were high for isometric (range 0.90-0.99) and isokinetic (range 0.96-0.97) strength measurements and good for speed of movement measurements (range 0.83-0.89). We can state that the Biodex dynamometer is a reliable tool for assessing muscle strength and force-velocity characteristics in older adults and the extensive protocol can be considered a methodological strength of this doctoral thesis.

In addition, *one repetition maximum* (1RM) strength tests were included in the intervention studies (***paper 2-4***) for measuring strength gains and for evaluating training intensities. One repetition maximum strength tests are performed on isotonic devices, which apply a constant resistance to the muscle and allow for variations in speed during movement. As activities of daily living also include accelerations and decelerations of a constant mass of the body, concentric and eccentric phases, isotonic strength tests have been suggested to be more closely related to real-life situations than isometric (static) or isokinetic (constant speed) strength tests (34).

Direct assessments of 1RM involve a trial and error procedure in which progressively heavier weights are lifted until the weight exceeds the subject's ability (18). The pitfalls of this procedure are the potential risk of injury in older adults (although not often reported) (119) and, more importantly, the fact that it is very time-consuming. Chapman et al. reported that it can take about 20min to complete a direct assessment of 1RM for one individual (29). As we were limited

to only one test leader, we decided to use a more time-efficient estimation method for evaluating leg extension 1RM.

Previous research has shown that the percentage of 1RM can be estimated from the number of repetitions (nRM) that can be performed with a given resistance (35). A logarithmic regression formula, based on the Oddvar Holten diagram (68), had already been shown to be appropriate for the leg extension exercise (data not published). Baseline comparison of the direct and estimation method in a group of 36 young adults (**paper 2**) showed a high intraclass correlation coefficient of 0.99 and only a small overestimation of 1.27kg. Given that direct assessments of 1RM are subject to underestimation because of fatigue caused by multiple trials (28), this small overestimation of our estimate might be negligible.

Nevertheless, we should recognize that the use of such estimate can be considered a methodological limitation. There are mixed reports in previous research as to the influence of training experience in estimating 1RM from repetitions to fatigue at submaximal weight (29,70). We cannot exclude that 1RM at posttests might have been more subjected to overestimation because of improvements in local muscular endurance. However, the finding that leg press 1RM, which was assessed using a direct method, followed a similar trajectory over a 12-week intervention period as leg extension 1RM is reassuring (**paper 3**). It can also be argued that our estimate for leg extension 1RM seems to recapitulate local muscular endurance measured on the same equipment. However, the average number of repetitions performed during both tests significantly differed (10.7 for 1RM versus 16.7 for endurance; $P < 0.001$). In addition, no significant correlation was found between leg extension 1RM (kg) and local muscular endurance (number of repetitions) (baseline $r = -0.041$; post $r = 0.150$; $P > 0.05$). Likewise, no significant correlation was found between percent changes from baseline to post for 1RM and local muscular endurance ($r = -0.153$; $P = 0.260$). These data seem to suggest that the two leg extension tests measure different aspects of muscular performance.

Physical frailty

In recent years, the Short Physical Performance Battery (SPPB) has been recommended by an international working group for use as a functional outcome measure in frail older adults (153). Since then, it has been widely used in clinical and research settings. The SPPB is a composite of a balance, walking and chair stand test (59) and has been shown to be reliable (113), predictive of adverse outcomes (58,59,127), and sensitive to change (113).

In **paper 1**, we decided to use the *modified Physical Performance Test* (mPPT) as functional outcome measure instead of the SPPB. The mPPT, as described by Brown et al. (19), combines the

balance and chair stand test of the SPPB (59) with the physical performance test of Reuben and Siu (125). It covers a broader range of functional items than the SPPB by also including upper extremity performance. Test-retest reliability in a population of elderly ≥ 78 years was 0.96 (15). As Brown et al. had already defined categories based the summary mPPT-score, we decided to use these categories and the corresponding terminology *'physical frailty'* in ***paper 1***.

It should be noted that we simply interpreted the term 'physical frailty' as 'functionally limited', while a consensus group recently defined 'physical frailty' as 'a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death' (104). To avoid confusion in the future, it would be best to only use the term physical frailty according to its recent consensus definition.

2.2.3.2. Finder and verification procedure for cutpoints

The cutpoints defined in ***paper 1*** demand replication. Typically, when the objective is to identify prognostic cutpoints, two samples - finder and verification - are used. For reasons related to the sample size, we decided not to divide our sample size in a finder and verification group in ***paper 1***. However, we did explore the 'finder and verification' procedure. When randomly selecting a finder group (±2/3 of the cases), both threshold values remained quite similar to the values obtained from the total study sample (unloaded speed of movement (SoM) = 360°/s versus 350°/s, isometric strength ($PT_{stat90°}$) = 1.47Nm/kg versus 1.46Nm/kg). Sensitivity and specificity were 79% and 71% for SoM, and 69% and 81% for $PT_{stat90°}$ respectively. The verification group using the remaining 1/3 showed that 89% to 100% of the women were correctly identified as being mildly frail and 62% as being not frail, respectively. The fact that we were able to confirm our findings by the 'finder and verification' method is reassuring. Nevertheless, we do acknowledge that our findings demand replication in a different group of older women.

2.2.3.3. Training volume

When comparing muscular and functional adaptations between resistance exercise protocols, one should take into account the volume of work (sets x repetitions per set x % resistance) performed during training. Increasing the number of sets in resistance exercise programs might result in greater hypertrophy and strength gains in both trained and untrained individuals (92,93).

In ***paper 2***, different exercise protocols were designed to obtain different combinations for levels of effort and external resistance within a similar number of repetitions (10-12): HI_{max} with high resistance and attaining maximal effort; LO_{max} with low resistance immediately after an intense

fatiguing protocol also attaining maximal effort; and LO with the same low resistance as LO_{max} but not attaining maximal effort. This approach inevitably led to a higher training volume for LO_{max}, which might have influenced the beneficial effect of LO_{max} over HI_{max} on isokinetic strength and speed of movement.

Therefore, the resistance exercise protocols in **_papers 3 and 4_** were designed to be equal in training volume. At the end of the training intervention, average training volume per session was calculated and compared between groups. It appeared to be higher in LOW than in both HIGH and LOW+. This difference in training volume between groups was probably a consequence of the strategy used to adjust training resistance over the training period. If maximal effort was not achieved within the prescribed number of repetitions, external resistance was increased for the next training session. This approach led to a higher external resistance in LOW than initially anticipated. Because of inter-individual differences in strength-endurance capacity, it is also difficult to predict the optimal training resistance in advance in high-repetition protocols.

A strategy often used to match training volumes between groups is to prescribe a fixed number of repetitions at a predetermined resistance (% 1RM). However, maximal effort would not have been reached in all participants when using this strategy. Based on the theoretical framework of the size principle (see chapter 2.4 of the introduction) and grounded by previous research, reaching maximal effort may be crucial to optimize hypertrophic gains in low-resistance exercise protocols (101).

Although recent work reported that low- and high-volume training induces similar adaptations in lower-body muscles after the first 12 weeks of training in older women (121), we corrected all analyses for average training volume as confounding factor to exclude potential interference.

2.2.3.4. Screening for malnutrition

In older individuals, malnutrition is a common phenomenon. Many older adults (almost 40% of people ≥70 years) do not consume sufficient amounts of dietary protein to meet the recommended dietary allowance (RDA) of protein (0.8g/kg/day) (73). Evidence-based recommendations even suggest that older adults should consume an average protein intake of 1.0-1.2g/kg/day in order to maintain physical function (6). Inadequate dietary protein intake may accelerate the age-related decline in skeletal muscle mass (151). Therefore, it is important to ensure that older people take in enough energy and protein, especially when engaged in a resistance exercise program. An adequate supply of amino acids is essential to produce muscle hypertrophy (157).

In our resistance exercise intervention of ***papers 3 and 4***, protein intake was not monitored, which can be considered a limitation of the study. Inadequate protein consumption could be part of the explanation for the modest improvements on muscle volume and on static and dynamic peak torques. A baseline screening for malnutrition by means of the Mini Nutritional Assessment (7), if necessary combined with a more detailed dietary record, would have been useful and should be included in future intervention studies. If the RDA of protein has not been met, dietary protein intake should be increased or protein supplementation immediately after an exercise session should be considered for optimizing hypertrophic gains (42).

Although not monitored in our study, the prevalence of malnutrition might have been limited in our study sample. A recent large-scaled study, including 4.507 older adults aged 65 years and older from 12 different countries, reported a low number of malnourished older adults (< 10%) in the community setting (82). Furthermore, if some of our participants were malnourished, they would have been randomized over the three intervention groups, so that malnutrition would not have had a major influence on between-group comparisons.

2.2.3.5. Absence of a no-treatment condition

In none of the intervention studies, a no-treatment condition was included. However, in ***paper 2***, one of the intervention arms trained at low resistance and low effort (LO), while the other two trained at maximal effort (HI_{max} and LO_{max}). Because HI_{max} and LO_{max} were expected to obtain greater gains in muscle strength and force-velocity characteristics than LO, the latter served as a control condition. As predicted, differences between LO and either HI_{max} or LO_{max} were found on most parameters.

The choice to not include a control condition in ***papers 3 and 4*** was based on the following reasons:

(1) The main aim of the study was to evaluate if low-resistance exercise is as effective as high-resistance exercise for inducing muscular and functional adaptations in older adults. In this regard, previous research already demonstrated that a high-resistance exercise condition is more effective than a no-treatment condition (16,52,132). If a low-resistance exercise condition appears to be as effective as a high-resistance exercise condition, it would most likely be superior to a no-treatment condition.

(2) We considered it unethical to assign older adults who are willing and motivated to engage in resistance exercise to a no-treatment condition. A more ethical approach would have been to include a waiting-list control condition. However, due to financial and

organizational limitations, we would not have been able to provide a 12-week supervised resistance exercise program to these subjects.

We acknowledge that the inclusion of a control condition would have given added value to **papers 3 and 4**, especially considering the small post-intervention improvements. However, we believe that all our intervention groups would be superior to a control group, based on data of previous resistance exercise intervention studies in our lab. Neither on isometric and isokinetic strength of the knee extensors nor on muscle volume of the upper leg were improvements detected in a control group of older adults after 12 weeks, 24 weeks or 1 year (16,126).

2.2.3.6. Responders versus non-responders

In **paper 3**, significant hypertrophy and strength gains were found in all training groups. However, we cannot ignore the fact that some older adults appear to exhibit no or only very limited hypertrophy or strength gain as response to an intensive 12-week resistance exercise intervention. One should be careful when interpreting the muscle volume data obtained at one particular portion of the thigh as training-induced muscle hypertrophy can also be non-uniform along the belly of the muscles and even between the individual components of the muscle groups (62,155).

The mean percent changes in muscle volume, ranging from 2.4 to 3.2%, did not differ between groups. However, it would be interesting to additionally evaluate whether high-resistance exercise resulted in more responders than low-resistance exercise. An interesting approach to distinguish responders from non-responders is based on the minimal detectable change of an instrument. Minimal detectable change (MDC) is defined as the minimal change that falls outside the measurement error of an instrument. It is calculated as the mean difference ± 1.96 x SD of test-retest data. As mentioned earlier, test-retest data of the CT-procedure of **paper 3** are currently unavailable. However, test-retest data of the procedure in **paper 1** indicate that percent changes should be higher than 3.86% to exceed measurement error and thus to define hypertrophic responders. Although measurement error is likely to be lower in **paper 3** (see chapter 2.2.3.1 of the discussion), the use of this MDC indicates that at least 8 (m=1, f=7) participants in HIGH, 7 (m=2, f=5) in LOW+ and 6 (m=4, f=2) in LOW can be considered as hypertrophic responders. Mean hypertrophic gains of responders, i.e. 6.6 ± 2.2% in HIGH, 5.9 ± 3.0% in LOW+ and 5.6% ± 1.1% in LOW, did not differ between groups (P = 0.506). These findings confirm that all training approaches resulted in equivalent, though limited, hypertrophy.

Responders did not differ from non-responders on any of the baseline parameters (all P > 0.05). Also, no difference was found in average training volume per exercise session between responders and non-responders (P = 0.252).

The variability in training responses between subjects might be linked with genetic susceptibility. To date, only few studies have focused on the association between genes and responses to resistance exercise. Although further research in this domain is necessary, there are some indications that genetic factors might influence strength training responses (64,141).

2.2.4 Suggestions for future research

In the light of the presented studies of this thesis, the following topics in particular are interesting for research to be performed in the future.

(1) From a clinical point of view, it would be interesting to investigate the feasibility and the effects of the proposed modes of exercise in older adults who are at high risk of steep functional decline. In addition, the effects on negative health outcomes (e.g. falls, fractures and institutionalization) should be examined in order to verify the cost-effectiveness of this approach.

(2) Fundamental research on the neural mechanisms underlying muscle function adaptations after low-repetition high-resistance exercise (constant or variable resistance) and high-repetition low-resistance exercise would allow us to better understand potential differences between such training protocols.

(3) Protein supplementation immediately after each exercise session might be investigated as a potential strategy to augment the hypertrophic response of older adults to our resistance exercise protocols.

(4) As muscle power appears to be a key component in functional performance, high-speed resistance exercise should be considered a topic of interest in older adults.

(5) Future research might focus on the impact of our different exercise protocols on:
- the cardiovascular system (acute responses and chronic adaptations)
- the joints (joint reaction forces – joint stress)
- the muscle-tendon unit
- bone mineral content

(6) For a better understanding of the phenomenon of responders versus non-responders, it would be interesting to investigate the association between genes and responses to resistance exercise.

(7) Future research should examine the minimum dose of resistance exercise required to maintain training adaptations and the potential benefits of systematic aerobic exercise during this maintenance phase.

(8) Given that long-term adherence to resistance exercise remains a challenge among older adults, it might be particularly interesting to explore strategies for improving long-term adherence. The Self-Determination Theory (SDT) has been postulated as a promising approach to facilitate behavioral change in the long run. According to the SDT, three basic psychological needs, i.e. the need for autonomy, for relatedness and for competence, are fundamental to obtain high-quality motivated engagement in any given behavior (129). Creating a need-supportive environment might thus be effective in facilitating exercise behavior. The need for autonomy can be satisfied by exploring options with participants and allowing them to self-select the training protocol or exercises. The need for competence can be fulfilled by appropriate goal-setting and by providing optimal challenges. Feelings of failure should be avoided. The need for relatedness can be supported by creating a meaningful relationship between coach and participant. This need can also be satisfied by creating social interactions with peers or significant others (e.g. group sessions).

3. Take home messages

(1) Resistance exercise interventions for older adults need to aim at improving muscle function in addition to muscle mass.

(2) Short-term low-resistance exercise until muscular failure can be as efficacious as high-resistance exercise for improving muscle mass, basic muscle strength and functional performance in older adults. The focus on external resistance as a crucial factor in muscle mass and function gains is too simplistic and inappropriate.

(3) Long-term maintenance of resistance exercise behavior remains a challenge among older adults. It provides an important issue for future research.

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APPENDICES

Professional career

In 2007, Evelien Van Roie graduated as Master of and Qualified Teacher in Physical Education at KU Leuven. Her major was 'Training and Coaching in Soccer'. Because of her interest in health-related fitness, she continued her studies for one more year and graduated as Master of Physical Education and Kinesiology with major 'Physical activity, Fitness and Health' in 2008. From January 2008 until September 2010, she had a part-time job as fitness instructor, where she was able to work with different populations, ranging from young and healthy adults to elderly, people with COPD, multiple sclerosis, or lower back pain. In November 2008, she started working as a research assistant under the supervision of Prof. dr. Christophe Delecluse at the Research Center for Exercise and Health, Department of Biomedical Kinesiology. While gaining scientific experience in the field of sarcopenia and resistance exercise, the framework of the doctoral project was delineated and collaboration was started with Prof. dr. Ivan Bautmans from the Gerontology Department of Vrije Universiteit Brussel. This collaboration resulted in a successful application for Ph.D. Fellow of Research Foundation Flanders and the start of a Ph.D. with joint degree. To bridge the gap between science and practice, Evelien voluntarily continued working as a fitness instructor during her Ph.D. studies.

Overview of the academic career

04.07.2007	Graduated 'cum laude' as Qualified Teacher in Physical Education (KU Leuven)
07.07.2007	Graduated 'magna cum laude' as Master of Physical Education, major 'Training and Coaching Soccer' (KU Leuven)
06.07.2008	Graduated 'summa cum laude' as Master of Physical Education and Kinesiology, major 'Physical Activity, Fitness and Health' (KU Leuven)
17.11.2008 – 30.09.2010	Ph.D. student (AAP) KU Leuven Department of Biomedical Kinesiology Research Center for Exercise and Health
01.10.2010 – 30.09.2014	Ph.D. student (Ph.D. Fellow of FWO) Research Foundation – Flanders KU Leuven, Department of Kinesiology, Physical Activity, Sports & Health Research Group Vrije Universiteit Brussel, Gerontology Department, Frailty in Ageing Research Group

List of publications

Papers

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Appositions – Bijstellingen

Bijstelling 1

In de huidige maatschappij wordt continu van mensen verwacht dat ze multitasken. Echter, multitasken is niet alleen bewezen als zijnde tijdsinefficiënt, het vergroot bovendien het aantal gemaakte fouten in vergelijking met het één voor één afwerken van verschillende taken.

Bijstelling 2

Fitnesscentra investeren vaak te veel in apparatuur en infrastructuur in plaats van in gekwalificeerd personeel. Het merendeel van de bevolking heeft juist nood aan wetenschappelijk onderbouwde bewegingscoaching in plaats van aan trendy apparatuur.

Bijstelling 3

Ervaren internationale topscheidsrechters van FIFA worden gedwongen om op pensioen te gaan op een leeftijd van 45 jaar. Scheidsrechters zouden beoordeeld moeten worden op hun fysieke paraatheid en beslissingsvaardigheden, niet op hun leeftijd.