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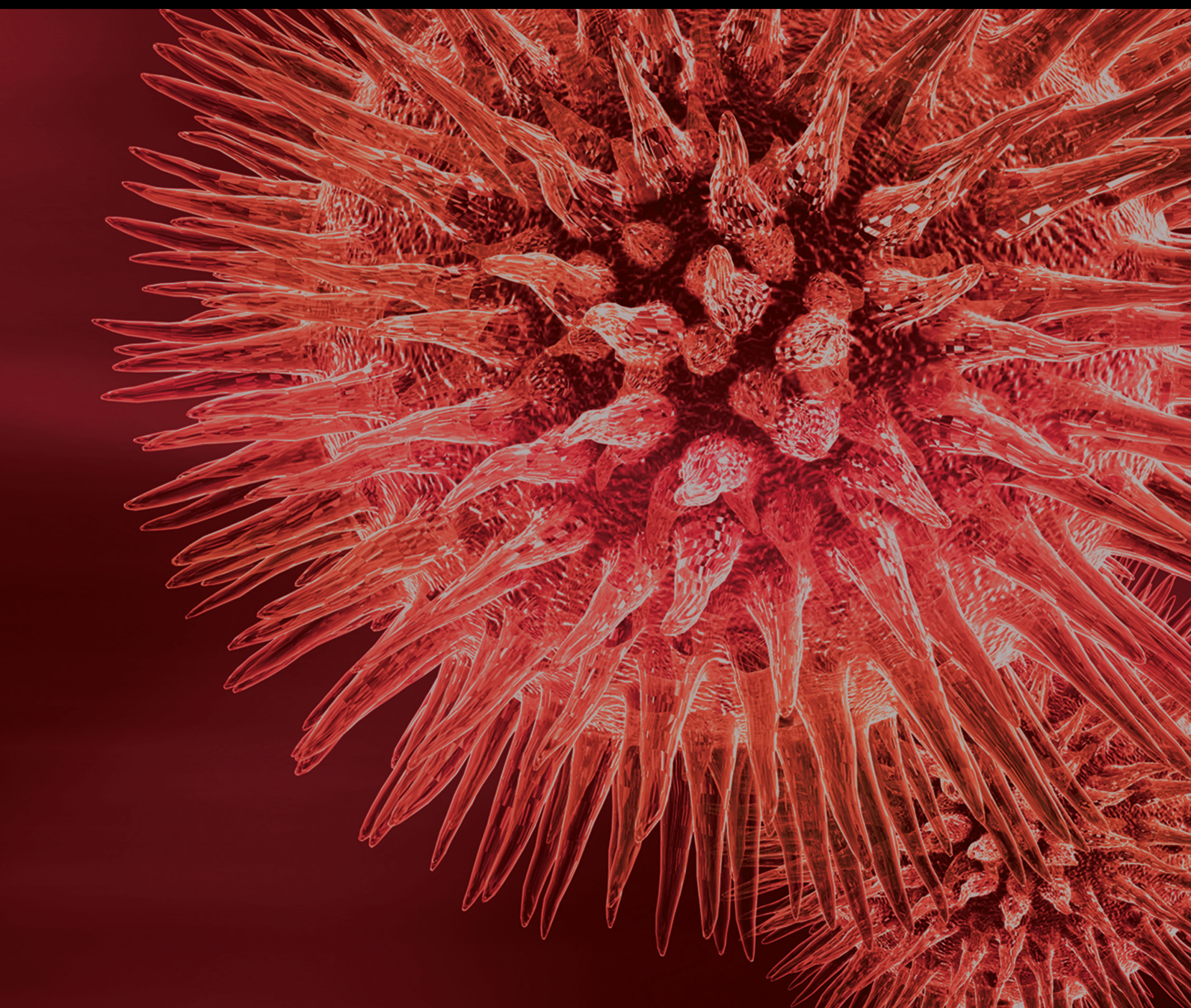
Lead Guest Editor: Birgitta Langhammer
Guest Editors: Astrid Bergland and Elisabeth Rydwik



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*Editorial*

# The Importance of Physical Activity Exercise among Older People

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In this special issue of BioMed Research International, the focus is on lifestyle and in particular physical activity (PA) as a driver for a healthy and long life for older people.

As populations continue to extend life expectancy, a central concern is whether the added time comprises years of healthy life and promotes a high health-related quality of life into old age. *PA* is defined as any bodily movement produced by skeletal muscles that result in energy expenditure. PA encompasses exercise, sports, and physical activities performed as part of daily living, occupation, leisure, or active transportation. *Exercise* is a subcategory of PA that is planned, structured, and repetitive and that has as a final or intermediate objective for improvement or maintenance of physical fitness. *Physical function* is the capacity of an individual to perform the physical activities of daily living. Physical function reflects motor function and control, physical fitness, and habitual PA [1].

PA is a protective factor for noncommunicable diseases such as cardiovascular disease, stroke, diabetes, and some types of cancer [2] and PA is associated with improved mental health [3], delay in the onset of dementia [4], and improved quality of life and wellbeing [5, 6]. The health benefits of PA are well documented with higher levels and greater frequency of PA being associated with reduced risk and improved health in a number of key areas [7].

The dose of PA or exercise is described by the duration, frequency, intensity, and mode [8]. For optimal effects, the older person must adhere to the prescribed exercise program and follow the overload principle of training, i.e., to exercise near the limit of the maximum capacity to challenge the body systems sufficiently, to induce improvements in physiological parameters such as VO2max and muscular strength [1].

Improvements in mental health, emotional, psychological, and social well-being and cognitive function are also associated with regular PA. Despite these health benefits, PA levels amongst older adults remain below the recommended 150 min/week [9]. The crude global prevalence of physical inactivity is 21.4% [10]. This translates to one in every four to five adults being physically inactive, or with activity levels lower than the current recommendations from WHO [11]. Inactivity and aging increase the risk of chronic disease, and older people often have multiple chronic conditions (NFH, 2010). The exercise recommendations from WHO include both aerobic exercise and strength exercise as well as balance exercises to reduce the risk of falls. If older adults cannot follow the guidelines because of chronic conditions, they should be as active as their ability and conditions allow [12]. It is important to note that the recommended amount of PA is in addition to routine activities of daily living like self-care, cooking, and shopping, to mention a few.

Inactivity is associated with alterations in body composition resulting in an increase in percentage of body fat and a concomitant decline in lean body mass. Thus, significant loss in maximal force production takes place with inactivity. Skeletal muscle atrophy is often considered a hallmark of aging and physical inactivity. Sarcopenia is defined as low muscle mass in combination with low muscle strength and/or low physical performance [13]. Consequently, low physical performance and dependence in activities of daily living is more common among older people [14, 15]. However, strength training has been shown to increase lean body mass [16], improve physical performance [17, 18], and to a lesser extent have a positive effect on self-reported activities of daily living [18]. These aspects are at focus in the papers of K. Kropielnicka et al. "Influence of the Physical Training on Muscle Function and Walking Distance in Symptomatic Peripheral Arterial Disease in Elderly" as well as G. Piastra et al. "Effects of Two Types of 9-Month Adapted Physical Activity Program on Muscle Mass, Muscle Strength, and Balance in Moderate Sarcopenic Older Women."

Participation in PA and exercise can contribute to maintaining quality of life, health, and physical function and reducing falls [19–21] among older people in general and older people with morbidities in particular. The increased attention to the relationship between exercise and HRQOL in older adults over the last decade is reflected in a recent review, which showed that a moderate PA level combining multitasking exercise components had a positive effect on activities in daily living, highlighting the importance of physical, mental, and social demands [22]. To reduce falls, balance training is also recommended to be included in physical exercise programs for older adults [12]. Exercise has also been shown to reduce falls with 21%, with a greater effect of exercise programs including challenging balance activities for more than 3 hours/week [23].

The gender perspective and motivators for fall prevention are at focus in M. Sandlund et al. qualitative study "Gender Perspective on Older People's Exercise Preferences and Motivators in the Context of Falls Prevention: A Qualitative Study," in this special issue.

Exercise training in older people has been associated with health benefits such as decreased cardiovascular mortality [24]. Explanatory mechanism likely to be involved following exercise was a change in the cardiac autonomic balance producing an increase, or a relative dominance, of the vagal component [25]. Furthermore, endurance exercise training in older people decreases resting and submaximal exercise heart rate and systolic and diastolic blood pressure and increases stroke volume [26]. This is especially notable during peak effort in which stroke volume, cardiac output, contractility, and oxygen uptake are increased, while total peripheral resistance and systolic and diastolic blood pressure decreased. Thus lowering after-load in the heart muscle, which in turn facilitates left ventricular systolic and diastolic function, emphasizes the importance of high intensity training also for the elderly. E. Tamuleviciute-Prasciene et al. focus on the frail elderly individuals and exercise in their contribution "Frailty and Exercise Training: How to Provide Best Care after Cardiac Surgery or Intervention for Elder Patients with Valvular Heart Disease."

Exercise may also have benefits for the brain centers that support executive control. It may be that strong executive functioning in itself may facilitate consistency for this challenging activity. Poor executive control has been associated with lower self-reported PA rates over a 2-year period [27, 28]. The executive control's contribution to PA has been found to be 50% greater in magnitude than the contribution of PA to subsequent changes in executive control [29]. In the paper of M. A. McCaskey et al. "Making More of IT: Enabling Intensive MOtor Cognitive Rehabilitation Exercises in Geriatrics Using INFORMATION Technology Solutions," the authors also include new technology to enhance and maintain exercise in cognitive rehabilitation.

In order to attain a high level of cardiorespiratory fitness, it is recommended to be physically active for 6 months or longer. These recommendations may also be applied to balance exercises in order to reduce falls [23]. Many elderly individuals are incapable of sustaining activities for this long on their own. Successful maintenance of PA typically requires substantial support and supervision. Even then, a high percentage of people drop out due to difficulties negotiating everyday costs of activity participation like scheduling conflicts and competing sedentary activities or health issues. This issue is highlighted in the study of T. Adachi et al. "*Predicting the Future Need of Walking Device or Assistance by Moderate to Vigorous Physical Activity: A 2-Year Prospective Study of Women Aged 75 Years and Above.*"

In addition, reduced bodily functions can make it difficult for elderly persons to maintain exercise under different environmental circumstances, which is demonstrated in the contribution of B. N. Balmain et al. "*Aging and Thermoregulatory Control: The Clinical Implications of Exercising under Heat Stress in Older Individuals*."

In this special issue, we have included papers that focus on the aging process and PA in a broad perspective, focusing on different aspects on PA, exercise, and older people. PA and exercise play an important role in the primary, secondary, and tertiary prevention, in the management of diseases, to counteract sarcopenia and falls as well as improving physical performance and activities of daily living, as these papers illustrate.

Promoting exercise among the older population is an important public health and clinical issue. A core issue is how to get older people with comorbidities to exercise.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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*Review Article*

# Making More of IT: Enabling Intensive Motor Cognitive Rehabilitation Exercises in Geriatrics Using Information Technology Solutions

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Although the health benefits of physical activity and exercise for older people are well established, a largely sedentary lifestyle still prevails in ageing western societies. Finding new ways to make exercise more accessible and acceptable for older adults must be developed to fully unleash its potential in preventing and weakening age-related physical and cognitive decline. Existing barriers to implement effective exercise-based treatment plans include motivational reservations on both the clinician's and patient's side, but also physical limitations caused by disease or deconditioning. Particularly in the more senior population, debilitating conditions do not allow adherence to currently recommended exercise regimes. A major rethinking of age- and user-adapted exercise is overdue. The high intensities required for physical and mental adaptations must be modifiable and personalized according to the functional status of each patient. Emerging information and communication technologies (ICT) have brought forward a plethora of attractive solutions for smart and adapted exercise, but there remains a vast gap between technological advancement and clinical relevance. Where in the beginning ICT for active ageing mainly focussed on aspects of usability and user experience, the current status of IT as applied in ageing populations noticeably shifted toward new services, applications, and devices that can be offered with the aim to prevent, compensate, care, and/or enhance daily life functioning of senior citizens. In this perspective paper, we aim to summarize the current state of the art in ICT-based interventions aimed at improved motor-cognitive control and make suggestions about how these could be combined with high-intensive interval exercise regimes to make rehabilitation for the impaired older adults more effective, and more fun.

## 1. Introduction

Driven by the observable patterns of ageing in western societies, attention towards healthy ageing as a means to preventing decline in functioning has been spreading rapidly over the last decade [1]. Today, the primary goal of public health is to increase the number of years of good health, and, thereby, to maintain independence and quality of life as long as possible. Healthy ageing is characterised by the avoidance of disease and disability, the maintenance of high physical and cognitive function, and sustained engagement in social and productive activities. These three components together define successful ageing [2]. In Europe it was the European Commission that identified active and healthy ageing as a societal challenge common to all European countries. Active ageing and independent living (http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing) is one of the pillars around which actions are focused [3]. The specific action proposed to address issues related to this pillar is to develop Information and Communication Technology (ICT) solutions to help older people stay more active, and independently mobile for longer [4–6] and, by achieving that, contribute to Compression of Morbidity [7]. The importance of prevention of age- and behaviour-associated physical function decline and disabilities should therefore be in the focus of society's attention [8, 9]. Older adults are less likely to remain living independently in the community when they lose their ability to move and interact within their environments without needing assistance. Exhibiting higher rates of morbidity, mortality, health care utilization, and cost next to experiencing a poorer quality of life are other consequences [10, 11].

Furthermore, frail older adults and geriatric patients are particularly susceptible to loss of health-related (e.g., muscle size and, to an even greater extent, muscle power) [12] and skill-related fitness components (e.g., balance and reaction time) [13]. Notwithstanding the fact that physical exercise is considered one of the most effective nonpharmacological interventions to improve mobility and independence in frail older adults, no clear guidance regarding the most effective program variables exists [14]. Moreover, it is well established that geriatric patients are particularly sensitive to prolonged bed-rest; there are no clear exercise-based recommendations for multimorbid patients recovering from an acute illness. Even when patients are admitted to rehabilitation, the activity levels and exercise intensities administered are lower than would be required for actual improvement [15]. The quality of life and ability to function in daily activities of living rely on minimal levels of neuromuscular function and rapid loss of muscle power in hospitalised geriatric patients is often the beginning of years lived in frailty [16]. Sudden immobility due to nonavoidable hospitalisation has been shown to lead to a significant reduction of functional capacity and is associated with a substantial and sustained decline in functional status [17, 18]. Less than a fifth of hospitalised older patients with remaining impairments regain normal personal ability to perform the activities of daily living one year after discharge. About a third of discharged patients further deteriorate within a year and show debilitating signs of reduced cognitive and physical performance [16]. This has wide socioeconomic relevance, as the demographic changes come along with souring numbers of emergency admissions of patients older than 75 [19]. Almost half of geriatric patients admitted to emergency treatments, e.g., after falls or cardiopulmonary symptoms, have been reported to be rehospitalised within 6 months [19, 20]. Thus, finding ways to effectively prevent deconditioning leading to frailty and to significantly reduce the number of readmissions of older patients after a critical illness and subsequent discharge is of high relevance.

We are faced with the challenge of how to support public health policies that would help senior citizens in achieving the goals of primary and secondary (i.e., reducing readmission rates) prevention with the aim to remain independent. An extended life should ideally also involve preservation of the capacity to live independently and to function well [21]. For this purpose it is important that we understand the best ways of providing effective answers to the need for specifically tailored physical activities, for the provision of intellectual stimuli that keep older adults at highest possible levels of cognitive functioning, or for definition of supporting systems that facilitate social integration by keeping in close contact with family and peers.

Physical activity and exercise for older adults are highly recommended in order to promote maintenance of physical and cognitive functioning [22–26] at the highest possible levels. However, maintaining motivation to continue and adhere to exercise is often difficult as participating in conventional exercise may not have such an appeal [27]. There is, therefore, an identified need to perform more research aimed at establishing the best ways to encourage older adults to be more physically active in the long term [28]. Older adults may misinterpret exercising as being dangerous since perceived barriers are thinking participation increases the risk of having a heart attack, stroke, or death, despite the minimal likelihood of these occurring [29]. Barriers to physical activity resolve around major themes such as social influences (valuing interaction with peers, social awkwardness, encouragement from others, and dependence on professional instruction); physical limitations (pain or discomfort, concerns about falling, and comorbidities); competing priorities; access difficulties (environmental barriers and affordability); personal benefits of physical activity (strength, balance and flexibility, self-confidence, independence, improved health, and mental well-being); and motivation and beliefs [30]. This makes motivation and encouragement for exercise and physical activity fostered by professional support important. Finally, while we know that early aerobic exercise training after acute illness could enhance cardiovascular fitness and improve functional recovery [31], patients with functional impairment often cannot adhere to the commonly prescribed high-volume low-intensity exercises [32]. Providing short and effective exercise and increasing self-efficacy could prevent fear-avoidance strategies and help restoring prehospitalisation functional status.

Incorporating progressively intense but short exercise as part of a tailored and combinatory program has shown to be beneficial for healthy older men [33] and also feasible for comorbid geriatric patients [34]. Evidence from animal models and experimental research suggests a causal relationship of exercise intensity with physical [35, 36] and mental [37–39] health. Several reviews have summarized the evidence of the benefits of such high-intensity interval training (HIIT) for mental and physical health [37, 40, 41]. While these articles provide comprehensive recommendations for HIIT implementations and its limitations, they do not address the issue of how frail older adults can overcome physical impairments to benefit from this promising intervention. The main objectives of this perspective review are to (1) critically appraise the literature on aerobic exercise for healthy ageing and (2) highlight its limitations in practical translation of current recommendations. We then (3) review the evidence to illustrate how HIIT can overcome these limitations and what effects it may have on improved cardiovascular fitness and cognitive functioning. Next, (4) we illustrate how the effect of physical exercise on cognitive function and physical health can be boosted by combined motor-cognitive exercises. Finally, (5) we propose novel training solutions based on information and communication technologies (ICT) that exploit the versatility of enjoyable games to improve adherence and increase cognitive load during exercise (i.e., exergames). The working hypothesis (6) is that combined intensive cognitive and physical exercise delivered as smart ICT-solutions has the potential to dampen the cognitive decline observed in older people in the early-to-middle stages of dementia [42] next to improving their physical functioning [43, 44]. We intend to illustrate how a successful implementation of these modern technologies in combination with short intense exercise bouts can help to make more of the little time invested in primary and secondary prevention.

## 2. Aerobic Exercise for Healthy Ageing: A Critical Appraisal of the Literature

Physical activity has been shown to be vitally important for maintaining endurance, strength, and function in older adults [45]. Optimisation of physiological function throughout the lifespan has been advocated as an important part of any contemporary biomedical policy addressing global ageing [46]. Reductions in both muscle volume and oxidative capacity per volume in the course of ageing result in declined oxidative capacity and appear to be an important determinant of the age-related reduction in aerobic capacity [47, 48]. These reductions are believed to explain the reduction in preferred walking speed in healthy older subjects, which requires a higher fraction of ventilatory threshold [49], which is also associated with cognitive [50] and mobility [51] decline.

Decay of cognitive performance in old age is predominant in most individuals, an observation confirmed, for example, by a large Italian epidemiological study demonstrating that ageing associated cognitive decline has a prevalence rate of 28% for people from 65 to 84 years of age, and cognitive decline without cognitive complaints summed up to 45% of people showing some kind of cognitive impairment without dementia [52]. Worldwide, the number of people living with dementia is estimated to be 47.5 million and by 2050 this figure will triple to 135.5 million [53]. Dementia is a broad category of brain diseases causing a long-term and often gradual decrease in the ability to think and remember and that is great enough to affect a person's daily functioning [54]. Although the signs and symptoms linked to dementia can be understood in three stages, training interventions ideally should address older people in the early-to-middle stages of dementia [55].

Research has pointed out recently that physical activity may be relevant for healthy brain ageing and may protect from cognitive decline and dementia [56–60]. Most physical intervention studies, which focused on adaptations in cognitive performance, brain function, or brain structure, applied aerobic-type exercise. Two meta-analytic studies reported that aerobic exercise is effective in increasing cognitive performance in general and executive function in particular [61, 62]. Studies that are more recent also found that strength and coordination training might positively affect cognitive abilities [63, 64]. Voelcker-Rehage et al. [65] demonstrated training specific functional plasticity in the brain based on functional magnetic resonance imaging data. It appears that aerobic training increases activation in the sensorimotor network and coordination training leads to a higher activation of the visuospatial network, whereas strength training changes the hemodynamic activity of brain regions associated with response inhibition processes.

Current recommendations for exercise prescription to reverse frailty follow the Frequency-Intensity-Time-Type training principles [66]. According to the literature, a frequency of 2-3 exercise bouts per week at progressive moderate to vigorous intensity is recommended [67]. The intensity has been further specified as 70% to 75% of the age-adjusted maximal heart rate [68]. As the review by Bray et al. [66] points out, duration should be adapted according to the frailty status, age, and consistency of exercise participation. Ideally, frail adults should train for 30-45min while prefrail adults should train for 45-60min. For frail older adults, a shorter duration is recommended as they may get easily fatigued [69]. The exercise should not be limited to one type of intervention. Rather, a multicomponent regime with different exercise components has shown to be most accepted and effective in older adults [66, 70]. Any program should, however, include and start with an aerobic warm-up component [66], which can also just be brisk walking [71]. The greatest unknown in exercise prescription for the older adults is the progression rate of intensity. To really benefit from any kind of exercise, tailored progression to reach and extend the individual's capacity limits is of particular importance. Only by continuously monitoring each patient's capacity and adapting the training intensity can long-term benefits be expected [66]. Meanwhile, for healthy older adults, the American College of Sports Medicine and the American Heart Association (2007) recommend moderate-intensity aerobic physical activity five days a week or vigorous-intensity on three days per week. Additional strength and flexibility exercises are recommended at least twice a week with incorporation of balance and coordination exercises to reduce risk of injury form falls [72].

## 3. Limitations in Practical Translation of Current Recommendations

The aforementioned recommendations for older adults demand physical activity on most or all days of the week. However, only 31% of persons, 65 to 74 years, report regularly engaging in moderate physical activity for 20 minutes or more three days a week [73]. By 75 years of age, the rate drops to a low level of 20% [73]. Furthermore, only less than 5% of older adults (60+ years) are physically active in terms of meeting the recommended 30 min a day [74, 75].

A reason might be that older adults may not be able to initiate physical activity at recommended levels [76]. A possible solution could be that, through appropriate and progressive increase in training amount, the recommendation for older adults can be achieved in rehabilitation or exercise settings [76]. Nevertheless, for many older adults with physical, cognitive, or combined physical-cognitive impairments the execution of physical exercise according to the recommended levels may never be possible [76]. Therefore, a need exists for innovative ideas and to develop training interventions that support physical and cognitive functioning and that facilitate exercise participation by considering holistic approaches (physical, cognitive, and social), current physical and mental status (user's profile), next to shorter training time requirement, and the consideration of innovative new technologies-based solutions [22]. At the moment, two interesting training approaches are discussed in the research field of physical activity in older adults: high-intensity interval training [77] and motor-cognitive training [44].

## 4. Higher Intensities Intervals for Better Efficacy?

The rise in research activities on the topic of high-intensity interval training (HIIT) is striking. The last decade has seen a more than tenfold increase in publications looking into the effects and mechanisms of HIIT. It has since been shown that HIIT is more effective at improving cardiovascular and cardiopulmonal function when compared to moderate intensity continuous training regimes [78]. Several individual studies with varying training modes and reviews with meta-analyses have confirmed these findings and also uncovered a row of unexpected beneficial effects on bodily functions: if properly implemented (e.g., $4 \times 4$ minutes of HIIT over at least 12 weeks), it has the potential to change molecular blood composition, reducing cardiovascular disease risks (e.g., reduction in blood pressure), and improving insulin sensitivity [32], and increase brain derived neurotrophic factors [37]. Importantly, HIIT has also undergone safety evaluations in animal and human studies, consistently reporting its safety, even in patients with cardiac or metabolic dysfunctions [79]. A study by Rosendahl et al. [80] demonstrated positive long-term effects in physical function of a high-intensity exercise program for older persons dependent in activities of daily living, of whom most had severe cognitive or physical impairments. No adverse events occurred in the study, despite the high prevalence of different diseases. HIIT training is also amenable with novel technologies [81]. A point that needs attention, however, is determination of the optimal dose-response for interval training. The studies discussed so far used different protocols with different intensities which may result in differing responses of the trainees [82]. Modulating the parameters of intense exercise using additional cognitive load and smart ICT solutions may provide a more potent stimulus for synaptic adaptions and potentially translate into improved physical function [83]. Moreover, if ICT based solutions can integrate the individual's vital signs and relevant biomarkers to adapt the training, safety and efficacy may also be improved. If, for instance, new technologies would allow surrogate measurement of oxidative-nitrosative-inflammatory stress during or before exercise, the exercise intensity could be adapted to prevent harmful blood-brain-barrier disruptions and potential maladaptation [37].

HIIT involves repeated bouts of high intensity effort followed by varied recovery times [84]. According to the American College of Sports Medicine (ACSM), each bout ranges from 5 seconds to 8 minutes performed at 80% to 95% of a person's estimated maximal heart rate. The ACSM recommends recovery periods to be performed at 40% to 50% of a person's estimated maximal heart rate [84]. This intermittent recovery phase allows untrained people with lower functional capacity, e.g., older adults [85], to work out harder than during continuous low-intensity exercises [86]. It has been labelled with "higher efficacy, tolerability, and adherence without compromising patients safety" [36]. Adapted to the capacity of the patients, HIIT presents a viable alternative to poorly adhered low-intensity exercise to reduce the risk for inactivity-related disorders [87]. However, recent concerns regarding the underinvestigated risks on brain health have given rise to more critical voices [37, 41]. One review found a slightly higher incidence of adverse response during or shortly after HIIT exercise in patients with cardiometabolic diseases [41]. Therefore, despite all the benefits of HIIT, the precautions taken before employing a HIIT program for patients should be taken at least as strict as before any other form of exercise. Patients must be stable and medical monitoring should be provided during the exercise. Table 1 shows an overview of selected high-intensity interventions for older people. Selection criteria were studies investigating HIIT in participants older than 65 years.

Adapted physical activity at high intensity is capable of counteracting age-related changes and performance loss not only in the cardiovascular and muscular system [91], but also on cognitive performance and brain structures [92]. Intense physical activity clearly improves cerebral blood supply and increases neuronal activity, which has been shown to stimulate neurogenesis [37]. The predominant hypothesis regarding this effect is that brain-derived neurotrophic factor (BDNF) is upregulated with higher protein concentrations observed in brain regions particularly important for learning and memory (e.g., hippocampus). BDNF plays an important role in neural plasticity and has been associated with cognitive performance in healthy and clinical populations [39, 93]. Just 20 minutes of HIIT has shown to increase BDNF serum levels with a relevant functional effect, i.e., to influence behavior and cognition [36].

A review of the literature by Penrose et al. suggests that, in order to better harvest the effects of exercise on cognitive function in patients with dementia, physical activity should be combined with cognitively stimulating activities [80, 94]. The next section takes a closer look at how current exercise regimes are employed in combination with cognitive loadings to improve mental and physical capacity.

## 5. Motor-Cognitive Exercise

Cognitive training studies have often shown highly task specific effects [95–99]. More widespread transfer effects were found when different cognitive abilities were combined in complex interventions or lifestyle changes [100]. Nevertheless, effects were often small, while aerobic training elicited both broad transfer and relatively large effects. These findings led to the assumption that not only the combination of different cognitive abilities, but also the combination of cognitive and physical training improves cognitive performance in old age to a greater extent than the training of an isolated ability [42, 101–104].

Most daily activities are an interaction of motor and cognitive functions. From an evolutionary point of view,

Table 1: Overview of selected HIIT studies for older people (>65 years).

| Reference | Intervention | Outcomes | Main finding |
|---|---|---|---|
| Rosendahl et al., 2006 [80]∗ | C=inactive controls<br>F=29 within 3 months<br>I="high intensity"<br>T=n/a<br>T= HIFE (functional exercise at high load) + Protein supplementation | Berg Balance Scale<br>Max Gait Speed<br>1 rep max (lower extremities) | ⬀<br>⬀<br>⬀ |
| Rosendahl et al., 2008 [88]∗ | C=inactive controls<br>F=29 within 3 months<br>I="high intensity"<br>T=n/a<br>T= HIFE | Fall rate | = |
| Littbrand et al., 2009 [89]∗ | C=inactive controls<br>F=29 within 3 months<br>I="high intensity"<br>T=n/a<br>T= HIFE | Barthel ADL | ⬀ |
| Saucedo Marquez et al., 2015 [36] | C=continuous exercise at moderate intensity (70% $HR_{max}$)<br>F=one-time intervention<br>I=90% $HR_{max}$ and recovery intervals 20% $HR_{max}$.<br>T=20 minutes<br>T= HIIT on cycle ergometer with intervals of 1 min duration. | BDNF serum levels | ⬀ |
| Wisloff et al., 2007 [90] | C=continuous walking at 70% HRpeak.<br>F=3/week<br>I=95% $HR_{peak}$ and recovery intervals at 50% to 70% $HR_{peak}$.<br>T=20 minutes.<br>T= 4 minutes HIIT with 3 minutes recovery interval. | Flow-mediated dilation<br>Muscle biopsy (Mitochondrial function)<br>Quality of life<br>$VO_{2peak}$ | ⬀<br>⬀<br>=<br>⬀ |

An overview of a selection of studies investigating types of high-intensity interval exercise in older people: C=comparator; F=frequency; I=intensity; T=duration/time; T=type; HR=heart rate; BDNF = brain-derive neurotrophic factor; ADL = activities of daily living; ⬀: in favour of intervention; ⬂: in favour of comparator; =: no difference between groups.∗: based on the same interventions with different outcomes.

tasks were always an interconnection of motor and cognitive functions [105]. However, training interventions of older adults are usually split into a physical and a cognitive part. Studies demonstrated that larger benefits could be induced by the combination of motor and cognitive exercise as the combination might generate more synergistic beneficial changes [101, 106]. Based on reports found in the scientific literature, the cognitive supplements should be selected such that they share similar mechanisms with exercise and, thus, theoretically have the potential to support the action of the physical exercise part [42] or vice versa. Moreover, an indication of previous studies was that the combination has to be simultaneously to evoke positive effects [107]. Therefore, a need exists to take both components into account to design effective interventions and to design multimodal interventions [101], c.f. with the help of exergames [83].

Environmental challenges cause plastic adaptations of the human brain. Physical and cognitive exercise might trigger similar neurobiological mechanisms that go hand in hand to induce plastic changes in the brain [106]. Physical activity seems to facilitate neuronal plasticity by upregulation of blood circulation, neurotrophic factors, neurogenesis, and synaptogenesis [107–109]. The concurrent cognitive stimuli might activate the synapses and this in turn supports the survival of newly generated synapses and their integration into preexisting neuronal networks [106, 110]. Moreover, motor-cognitive exercise might also improve the synapse communication in brain networks that are responsible for movement coordination and execution because of the motor stimuli. This in turn could positively influence the communication from the motor area of the brain to the muscles. An efficient brain-body communication might contribute to motor performance (e.g., balance and strength). Furthermore, adaptions in the muscles and in the cardiovascular system might depend on the movements that are executed for the motor part.

Various applications exist that include the training of motor and cognitive abilities. Dancing and Tai Chi are examples of motor-cognitive exercises. Dance movements and Tai Chi both combine physical activity, sensorimotor interaction, and cognitive functioning in a possible social environment. Studies showed that dancing has positive effects on different cognitive functions, e.g., reaction time, working memory, and flexible attention, and on lower body muscle endurance, strength, and balance in older adults [111–114], however, only when an appropriate dose level of dancing training is reached

[115]. Also Tai Chi performance showed positive effects on physical functions and ameliorated cognition in older adults [116–118].

More recently an emerging complementary tool in exercise and rehabilitation in the older population has been exergames [119]. Exergaming combines motor and cognitive exercises as video games that have to be played by being physically active. The exergames used in research range from commercially available games (Nintendo Wii Fit, Xbox Kinect, and Dance Dance Revolution) to purpose-developed systems. Exergame studies demonstrated positive benefits for cognition and/or physical functioning in older adults [42, 120–124]; however, the training principle of specificity seems to apply to exergaming. The choice of exergame console [125] and game content used for training [126] influences the areas of (postural) control trained and improved. Which motor and cognitive functions will be or can be improved and triggered through exergaming most likely also depends on the consideration and implementation of training principles (e.g., intensity, frequency, and user-centred).

## 6. Personalized ICT Interventions for Active Ageing

In this section we will explore how the societal challenge of active and healthy ageing that is common to all European countries might be approached through the purposeful development of smart ICT technologies. We will begin by discussing general solutions that address behaviour associated and physical function decline with age [8, 9]. We will then put our focus on existing solutions that incorporate HIIT training [127].

In parallel to the push by scientists, industry leaders, and government officials to make medicine more personalized [128], there is a call for development of preventive physical activity strategies towards personalized exercise programs. In this context, ICT solutions have been reported as promising [129, 130] and exergames lend themselves to personalization of interventions [131]. Various ICT based solutions for optimised tailoring of exercise interventions have been proposed to support not only people with dementia but also their families and caregivers [132, 133]. Video game play-driven physical activities require mental engagement and would, thus, be in line with recommendations of the Global Council on Brain Health [134].

Various ICT-based applications for geriatric physical and mental training or therapy with older adults as well as specific recommendations for the design of these solutions are available; see [133] for a comprehensive overview. ICT may serve, for example, to mitigate some of the negative side effects of ageing (e.g., physical and cognitive decline) but can also serve to develop new capability enhancing opportunities. Where in the beginning information technology for active ageing mainly focussed on aspects of usability and user experience, the current status of IT as applied in ageing populations noticeably shifted toward new services, applications, and devices that can be offered with the aim to prevent, compensate, care, and/or enhance daily life functioning of senior citizens [133].

The Human-Computer-Interaction and the game design communities provide useful research and development examples that integrate effective exercises and training for older adults in an attractive and motivating multimedia design. The spectrum includes a wide range of innovative applications supporting patients and their relatives as well as caregivers (Figure 1). Well known examples include the social robots, like Zora or Paro. While social robots are designed to facilitate social interactions between patients as part of a multisensory behaviour [135], virtual coaches (e.g., CareCoach) use motivational cues for older people to maintain daily activities [136]. While such solutions provide some form of companionship and monitoring, they do not engage users in any meaningful physical activities. So-called social exergaming solutions, on the other hand, include joyful and purposeful physical activity while simultaneously stimulating social interaction to counter isolationism and loneliness [137].

*6.1. Exergames for Older People.* Exergames (Figure 2) are games, which are controlled by physical activity and body movements of the player (exertion/exercise + gaming) [138]. Exergames have been approved to be a suitable tool, which, if designed properly, engages seniors in physical activity in an effective (by integrating different training aspects and principles) and attractive manner (by implementing motivational designs). Depending on the virtual game scenario, the required in-game tasks, and the respective movement-based controller system (e.g., haptic or gesture-based input devices), different motor-cognitive functions and other health parameters can be improved when playing exergames.

*6.2. High Intensity Interval Exergames for Older People.* Gerontology research has provided insights into the impact of exergames-based interventions on seniors' motor-cognitive abilities [42, 120, 121, 123, 124]. A recently published, comprehensive systematic review provides an extensive overview of existing studies with exergames and their effects on older adults' level of physical activity [139]. Their findings support the usage of exergames in older adults, as shown by increased motivation and engagement of older people in general physical activity. Further systematic reviews have summarised evidence supporting the effectiveness of exergames to treat age-related chronic disease in terms of physical, psychological, and cognitive rehabilitative outcomes [140, 141]. However, research of exergame effects on aerobic capacity is largely missing. Currently, it is assumed that exergames are merely able to elicit light intensity energy expenditure when employed in community-dwelling older people [142]. But exergaming has also been described as an acceptable, safe [143], and innovative way to design enjoyable high-intensity interval training [81]. Only very few studies and game developers have specifically considered aerobic training in general [119] and HIIT specifically for seniors. To the best of our knowledge there are three studies examining HIIT and exergaming: one study used a boxing approach in young adults and adults [144], another study was performed with young adults on ergometers [81], and one program was


Figure 1: Selection of ICT-based solutions for seniors.


Figure 2: Selection of specifically developed (left) and general game market (right) commercially available exergames for seniors.

designed for older adults that has to be performed in standing position on a pressure-sensitive plate [127] (c.f. Figure 3). The latter study was performed at the Institute for Human Movement Sciences and Sport (ETH Zurich) while the other two studies were found by a literature search on Scopus using the keywords exergaming and high-intensity interval training.

*6.3. Sport Scientific Recommendations for Personalized Exergames for HIIT and Motor-Cognitive Training in Older People.* Based on theoretical considerations [145] combined with exercise recommendations for older adults [22] and knowledge from an effectively implemented HIIT training in older adults [146], an ergometer-based exergame HIIT program could be designed that considers 4x4 minutes >90% of peak oxygen consumption [$VO_{2\ peak}$] with 3 minutes' pedaling at no load on an ergometer on 3 days per week. The training can be extended with 2 days per week treadmill walking (45 minutes at 70% of $VO_{2\ peak}$). Before each activity, there is 5–10 min of warm-up and cool-down activities. Exercises for older adults should consider a Rate of Perceived Exertion 11–14 (6–20 scale). Furthermore, exercise with integrated cognitive challenges should target executive functions (e.g., inhibition, working memory, and flexibility) and White Matter Hyperintensity (WMH; Figure 3) [120, 121, 147]. Cognitive stimuli can be presented via visual (e.g., frontal screen) [120, 121] or acoustic (e.g., music player) systems [148] whereby the trained cognitive function determines the composition of the stimuli (e.g., inhibition: participants have to react to key stimuli and suppress reactions to other stimuli). Reactions can be recorded via the training device (e.g., step sequences, see

Figure 3: Dividat Senso plate with HIIT module for seniors [127].

Figure 3), pressing a button, or speech sounds depending on the wanted accuracy and objective. For a HIIT training, it might be reasonable to adjust the intensity of the cognitive load to the physical load of the exercise (e.g., more stimuli during the low-intensity exercises phases) to achieve an optimal challenge [149]. An optional complementation could be pedometers to increase lifestyle physical activity. Training program duration should be 6 weeks to see an effect in measures of aerobic capacity [146] and 12 weeks for changes in WMH with task-oriented training in standing position and targeting timing and coordination of gait [150].

Considering the above-mentioned points, a program that consisted of an exergame-based HIIT performed while standing on a pressure sensible platform (Dividat Senso Step Plate, Schindellegi, Switzerland, 93/42/EWG certified) and cognitively interacting with an on-screen scenario with audio-visual feedback might be designed as follows: short intervals of higher intensity exertion (fast alternating steps to keep a rocket in the air; 70-90% of maximum heart rate (HRmax)) alternated with active rest periods (50-70% of HRmax) for a total of up to 25 minutes. Important in this context is the reliable determination of HRmax values. Where the rating of perceived exertion using the 20-point Borg-scale seems valid and reliable for older adults [151], it seems important not to underestimate the true level of physical stress in older trainees in relation to reaching the appropriate intensity of exercise [152]. The intervention should be performed individually three times per week (to be in line with exercise recommendations related to frequency of training) for a period of four weeks with twelve sessions. Each training session is partitioned into three parts: five minutes' warming-up on a cycle ergometer at 50-70% of HRmax, followed by up to 25 minutes of HIIT, using different exergames on the pressure sensible platform. The sessions are finished with a cool-down of five minutes on an ergometer. Participants are expected to complete twelve training sessions while being monitored by a trainer, who systematically observes and supervises participants throughout the training. The program is individually tailored to each participant according to a training protocol based on the guidelines published by the American College of Sports Medicine [153] and is aimed at increasing endurance capacity. Table 2 includes an exemplified HIIT protocol that can be included into the exergame training program.

## 7. A Call for More HIIT in Exergames for Older Adults

Our review revealed that there are currently only two exergame HIIT training programs [81, 127] and only one that is specifically designed for older adults. Following and based on our longstanding experience in designing and researching holistic, research-based and user-centred state-of-the-art exergames for and with various, heterogeneous target groups, we aim to contribute to the ongoing debate and make some recommendations for the design of personalized exergames for HIIT and rehabilitation in seniors.

*7.1. Interdisciplinary Collaboration.* To create a holistic and user-centred design, it is recommendable to work with interdisciplinary developer teams of experts from all related fields. In the context of personalized exergames for HIIT and rehabilitation in seniors, the team should consist of older people, therapists, movement and sports scientists, game designers, and industrial and interaction designers as well as Human Computer Interaction researchers, who can provide relevant knowledge from different perspectives.

In this scenario, the targeting group (older people, therapists, and relatives) is part of the developer team and is directly involved in the participatory and user-centred design process. It can be further distinguished between the first stage- (seniors, who will play the game as single and/or multiplayer game) and the second-stage-targeting group (therapists and relatives, who will attend the senior while playing and/or could be involved in the gameplay).

### *7.2. Design Recommendations for Exergames in Older People*

*7.2.1. Multilayered Design.* The holistic design process should focus on three design levels, which need to be covered symbiotically and in relation to one another (Figure 4).

(1) Body: targeting group-specific, physical requirements need to be taken into account and specific training/exercise concepts (adapting to the training progress) must be developed including the individual and social body as play element. In the context of HIIT and motor-cognitive training, designers should especially focus on movements from traditional HIIT

Table 2: Example of a theory-based HIIT training protocol schedule designed for the Dividat Senso plate (Figure 3).

| | | |
|---|---|---|
| Week 1 (Trainings 1-3) | High-intensity interval: 4x1 min up to 9x1 min at 70-80% of HRmax+10%, Borg 12-14<br>Active recovery interval: up to 8x2 min at 50-70% of HRmax+10% | If participant was already working at ~80% level of HRmax+10% at the end of week 1, keep continuing at ~90% level of HRmax+10% |
| Week 2 (Trainings 4-6) | High-intensity interval: 3x2 min up to 6x2 min at 70-80% of HRmax+10%, Borg 12-14<br>Active recovery interval: up to 5x2 min at 50-70% of HRmax+10% | If participant was already working at ~80% level of HRmax+10% at the end of week 2, keep continuing at ~90% level of HRmax+10% |
| Week 3 (Trainings 7-9) | High-intensity interval: 3x2 min up to 6x2 min at 80-90% of HRmax+10%, Borg 15-17<br>Active recovery interval: up to 5x2 min at 50-70% of HRmax+10% | |
| Week 4 (Trainings 10-12) | High-intensity interval: 5x2 min up to 8x2 min, at 80-90% of HRmax+10%, Borg 15-17<br>Active recovery interval: up to 7x1 min at 50-70% of HRmax+10% | |

The participant performs alternating steps on the plate and, by doing that, keeps a rocket above a certain threshold line. The trainee may face different cognitive challenges by having to control the rocket along a straight line in the air using different stepping speeds or through having to manoeuvre the rocket in between obstacles.


Figure 4: Three levels of research-based and user-centred design in exergames (source: Martin-Niedecken, 2017).

and motor-cognitive training/rehabilitation interventions and take or modify these into game-related input movements.

(2) Controller: choose and experiment with targeting group-specific game devices such as specifically developed input devices and/or therapy/training devices, which are used to transfer the player's body movements to the game and which could provide an additional playful experience beside the virtual game scenario. Equally to the body design level, it is important to think about devices, which allow for the implementation of different motor-cognitive stimuli as well as for HIIT movements and which easily can be integrated into the specific body movements rather than disturbing the flow of movements and gameplay.

(3) Game: the game should include varied and balanced game mechanics, feedback, aesthetics, dynamics, story, and sound, which suit the targeting group's requirements and preferences. Furthermore, it is important that the game takes up the expert knowhow on specific useful cognitive stimuli and HIIT and provide a playful representation and a well-balanced feedback loop for the player.

Furthermore, in the context of geriatric rehabilitation, it is very useful to feature an additional tool for the therapists and/or caregivers, which allows organizing and evaluating training sessions and plans. Such a therapist-UI could also be used to manually adapt specific in-game parameters as well as controller settings and input movements to the current physical and emotional needs and states of the patient during an exergame-based training/therapy session.

To sustainably enhance the effects of exergame training/therapy and support adherence of seniors in playful exercising, designers should create applications which can be used in a clinical setting and in the presence of a therapist or caregiver, as well as applications for the home use, which are easily accessible and can be used alone by older people.

*7.2.2. Multilevel Process: Design, Evaluation, and Redesign.* Following a traditional user/player-centred game design approach [154], developer teams should always start with a review (and testing) of related R&D work on all three design levels and use the gained knowledge as base for their first concepts.

Among others, the designs of all elements related to the three design levels should be based on theories and approaches like the "game flow" [155] and the "dual flow" [156] to allow for a maximum attractive and effective training/gameplay experience through an individually adaptable game difficulty and complexity and in terms of a multiplayer, a dynamic grading, and balancing of all players even if they have different skills [157]. Additionally, findings from the interdisciplinary research debate with and on exergames provide further insights into the impact of various controller technologies [158], body movements [159], social exertion, and bodily interplay [160] as well as various design parameters (visuals, audio, perspectives and points of view, etc.) on the player's gameplay/training experiences. This knowhow should also be taken into account, when designing a targeting-group specific exergame.

Another promising and valuable approach is the involvement of older adults' relatives and especially of their grandchildren into a multiplayer game setting [161]. An intergenerational design approach can allow for new (social) interaction mechanisms and holds great potential for future exergame developments for seniors. Furthermore, experimenting with mixed realities (augmented and virtual realities) and/or mixed genres (exergames meet strategy games) in could open up new design patterns.

By involving the targeting group(s) into the design process from the very beginning, designers can easily gain valuable insights into personal preferences, needs, and requirements and enhance identification of their targeting groups with the final product.

To start working with the targeting group(s), powerful and effective methods are guideline-based focus group interviews and the use of first draft paper prototypes, sketches, movement concepts, and input device prototypes as inspiration and basis for the discussion. Developer teams should run several user-tests and collect the feedback from all user perspectives (e.g., older people, therapists, and relatives).

After the first explorative phase, developers should start implementing first design drafts and let their targeting group(s) test them again immediately to get feedback, which could then be implemented in the further development of various or individual concepts.

Figure 5: User-centred and adaptive single and multiplayer exergame environment "Plunder Planet," which was developed with and for children and young adolescents which can be played with different motion-based controller devices challenging the motor-cognitive, coordinative, and endurance abilities of the players [149].

As soon as a holistic prototype is ready after some design iterations, developer teams should run first user studies on specific research questions to gain deepened insights and knowledge on the attractiveness and effectiveness of their exergame. Again, the results will be used as basis for the redesign. This dynamic process can be repeated several times until the final product is ready.

So far, and to the best of our knowledge, there are any exergame projects or products for HIIT or motor-cognitive training/rehabilitation in seniors, which focused on this exact holistic and symbiotic approach.

However, in current studies, Martin-Niedecken and colleagues could show the positive impact of an adaptive and user-centred exergame training environment on dual flow, motivation, and training performance of children with and without previous gaming and sports experience [162–165]. The fitness game "Plunder Planet" (Figure 5) was developed following an iterative, research-based, and user-centred design approach like outlined above.

## 8. Conclusion

To conclude, we would like to point out the need for future projects and works, which take these guidelines and recommendations into account and, through the implementation of personalized, state-of-the-art designs and the interdisciplinary collaboration, help to improve the feasibility and acceptance of exergames as a beneficial tool in the context of geriatric training and rehabilitation in general as well as for exergames for HIIT training.

Public policy makers bear responsibility in the context of supporting healthy ageing [166] and must recognise the needs for prevention by working towards environments, societies, and building infrastructure that facilitate active living of seniors. Innovative public health policy should allocate attention to technology, in terms of advanced instruments for healthcare and in terms of support that can be provided to supporting performance of everyday activities of older individuals. Although technology is permeating our everyday lives, most solutions target tech-savvy people, e.g., persons "well informed about or proficient in the use of modern technology, especially computers [https://en.oxforddictionaries.com/definition/us/tech-savvy]," and do not specifically focus on older users [166].

## Conflicts of Interest

M. A. McCaskey and A. Schättin have no conflicts of interest to report. E. D. de Bruin and A. L. Martin-Niedecken are involved in research supporting the development of different ICT-based technologies. E. D. de Bruin was a cofounder of Dividat, the spin-off company that developed the video step platform discussed as an example in this perspective review, and is associated with the company as an external advisor. No revenue was paid (or promised to be paid) directly to E. D. de Bruin or his institution over the 36 months prior to submission of the work. A. L. Martin-Niedecken was the initiator and lead of the R&D project on "Plunder Planet," which is also discussed as an example in this paper, and is cofounder of Sphery, a company which focuses on the development of playful fitness training settings.

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*Research Article*

# Effects of Two Types of 9-Month Adapted Physical Activity Program on Muscle Mass, Muscle Strength, and Balance in Moderate Sarcopenic Older Women

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The present study aimed to evaluate the effects of two types of 9-month adapted physical activity (APA) program, based on a muscle reinforcement training and a postural training, respectively, on muscle mass, muscle strength, and static balance in moderate sarcopenic older women. The diagnosis of sarcopenia was done in accordance with measurable variables and cut-off points suggested by the European Working Group on Sarcopenia in Older People (EWGSOP). Seventy-two participants were randomly assigned to two groups: the muscle reinforcement training group (RESISTANCE) (n=35; 69.9 ± 2.7 years) and the postural training group (POSTURAL) (n=37; 70.0±2.8 years). Body composition, muscle mass, skeletal muscle mass index (SMI), and handgrip strength (HGS) were evaluated for sarcopenia assessment, whereas Sway Path, Sway Area, Stay Time, and Spatial Distance were evaluated for static balance assessment. Sixty-six participants completed the study (RESISTANCE group: n=33; POSTURAL group: n=33). Significant increases of muscle mass, SMI, and handgrip strength values were found in the RESISTANCE group, after muscle reinforcement program. No significant differences appeared in the POSTURAL group, after postural training. Furthermore, RESISTANCE group showed significant improvements in static balance parameters, whereas no significant differences appeared in the POSTURAL group. On the whole, the results of this study suggest that the APA program based on muscle reinforcement applied on moderate sarcopenic older women was able to significantly improve muscle mass and muscle strength, and it was also more effective than the applied postural protocol in determining positive effects on static balance.

## 1. Introduction

The older population in the world is predicted to increase by threefold within 50 years, from 600 million people in 2000 to over two billion in 2050. This increase may be viewed as one of society's greatest achievements, but preserving older adults' independence and quality of life remains one of the major clinical and public health challenges [1]. A severe change associated with aging is the progressive and apparently inevitable process of loss of muscle mass and strength [2] referred to as sarcopenia [3]. Although consensus definition and diagnosis criteria have not been reached, the bidimensional nature of sarcopenia is increasingly accepted, encompassing both the quantitative and qualitative declines of skeletal muscle and being characterized by a loss of muscle mass, strength, and power [4, 5]. This condition, which involves primarily women [6], has been associated with the atrophy of fast twitch type II muscle fibers and the substitution of functional tissues by

Table 1: Participant characteristics at baseline. Data are means ± SD.

| | RESISTANCE (n=35) | POSTURAL (n=37) | p-value |
|---|---|---|---|
| Age (years) | 69.9±2.7 | 70.0±2.8 | n.s. |
| Height (cm) | 1.62±0.02 | 1.59±0.01 | n.s. |
| Body mass (kg) | 63.86±1.75 | 63.77±2.15 | n.s. |
| Body mass index (kg/m$^2$) | 24.34±0.72 | 25.23±0.86 | n.s. |
| Handgrip strength (kg) (mean of the two sides) | 17.84±4.97 | 17.86±5.3 | n.s. |

adipose and fibrotic tissues that have reduced rates of protein synthesis, thus leading to reduced muscle efficiency [7].

The impaired state of health induced by sarcopenia is closely related to a risk of adverse outcomes such as physical disability, poor quality of life, impaired ability to perform activities of daily living [8, 9], and, mostly important, risk of falls and fractures, which represent the main causes of a downward spiral of loss of confidence and social withdrawal, which may ultimately lead to loss of independence [10]. The decrease in maximal muscle strength could be a main cause of postural instability [11], and the consequent reduced ability of old adults to adequately react to unexpected perturbations and to successfully regain balance is important intrinsic risk factor for falling [12–14].

Exercise has been shown to reduce the incidence of falls by 13% to 40%, which has led to a broad consensus among experts that older adults should be offered exercises that incorporate elements of balance and strength training [15]. Pieces of evidence support the notion that regular physical activity, in combination with appropriate nutritional support, is the most effective strategy for improving sarcopenia and physical function and preventing disability [16]. There are four types of exercises recommended in adapted physical activity (APA) for older adults: aerobic exercises, progressive resistance training, flexibility exercises, and balance training [17]. Particularly, progressive resistance training has been demonstrated to attenuate development of sarcopenia, by improving muscle size and function, reducing balance and flexibility problems, and reducing also the risk of development of other sarcopenia-related comorbidities [18]. The role of exercise in sarcopenia was investigated in several studies [19–22], but to the best of our knowledge, no standardized training protocol has been developed for healthy older people to induce positive quantitative and qualitative effects on muscle function and to improve balance. The aim of this study was to evaluate the effects on muscle mass and muscle strength and on static balance of two types of 9-month adapted physical activity (APA) programs based on muscle reinforcement training and postural training [23], respectively, in moderate sarcopenic older women.

## 2. Materials and Methods

*2.1. Participants.* Initially, 82 potential participants were assessed for eligibility from the community through advertisements in the notice board of the Public Health Service ASL 4 Chiavari, Italy, and in the local newspaper and the screening period was conducted between August and September 2016.

The recruitment process consisted of a medical evaluation to assess their good health and the absence of any contraindication to participation in adapted physical activity programs.

Participants were required to be at least 65 years of age and they were excluded if they had a pacemaker (due to the use of bioelectrical impedance analysis) or previous health problems such as neurological or cardiovascular diseases that would limit participation in the APA programs.

During enrolment, 10 potential participants were excluded, because 6 did not meet inclusion criteria and the other 4 declined to participate.

At the end of the recruitment, 72 participants were enrolled for the study and they were randomly divided into two groups assigned to one of the two APA programs: muscle reinforcement training group (RESISTANCE) (n=35) and postural training group (POSTURAL) (n=37). Two out of 35 participants of the RESISTANCE group and 4 out of 37 participants of the POSTURAL group did not complete the training programs. A flow diagram of the study is reported in Figure 1.

The participant characteristics of the two groups at baseline are reported in Table 1.

The experimental protocol was approved by the Ethics Committee of the University of Genoa and, after explaining the aim and the procedure of the study, all participants gave their informed consent for intervention.

*2.2. Sample Size.* Estimation of sample size for this investigation was performed using handgrip strength as one of our primary outcome measures. Sample size was estimated combining the normative data and the genuine change in grip strength determined in previous works [24, 25]. These assumptions generated a desired sample size of at least 30 participants. However, we recruited 72 participants, 35 in the RESISTANCE group and 37 in the POSTURAL group, to allow for drop-out during the intervention period.

*2.3. Testing Procedures.* Testing was conducted before (T0) and after (T1) the APA intervention.

*2.3.1. Food Questionnaire.* Before starting the APA program, all the participants were asked to answer to a food questionnaire in order to check a balanced daily intake of nutrients.

*2.3.2. Anthropometry and Body Composition.* Body mass and height were measured to the nearest 0.1 kg and 0.5 cm, respectively, using a mechanical column scale and a stadiometer. Body composition evaluation was performed using a bioimpedance scale (InBody 320, GBC BioMed, NZ)

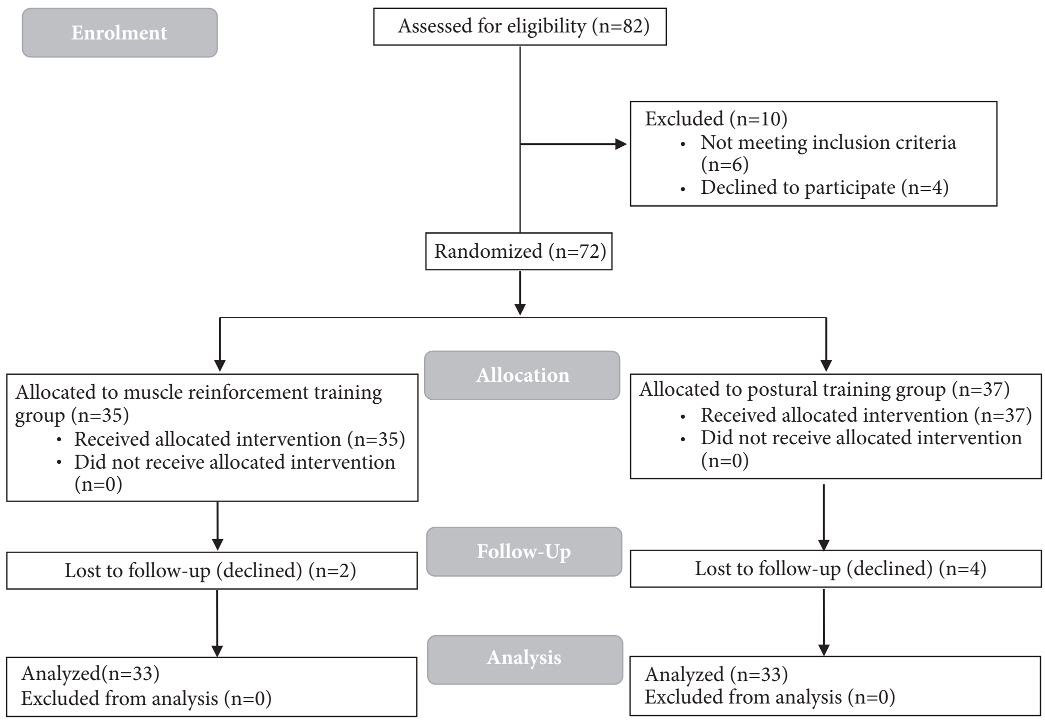


Figure 1: Flow diagram of the study.

at least 2 hours after the meal and participants were required to wear light clothing with bare feet. After ensuring proper feet placement and hold of hand electrodes, participants were instructed to stay relaxed during the measurements, maintaining a normal standing position, with arms and legs extended. The parameters used to measure the body composition were weight (Kg), body mass index (BMI), and muscle mass (Kg).

The skeletal muscle mass (SM) was calculated with the regression equation (1) as described by Janssen et al. [26]:

$$\mathrm{SM}\ (\mathrm{kg}) = \left[\left(\frac{\mathrm{Ht}^2}{R} \times 0.401\right) + (\mathrm{gender} \times 3.825) + (\mathrm{age} \times -0.071)\right] + 5.102 \quad (1)$$

where Ht is height in centimeters; $R$ is BIA resistance in ohms; for gender, men = 1 and women =0; and age is in years.

The same authors defined SM index (SMI) considering SMI as SM (Kg), obtained from the above-mentioned prediction equation, adjusted for the squared height (SM/height$^2$, Kg/m$^2$).

*2.3.3. Sarcopenia Assessment.* Sarcopenia was diagnosed in accordance with EWGSOP criteria [8]. Particularly, we adopted the following measurable variables and cut-off points to diagnose sarcopenia presented in the above cited EWGSOP report: SMI, using BIA predicted skeletal muscle mass (SM) equation (SM/height$^2$), and the handgrip strength. Concerning SMI, the cut-off values used by the EWGSOP were moderate sarcopenia when SMI is between 8.51 and 10.75 kg/m$^2$ (men) or 5.76 and 6.75 kg/m$^2$ (women) and severe sarcopenia when SMI is ≤8.50 kg/m$^2$ (men) or ≤5.75 kg/m$^2$ (women) [27]. HGS cut-off values for the diagnosis of sarcopenia were ≤ 30 kg (men) and ≤ 20 kg (women) [8, 27]. All the participants in our study showed a moderate sarcopenia. Muscle strength was assessed by handgrip strength, a proxy index of overall muscle strength [28], measured with a Jamar hydraulic hand-held dynamometer (Sammons Preston, Rolyan, Bolingbrook, IL, USA) with the second handle position for all participants and expressed in kg [29]. Additionally, the Jamar hand dynamometer has been shown to have acceptable concurrent validity in young and adults [30, 31]. Participants seated on a chair with their feet flat on the floor, holding the handgrip with their wrist in line with their elbow, and they were instructed to press the dynamometer as hard as possible. Participants performed a maximum voluntary isometric contraction of finger flexor muscles, three measurements were taken with 10-second intervals between each trial for both body sides (dominant and nondominant), and mean value of the two body sides was indicated as whole body handgrip strength (HGS). The maximum values were considered for statistical analysis [32].

*2.3.4. Static Balance.* All participants performed the balance assessment on a static force platform (ARGO, RGM Medical Devices S.p.A., Genoa, Italy). The ARGO static force platform has a large platform surface area (600 x 600 mm) and a high sampling frequency (100 Hz). This platform, even with short measurement times, allows a reliable harmonic analysis of sway density parameters [33].

Participants were asked to stand with their feet joined and parallel on the barefoot, with their arms hanging loose at sides, and with closed mouth and unclenched teeth, looking at a target placed at their eye level about 1 m in front of them, in an acoustically isolated room and darkened when they were in closed eyes (CE) condition. Participants executed two trials in two different randomized modalities: with open eyes (OE) and with closed eyes (CE). Each assessment lasted 40 seconds preceded by a 5-second waiting time that allowed the participants to become familiar with the position, thus reducing the adaptation artifact [34, 35]. The parameters used to evaluate the static balance were as follows:

(1) Sway Path (SP) (mm/s), defined as Length of the Sway Path, normalized with respect to the duration of the acquisition interval;

(2) Sway Area (SA) ($mm^2/s$), defined as the Sway Area by the radius connecting each subsequent point of the statokinesigram to the average position of the Centre of Pressure (COP), normalized with respect to the duration of the acquisition interval;

(3) Stay Time (ST) (s), the mean Stay Time spent by the COP trace in the neighbourhood of each peak, over the observed sway of each subject;

(4) Spatial Distance (SD) (mm), the average displacement of the COP trace between one peak and the next one.

*2.4. APA Exercises.* The two different APA programs were performed twice a week, for 36 weeks, and every session lasted for 60 minutes. The APA sessions were performed in a gym and conducted by an instructor in groups of a maximum of 20 participants.

Each session of the muscle reinforcement training was divided into three phases: (1) standing 15′ warming up and motor coordination exercises; (2) standing/on the ground 30′ muscle toning at low/moderate intensity for different muscular districts (primarily abdominal and both lower and upper limbs) with low weight loads (0.5, 1, or 1.5Kg); (3) cooling down 15′ and relaxation/stretching of the muscle systems with specific exercises [23].

Each session of the postural training was divided into three phases: (1) standing 10′-15′ cardiovascular activation, shoulder and coxofemoral joints mobilization, lower limbs reinforcement; (2) sitting 10′-15′ neck and shoulders mobilization; (3) on the ground, 5-30′ spine mobilization, abdominal muscles reinforcement, gluteal and spine extensor muscles reinforcement, spine stretching, hamstring and psoas muscle reinforcement and self-stretching, and final relaxation [23].

Both muscle reinforcement exercises and postural exercises were adapted to the participant's abilities and were progressive in repetitions and difficulties over time.

*2.5. Data Analysis.* Shapiro-Wilcoxon tests were used to evaluate whether the outcome variables were normally distributed.

SM, SMI, and HGS of the two groups were normally distributed and were compared before (T0) and after (T1) the intervention by means of a repeated measure ANOVA, with TIME (2 levels, T0 and T1), as within-subject factor, and GROUP (2 levels, RESISTANCE and POSTURAL), as between-subject factor. Newman-Keuls post hoc test was used to evaluate significant interactions.

Static balance data of the RESISTANCE and POSTURAL groups acquired with CE and OE were not normally distributed. Therefore, Mann-Whitney tests were used to evaluate differences between groups at each time epoch (T0 and T1), whilst Wilcoxon tests were applied to assess changes in each group. Significance for all procedures was set at a level of 0.05.

Data are presented as mean ± SD for normally distributed data and as median associated with the interquartile range for not normally distributed data.

## 3. Results

*3.1. Effects on Sarcopenia.* The statistical analysis on lean mass expressed as % of the total weight and in kg showed a significant effect of the factor TIME (%: $F(1,64)=22.70$, $p<0.001$; kg: $F(1,64)=18.25$, $p<0.0001$). Furthermore, a significant TIME∗GROUP interaction appeared (%: $F(1,64)=24.82$, $p<0.0001$; kg: $F(1,64)=29.53$, $p<0.0001$), and post hoc comparisons revealed a significant increase of lean mass values from T0 to T1 only in the RESISTANCE group (mean±SD; %: T0=30.10±8.44 %, T1=33.11±7.29 %; kg: T0=19.50±6.59 kg, T1=21.25±6.05 kg), whilst not significant differences appeared in the POSTURAL group (mean±SD; %: T0=30.52±5.93 %, T1=30.45±5.51 %; kg: T0=19.85±7.39 kg, T1=19.63±6.49 kg).

Data concerning skeletal muscle mass (SM) values before (T0) and after (T1) the intervention program are represented in Figure 2(a). The results of the statistical analysis showed a significant main effect of the factor TIME ($F(1,64)=17.76$, $p<0.001$) and a significant TIME∗GROUP interaction ($F(1,64)=29.04$, $p<0.0001$). Post hoc test revealed a significant increase of SM value only in the RESISTANCE group (mean±SD: T0=17.31±1.16 kg, T1=19.02±6.58 kg, $p<0.001$), whilst no differences were found between T0 and T1 in the POSTURAL group (mean±SD: T0=17.59±7.31 kg, T1=17.53±6.39 kg).

The statistical analysis on SMI values showed a significant effect of the factor TIME ($F(1,64)=19.89$, $p<0.0001$) and a significant TIME∗GROUP interaction ($F(1,64)=29.20$, $p<0.0001$). A significant increase of SMI values was found only after muscle reinforcement program (mean±SD: T0=6.48±2.75 $kg/m^2$, T1=7.36±2.31 $kg/m^2$, $p<0.001$). No significant differences appeared after POSTURAL training (mean±SD: T0=6.74±2.46 $kg/m^2$, T1=6.67±2.17 $kg/m^2$) (see Figure 2(b)).

Results of the handgrip test are represented in Figure 2(c). The statistical analysis on the mean of HGS of both hands showed a significant effect of the factor TIME ($F(1,64)=7.94$, $p<0.01$) and a significant interaction between TIME and GROUP ($F(1,64)=14.37$, $p<0.001$). A significant increase of HGS values was found only in the RESISTANCE group (mean±SD: T0=17.84±4.91 kg, T1=19.86±5.22 kg, $p<0.001$) and no differences appeared in the POSTURAL group (mean±SD: T0=17.84±5.25 kg, T1=17.55±4.85 kg).

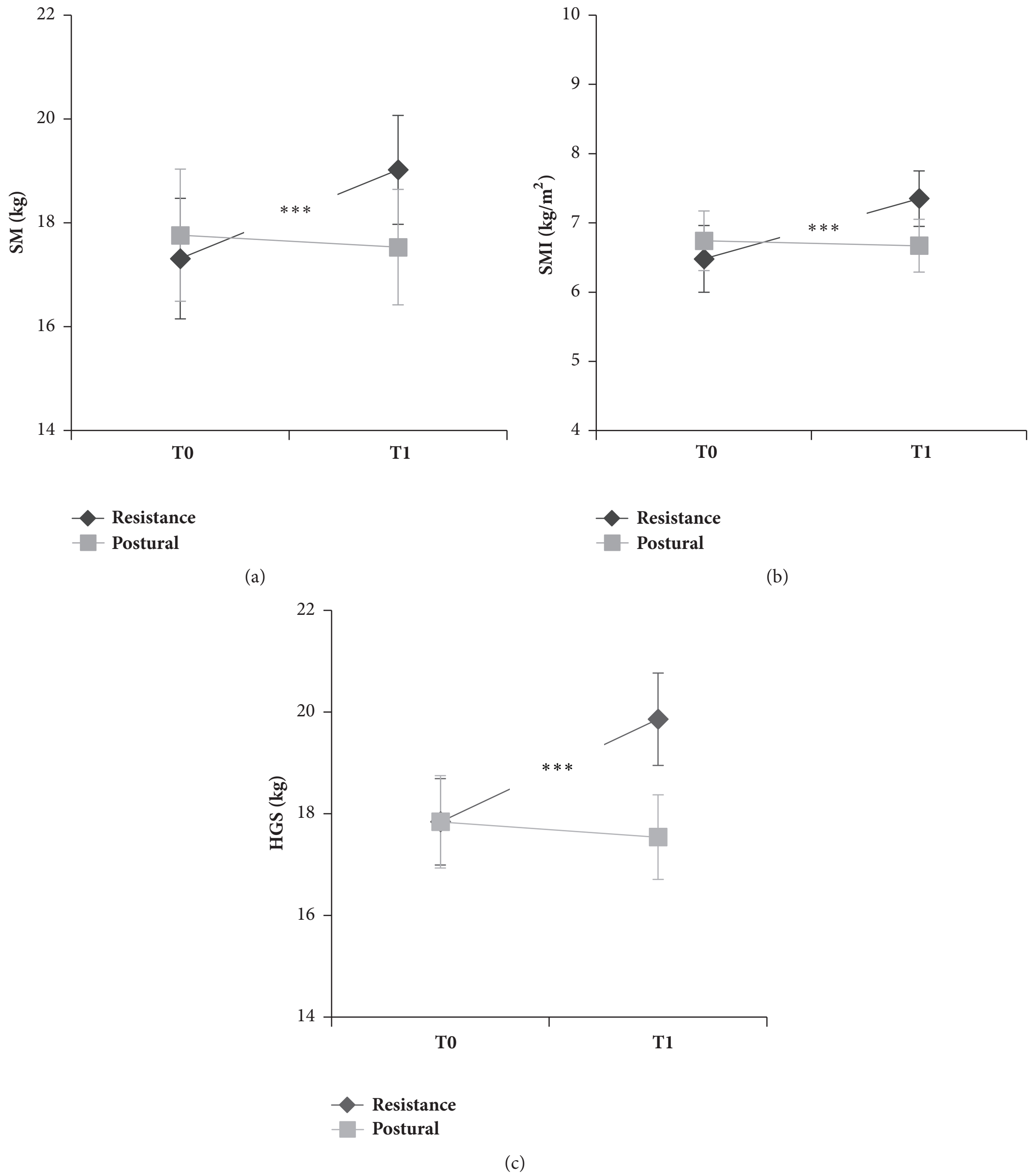


Figure 2: Values of skeletal muscle mass (SM) (a), skeletal muscle mass index (SMI) (b), and handgrip strength (HGS) (c) of the muscle reinforcement training group (RESISTANCE, black lines) and postural training group (POSTURAL, grey lines) before (T0) and after (T1) the intervention. Values are means ± SE. $***$ indicates $p<0.001$.

*3.2. Effects on Balance Parameters.* The static balance data are represented in Figure 3 and the descriptive statistics are reported in Table 2. The results of the Mann-Whitney test comparing the parameters of the two groups showed significant differences after the treatment, whilst no differences were observed at baseline. Furthermore, the results of the Wilcoxon test comparing the parameters related to each group acquired in T0 and T1 epochs revealed significant differences between the effects evoked in the two groups. Hereafter we will report only significant results.

*3.2.1. Sway Path (SP).* Wilcoxon tests comparing the Sway Path acquired with close eyes (SP CE) before and after treatments revealed a significant decrease of its value after muscle reinforcement training (*Z=3.53, p<0.001*) and a significant increase after the postural training (*Z=3.29, p<0.001*). When the test was repeated with eyes open a significant decrease was observed after muscle reinforcement training (*Z=3.94, p<0.001*), whilst no differences were observed in the POSTURAL group. The different effects of the two treatments appeared also when comparing Sway Path values at T1 in both

Table 2: Static balance data expressed as median associated to the interquartile range. CE: closed eyes; OE: open eyes; n.s.: not significant.

| | RESISTANCE training group | | | POSTURAL training group | | | RESISTANCE vs. POSTURAL |
|---|---|---|---|---|---|---|---|
| | T0 | T1 | p | T0 | T1 | p | |
| **Sway path (mm/s)** | | | | | | | |
| **CE** | 16.78 [13.16,24.21] | 15.44 [12.13, 20.59] | <0.001 | 19.57 [14.02, 24.96] | 23.59 [15.82, 29.42] | <0.001 | T0: n.s.; T1: p<0.01 |
| **OE** | 11.76 [9.27, 14.65] | 9.75 [7.58, 11.76] | <0.001 | 12.13 [10.15, 13.68] | 11.23 [10.16, 13.68] | n.s. | T0: n.s.; T1: p<0.05 |
| **Sway area ($mm^2/s$)** | | | | | | | |
| **CE** | 40.64 [28.75, 59.39] | 26.55 [16.85, 49.96] | <0.001 | 44.38 [20.04, 68.56] | 52.25 [27.13, 76.98] | n.s. | T0: n.s.; T1: p<0.01 |
| **OE** | 19.36 [12.84, 32.15] | 12.68 [9.14, 17.11] | <0.001 | 18.99 [11.58, 27.49] | 17.74 [13.50, 24.89] | n.s. | T0: n.s.; T1: p<0.05 |
| **Stay time (s)** | | | | | | | |
| **CE** | 0.65 [0.49, 0.73] | 0.87 [0.59, 1.10] | <0.001 | 0.59 [0.43, 0.88] | 0.48 [0.35, 0.69] | <0.05 | T0: n.s.; T1: p<0.001 |
| **OE** | 1.11 [0.81, 1.31] | 1.37 [1.01, 1.85] | <0.001 | 0.99 [0.87, 1.38] | 1.09 [0.89, 1.35] | n.s. | T0: n.s.; T1: p<0.01 |
| **Spatial distance (mm)** | | | | | | | |
| **CE** | 6.71 [4.51, 8.71] | 4.65 [3.07, 6.97] | <0.001 | 6.19 [3.86, 9.41] | 7.70 [4.79, 10.61] | <0.01 | T0: n.s.; T1: p<0.01 |
| **OE** | 3.78 [2.55, 4.31] | 2.61 [1.99, 3.41] | <0.001 | 3.28 [2.57, 4.33] | 3.06 [2.74, 4.15] | n.s. | T0: n.s.; T1: p<0.05 |

conditions (CE and OE); indeed, SP in RESISTANCE group was significantly lower than SP in POSTURAL group (CE: *Z=-3.23, p<0.01*; OE: *Z=-2.46, p<0.05*). Data are represented in Figures 3(a) and 3(b).

*3.2.2. Sway Area (SA).* In the RESISTANCE group Sway Area decreased significantly after the treatment in both conditions (CE: *Z=5.01, p<0.001*; OE: *Z=4.89, p<0.001*), whilst no differences were observed in the POSTURAL group. Furthermore, the Mann-Whitney test comparing SA at T1 showed in both conditions that SA associated with the RESISTANCE group was significantly lower than that associated with the POSTURAL group (CE: *Z=-2.96, p<0.01*; OE: *Z=-2.23, p<0.05*). Data are represented in Figures 3(c) and 3(d).

*3.2.3. Stay Time (ST).* After the intervention, ST increased significantly only in the RESISTANCE group in both conditions (CE: *Z=4.01, p<0.001*; OE: *Z=4.69, p<0.001*), whilst a significant decrease after the postural training was observed only in CE condition (*Z=2.49, p<0.05*). The comparison between the two groups at T1 showed that ST associated with RESISTANCE group was higher than that in the POSTURAL group in both conditions (CE: *Z=3.65, p<0.001*; OE: *Z=2.64, p<0.01*). Data are represented in Figures 3(e) and 3(f).

*3.2.4. Spatial Distance (SD).* In the RESISTANCE group the results of the Wilcoxon tests showed a significant decrease of SD value in both conditions (CE: *Z=4.44, p<0.001*; OE: *Z=4.74, p<0.001*), whilst a significant increase was obtained after the postural training only in CE condition (*Z=2.72, p<0.01*). Data are represented in Figures 3(g) and 3(h).

## 4. Discussion

The results of this study, performed in moderate sarcopenic older women, demonstrate that the RESISTANCE group showed significant improvements in muscle mass and function after the proposed muscle reinforcement program, whereas no significant differences were found in the POSTURAL group, after the adopted postural training. Furthermore, the muscle reinforcement program was able to induce in RESISTANCE group significant improvements in static balance parameters, whilst no significant differences in these values were found in the POSTURAL group, after the postural training. On the whole, the proposed muscle reinforcement program was able to induce positive effects both on sarcopenia and on postural parameters.

Sarcopenia is closely related to a risk of adverse outcomes, including poor quality of life and impaired ability to perform activities of daily living [8, 9], but, mostly important, it increases the risk of falls and fractures [10]. At the same time, the decrease in muscle strength could be also an important cause of postural instability [11], and, therefore, it represents an intrinsic risk factor for falling, by reducing the ability of older adults to adequately react to unexpected perturbations and to successfully regain balance [12–14].

Structured physical activity interventions are known to delay the onset of disability in older adults, improving clinical outcomes such as physical performance, gait speed, overall survival, fall risk, and quality of life [36]. So far, there are heterogeneous findings regarding the effects of exercise interventions on the maintenance of functional fitness, including sarcopenia [37].

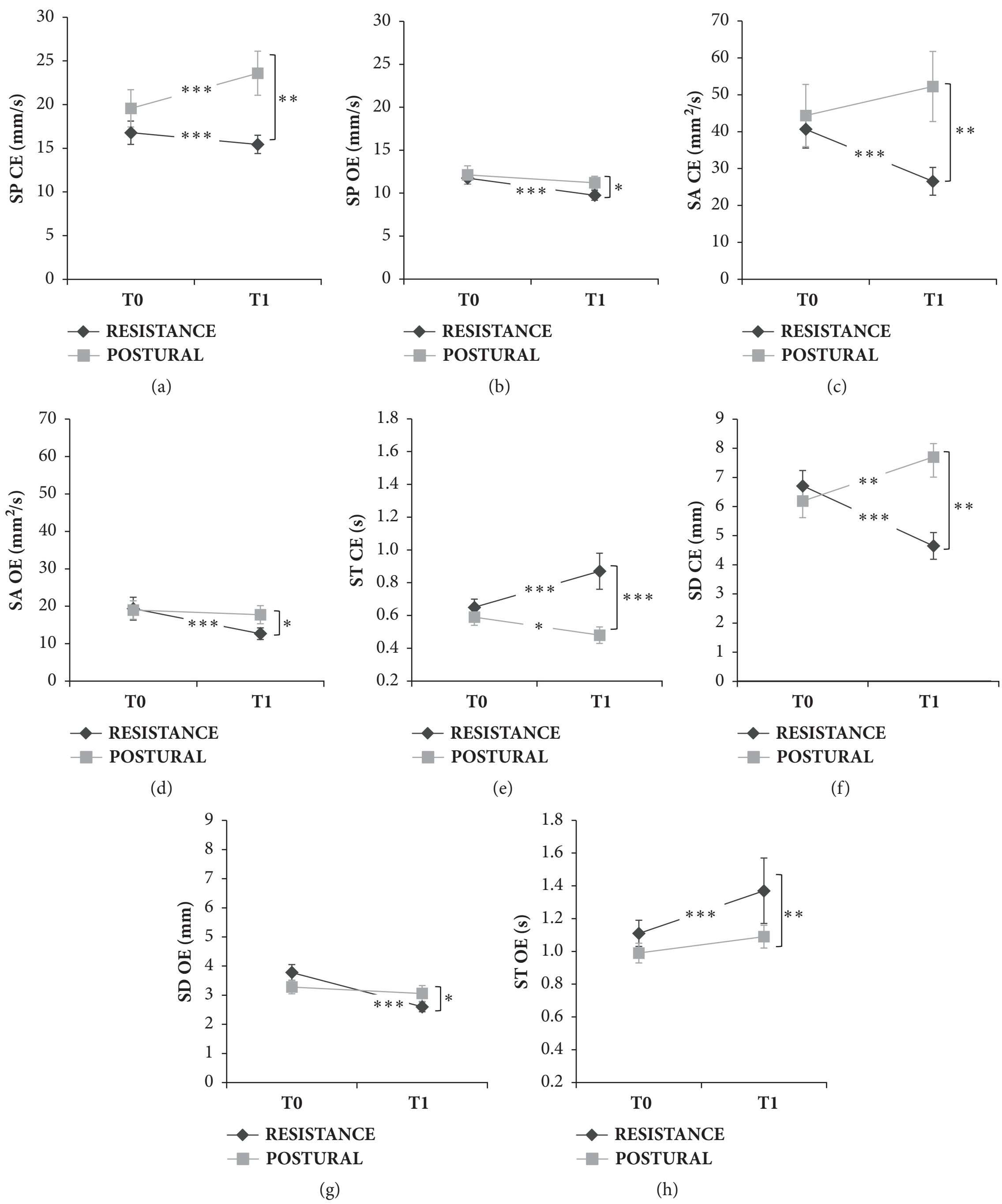


FIGURE 3: Static balance data of the RESISTANCE and POSTURAL groups, acquired with closed eyes (CE) and open eyes (OE) before (T0) and after (T1) the intervention. SP: Sway Path; SA: Sway Area; ST: Stay Time, and SD: Spatial Distance. Values are medians ± SE. ∗∗∗ indicates $p<0.001$, ∗∗ indicates $p<0.01$, and ∗ indicates $p<0.05$.

Two milestone studies have been performed to standardize exercise interventions and elders related outcome measurements [38–40]. Namely, the LIFE study was aimed at investigating the effectiveness of physical interventions in sedentary community dwelling older adults without comorbidity. The main results indicated that the longitudinal improvement of functional fitness was a general positive end point by virtue of a structured moderate physical activity program compared with health education program. Although reduced major disability over 2.6 years was observed, high heterogeneity of important cut points was identified, representing a clinical important challenge.

The SPRINT study was also aimed at assessing longitudinal mobility disability prevention in older adults by virtue of combined nutritional and physical interventions to improve sarcopenia and physical frailty. This study was geared to produce systematic advancements in the management of frail older adults by a multifactorial set of interventions that included physical activity.

A recent systematic analysis has pointed out how exercise interventions are beneficial to body composition and muscle strength [41]. However, the training effect is generally inconsistent due to heterogeneity in exercise mode, duration, and intensity, which makes a generalization of training approaches impossible [42, 43].

To overcome this difficulty, we assigned a homogeneous group of seventy-two older women with moderate sarcopenia, according to EWGSOP criteria [8], to two types of 9-month adapted physical activity program: the first one focused on muscle reinforcement, and the second one focused on postural exercises. Due to the importance of a balanced diet for sarcopenic people [44], before starting the physical activity program all the participants were asked to answer to a self-administered food questionnaire that demonstrated that participants had a balanced daily intake of nutrients. We showed that the muscle reinforcement program significantly increased the absolute and the percent lean mass, the skeletal muscle mass (SM), and the skeletal muscle mass index (SMI), obtained by BIA predicted skeletal muscle mass (SM) equation (SM/height$^2$). Furthermore, this type of APA program applied to the RESISTANCE group significantly improved handgrip strength (HGS), a parameter that well correlates with leg strength [8], sarcopenia, and physical function [43, 44]. The improvements in muscle mass, SMI, and muscle strength can be considered clinically relevant because the participants moved from a condition of moderate sarcopenia at baseline to a condition of normality after the muscle reinforcement intervention, according to the criteria used to diagnose sarcopenia.

It has been reported that postural control is improved by balance exercise intervention, whereas strength exercises or multicomponent interventions do not significantly influence such postural measurements [45]. In this study we investigated the effects of a muscle reinforcement protocol in improving balance parameters, such as Sway Path, Sway Area, Stay Time, and Spatial Distance, and we compared these effects with those obtained in another group of moderate sarcopenic older women that underwent an APA program focused on a postural training. Our findings showed that our muscle reinforcement program was more beneficial than the postural intervention in improving balance parameters of moderate sarcopenic older women. Therefore, under our experimental conditions, the results of this study suggest that the improvement of parameters for static balance can be more effectively obtained by the enhancement of muscle strength and functioning than by a postural training. This is an important achievement that obviously deserves further in-depth analysis, including the coassessment of other postural parameters, as well as the evaluation of potential biases.

A limitation of this study is the inability to establish a clear dose-response relationship along with individual functional fitness trajectories, due to the lack of baseline comprehensive geriatric assessment and polypharmacy analysis. In addition, the lack of osteoporosis assessment could prevent an accurate evaluation of osteosarcopenia, a common clinical condition in older people correlated with adverse clinical outcomes. On the other hand, the strengths of the study lie in the real-world assessment of an older adult population by a standardized adapted physical approach like that proposed in our APA project. Another limitation of the study is that we did not assess functional improvements in balance after the intervention period. It would be interesting to investigate, in further studies, whether the observed effects after a period of specific muscle reinforcement training are accompanied also by functional improvements.

## 5. Conclusions

The present findings show the effectiveness of a muscle reinforcement program on muscle mass and function, as well as on static balance parameters in moderate sarcopenic older women, thus suggesting that this type of intervention could represent a significant approach to reducing important risk factors for falling, such as sarcopenia and balance impairments. However, the limitations of this study and the potential biases must be considered before drawing firm conclusions, and further studies are required to deeply evaluate the effectiveness of different types of adapted physical activity program in muscle mass and function and in balance. On the whole, this study allows moving a step forward in the understanding of the clinical beneficial effects of adapted physical activity in an older population. The longitudinal assessment of this population, including physical activity training adherence over time, that is part of an ongoing study and the inclusion of geriatric assessment parameters will help understanding the elders risk stratification, on the basis of functional fitness and frailty prevention.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

## Authors' Contributions

G. Piastra and L. Perasso contributed equally to the work

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*Research Article*

# Influence of the Physical Training on Muscle Function and Walking Distance in Symptomatic Peripheral Arterial Disease in Elderly

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*Introduction*. A typical symptom of chronic lower-limb ischaemia is lower-limb pain, which occurs during walking forcing the patient to stop, intermittent claudication (IC). Exercise rehabilitation is the basic form of treatment for these patients. *Aim.* The aim of this study was to compare the effectiveness of three types of physical training programmes conducted over a 12-week period in patients with chronic lower-limb arterial insufficiency. *Materials and Methods*. Ninety-five people qualified for the 3-month supervised motor rehabilitation programme, conducted three times a week. The respondents were assigned to three types of rehabilitation programmes using a pseudo-randomization method: Group I (TW), subjects undertaking treadmill walking training; Group II (NW), subjects undertaking Nordic walking training; Group III (RES+NW), subjects undertaking resistance and Nordic walking training. Treadmill test, 6 Minute Walk Test (6MWT), and isokinetic test were repeated after 3 months of rehabilitation, which 80 people completed. *Results*. Combined training (RES+NW) is more effective than Nordic walking alone and supervised treadmill training alone for improving ankle force-velocity parameters ($p<0.05$) in patients with intermittent claudication. Each of the proposed exercise rehabilitation programmes increased walking distance of patients with intermittent claudication ($p<0.05$), especially in 6MWT ($p=0.001$). Significant relationships of force-velocity parameters are observed in the maximum distance obtained in 6MWT, both in Group III (RES + NW) and in Group II (NW) at the level of moderate and strong correlation strength, which indicates that if the lower limbs are stronger the walking distance achieved in 6MWT is longer. *Conclusions*. Given both the force-velocity parameters and the covered distance, the training RES + NW gives the most beneficial changes compared to training TW alone and NW alone. All types of training increased walking distance, which is an important aspect of the everyday functioning of people with IC.

## 1. Introduction

Atherosclerotic arterial occlusive disease is the most common cause of peripheral arterial disease (PAD) and lower-limb ischaemia. As a result of the narrowing/occlusion of leg arteries and consequently skeletal muscle hypoxia, the muscles' ability to work decreases [1, 2]. One of the most common symptoms of PAD is intermittent claudication, which manifests itself in lower extremity muscle pain during walking, which subsides after short rest [3]. Repeated episodes of muscle pain contribute to the lowering of physical activity of people with PAD, contributing to disease progression. The chronic ischaemic process leads to a significant reduction in muscle strength, which is most often the result of muscle atrophy and metabolic changes in muscle fibres. In patients with progressive ischaemic disease of the lower limbs, structural changes in skeletal muscles develop due to the process of denervation, myocyte depletion, and selective loss of type II fibres against type I fibres, along with a reduction in the number of motor units [1, 4, 5].

Physical exercise is considered the most important component of the comprehensive treatment process in patients with chronic lower-limb ischaemia, as confirmed in many clinical trials [6–17].

According to the ACC/AHA (American College of Cardiology/American Heart Association) guidelines for the treatment of patients with intermittent claudication, a rehabilitation programme lasting three to six months for 30–45 minutes at a time three times a week is recommended [18, 19]. It is also emphasized that walking training is an integral part of the conservative treatment in combination with prophylaxis and pharmacotherapy.

If conservative treatment does not bring the desired results, endovascular or surgical revascularization is carried out [20].

The purpose of physical training in patients with PAD is to enhance muscle strength, extend the distance of claudication, improve exercise tolerance, haemodynamic parameters, neuromuscular coordination, and quality of life, and postpone surgical treatment [3, 21–23]. At present, the gold standard of rehabilitation for patients with intermittent claudication is supervised walking training on a treadmill. The TASC II (*Trans-Atlantic Inter-Society Consensus II, 2007*) recommendations propose a programme in which both the treadmill angle and speed should be suitably adapted to the patient's abilities, so that between the third and fifth minute of walking, pain of medium intensity occurs (pain intensity according to the ESC scale where 1 means no pain and 5 is maximum pain intensity) [18].

Recently, there have been many scientific publications on Nordic walking training, although it has not been mentioned in recommendations for the rehabilitation process of this group of patients [24]. Briefly, this form of movement is walking with the use of poles, based on a natural human gait. The advantage of Nordic walking training over other aerobic forms (marching, jogging) is higher oxygen consumption and energy expenditure with a lower level of perceived fatigue [25–27]. Upper- and lower-body parts are involved, improving 70–90% of the entire body's muscles [28]. Nordic walking is a simple and easily accessible physical activity, recommended for people of all ages, mainly due to the low risk of falling and injury.

It has been confirmed that regular Nordic walking training in the group of people with PAD influences the claudication distance by extending it [29–32], it improves exercise tolerance [30, 33], and it reduces ischaemic pain [30, 31, 33].

Another type of training dedicated to patients with intermittent claudication is resistance training. Strengthening the muscles of the lower limbs slows down the degenerative processes resulting from chronic ischaemia, as confirmed in studies by McDermott et al. [34]. It turns out that systematically undertaken resistance training increases the volume of muscle fibres of both type I and type II, increases the density of capillaries and muscle strength in general, and also extends the distance of claudication [35–37]. Despite the beneficial effects of resistance exercise, they still attract little attention, both in clinical practices and in scientific research regarding PAD issues.

At each and every stage of the rehabilitation process, physical exercises do bring unquestionable health benefits, in both a somatic and mental capacity. One of the most frequently achieved ambulatory rehabilitation outcomes in patients with intermittent claudication is the extension of claudication distance, which is of great importance in these patients' daily living. However, the exact mechanisms responsible for this are still not fully understood [8, 38].

*Study Aim*. The aim of this study was to compare the effectiveness of three types of physical training programmes conducted over a 12-week period in patients with chronic lower-limb arterial insufficiency.

## 2. Materials and Methods

This publication is part of a project called "WROVASC–An Integrated Cardiovascular Centre", which was cofinanced by the European Regional Development Fund (POIG.01.01.02-02-001/08-03), within the Operational Programme Innovative Economy, from 2007 to 2013. The study was carried out at the Research and Development Centre of the Regional Specialist Hospital in Wroclaw.

The study was approved by the Ethics Committee of the Medical University of Wroclaw, Poland (Ref. KB-130/2008).

*2.1. Subjects.* Recruitment for the exercise rehabilitation program was carried out at healthcare facilities in Wroclaw during "White Saturdays" on which the patients had free access to consultations with angiologists. The information about "White Saturdays" was promoted by local newspapers, TV, radio, posters, and leaflets.

Over one thousand people were examined, of which 545 reported vascular symptoms. Peripheral vascular disorders (by ABI and Doppler ultrasound) were diagnosed in 219 people. The qualification to the exercise training was continued by Department of Rehabilitation. 144 persons of 219 qualified have agreed to participate in the exercise rehabilitation program.

Inclusion criteria for the exercise training were as follows: over 50 years of age, documented PAD, and lower-limb ischaemia and intermittent claudication distance of 30-400 meters (Fontaine's classification IIa and IIb) stable for at least 3 months, ABI<0.9, sound clinical condition of the patient, and written consent of the patient to participate in the project.

The exclusion criteria included PAD Fontaine stage I (painless distance, no impairment of walking capacity), stage II with walking distance > 400 m and Fontaine stage III/IV (pain at rest / trophic ulcer), uncontrolled arterial hypertension and/or diabetes, decompensated congestive heart failure, level of subjective fatigue above 7 points according to the 10-point Borg scale, cardiovascular incidents (MI, stroke) in the last year prior to the rehabilitation program, revascularization procedures performed during the last 3 months, generally poor patient health, incapacity to perform functional tests in motor terms, mental illness, and participation in another scientific research program.

The patients were qualified by angiologists, cardiologists, and physiotherapists.

A detailed process of patient recruitment for the rehabilitation program is presented in Figure 1. Finally, 95 people qualified for the 3-month supervised exercise rehabilitation programme, conducted three times a week. The respondents were assigned to three types of training using a pseudo-randomization method.

(i) Group I (TW): subjects undertaking treadmill walking training

(ii) Group II (NW): subjects undertaking Nordic walking training

(iii) Group III (RES+NW): subjects undertaking resistance and Nordic walking training

Clinical and functional examinations were repeated after 3 months of rehabilitation; 80 people completed the training programs and final testing (Figure 1).

Functional tests, the results of which are presented in this paper, were carried out in the Department of Functional Studies of the Physiotherapy Department at the University of Physical Education in Wroclaw with the assistance of a cardiologist. Characteristics of patients qualified for the rehabilitation programme are presented in Table 1.

### *2.2. Functional Tests*

*2.2.1. Stress Test on a Treadmill.* The test was conducted on a treadmill with a 12-lead electrocardiogram (ECG) and a blood pressure (BP) reading. A Gardner–Skinner protocol was used for the tests, in which belt speed was constant at 3.2 km/h (2.0 mph) and the angle of inclination changed by 2% every 2 minutes. The exercise test was carried out until a maximum claudication pain was reached, fatigue or shortness of breath was reported, or if heart disorders or other disturbing symptoms occurred. Heart rate (HR) and BP measurements were taken before and after each exercise test. The test was performed twice during the morning hours with electrocardiography monitoring in a period of one week. Initial distance of claudication and maximal distance were included in the analysis.

*2.2.2. 6-Minute Walk Test (6 MWT).* A 6-minute walk test was conducted in accordance with the American Thoracic Society (ATS) Statement recommendations on a marked 30-meter corridor. The test consisted of the patient's walking at a comfortable pace that he or she generally use on a daily basis. In the situation of maximum pain, which forced the patient to stop during the test, the measured time was not halted. Expressed in meters, the result of the test consisted of the distance of claudication and maximal distance. In this study maximal distance was analysed. The degree of subjective level of fatigue was assessed according to Borg's 10-degree scale. Before the test, subjects were informed that they could rest during the test in a standing or sitting position, if they experienced intensifying symptoms of exercise intolerance. If during the test severe symptoms of exercise intolerance occurred, which did not disappear despite a temporary rest, the test was immediately stopped. Intensifying symptoms of exercise intolerance that could interrupt the test included shortness of breath, dizziness, blurred vision, sudden sweating, cyanosis, tinnitus, loss of verbal control, general weakness, and fatigue. Before and after the 6MWT test, BP and HR measurements were taken using an automatic sphygmomanometer [39].

*2.2.3. A Study of Force-Velocity Parameters of Flexor and Extensor Muscles in the Knee and Ankle Joints.* The study was carried out in order to objectively assess the strength of flexor and extensor muscles of the knee joint as well as dorsal and plantar flexor muscles of the ankle joint using a functional dynamometer (Biodex System 4 Pro).

The seat, dynamometer, and a suitable attachment were adjusted so that the tip of the dynamometer became an extension of the axis of rotation in the examined joint. For all respondents the same range of flexion and extension at 90° was determined with an adjustment of the force of gravity. The thigh and pelvis of the respondent were stabilized using straps attached to the chair, so as to eliminate movements in neighboring joints. The starting position was a maximum bending of the lower limb in the investigated joint. The appropriate test protocol was selected, in isokinetic conditions for concentric work.

Before starting the actual measurement, the subject performed three submaximal flexions and extensions and one maximum movement in order to become familiar with a given load. The following loads were applied: for the knee joint, respectively, 180, 60, and 120°/s were used, while for the ankle joint 60 and 120°/s were used. In each test, the respondent performed five alternating limb flexions and extensions in a given joint. It was imperative for participants to exert maximum muscle force in the shortest possible time for each movement. There was a 60-second break between subsequent attempts. During the test, muscle function parameters were recorded: peak torque (PT), total work (TW), and estimated average power (AP).

*2.2.4. Training Methods.* Physical rehabilitation took place in a 3-month cycle, 3 times a week (36 training units) with a 45-minute duration.

Patients participated in one of three types of training.

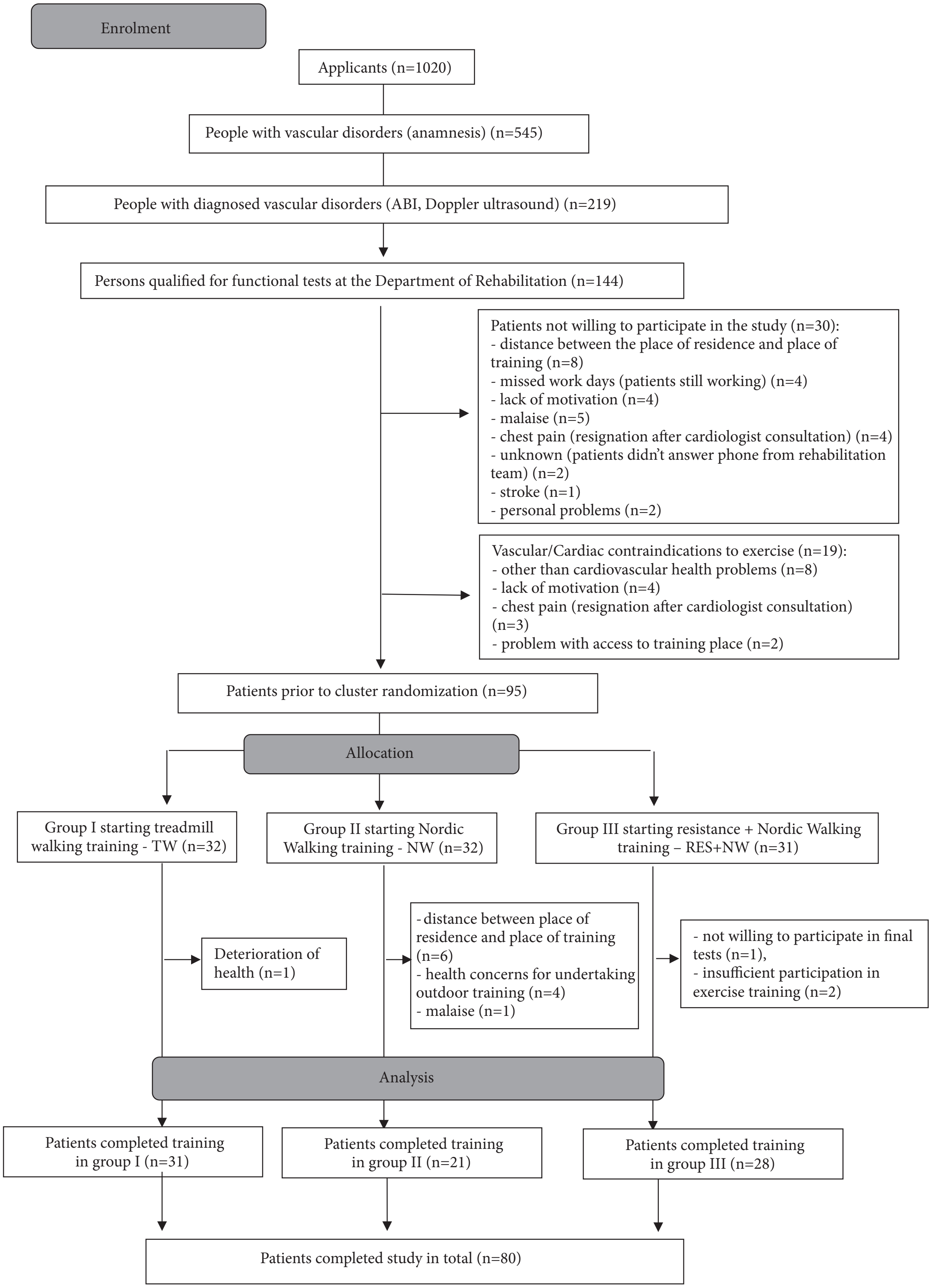


Figure 1: A detailed process of patient recruitment for the rehabilitation programme.

Table 1: Anthropometric characteristics of patients with PAD and Ankle Brachial Index (ABI).

| Variables | Group I (TW) (n=31) Mean ± SD | Group II (NW) (n=21) Mean ± SD | Group III (RES+NW) (n=28) Mean ± SD | p |
|---|---|---|---|---|
| Age (years) | 67.00 ± 7.43 | 67.00 ± 9.32 | 67.82 ± 8.49 | 0.92 |
| Body height (cm) | 168.03 ± 8.56 | 166.81 ± 7.4 | 169.54 ± 9.07 | 0.53 |
| Body weight (kg) | 79.02 ± 14.31 | 74.44 ± 12.44 | 78.84 ± 15.43 | 0.47 |
| BMI (kg/m$^2$) | 27.85 ± 3.72 | 26.77 ± 4.34 | 27.28 ± 4.01 | 0.63 |
| ABI R | 0.68 ± 0.19 | 0.76 ± 0.17 | 0.76 ± 0.19 | 0.14 |
| ABI L | 0.68 ± 0.16 | 0.71 ± 0.22 | 0.7 ± 0.19 | 0.84 |

∗ $p<0.05$; body mass index: BMI and Ankle Brachial Index: ABI.

(i) Treadmill walking training in Group I (TW) was carried out in accordance with the TASC II recommendations. The patient walked on a moving belt on the HX-100 treadmill with a constant speed of 3.2 km/h at 12° angle of inclination. The training took place in line with interval training principles. The duration of walking was determined by the onset of submaximum claudication pain (level 4 according to the 5-level ACSM scale), after which the patient rested on the nonmoving side strips of the treadmill until the pain subsided (level 0 or 1 according to the ACSM scale). However, the rest period did not exceed 2 minutes. Extending the distance covered was done gradually: at the start the patient covered four sections with breaks for a rest and withdrawal of pain. As the walking capacity improved, the training was extended so that within 45 minutes the patient could walk the longest distance possible. After each section the patient monitored their HR using sensors built into the treadmill grips. The training was individualized and was run concurrently on two treadmills (2 people exercising at the same time).

(ii) Nordic walking training in Group II (NW) was carried out by experienced NW instructors in accordance with the INWA. At the beginning of the training a general warm-up was performed (up to 10 min) using the NW poles (KV+ Campra Clip), followed by walking training with a NW technique using an interval method according to the same rules as in treadmill training. At the end, stretching and breathing exercises were carried out (5 min). After each section, the patient monitored his or her own HR on the radial or carotid artery. Patients walked around the circumference of a large wheel in outside conditions (park) or in a sports hall (in case of bad weather), which allowed for them to be continuously monitored. The first sessions (6–9 units) were devoted to learning a correct NW technique; the following classes were for improvements. The training was performed in groups (up to 12 people in one group).

(iii) Combined training of resistance + Nordic walking in Group III (RES+NW) was carried out alternately (Mon: NW, Wed: RES, Fri: NW, Mon: RES, etc.). The NW training was conducted according to the same rules as in the training above. Isokinetic training (resistance), i.e., conducted under constant angular velocity, while ensuring constant resistance, was based on biological feedback using functional dynamometry on the Biodex S4 Pro. While performing a given movement, the patient controlled its effect on the computer's monitor (biofeedback). Before starting proper training, the patient performed five repetitions at an initial angular velocity of 60°/s (3 reps for warm-up with submaximal force (~70% Fmax) and two with maximum force, in order to determine the training level). After performing a repetition with maximal strength, 70–80% of the maximum value [Nm] was determined for both muscle groups (plantar and dorsal flexors of the ankle joint, or in the case of patients with high arterial occlusion, training for flexors and extensors of the knee joint in both limbs was introduced). The patient's task was to perform a movement with a force that allowed one to reach a limit set at the beginning of the training (70–80%) by means of visual control (on the monitor), in line with the specificity of the biofeedback training. The patient performed 10 repetitions for a given velocity: 60, 120, 180, 240, and 300 and 300, 240, 180, 120, and 60°/s (according to the pyramid rule), altogether totaling 100 movements per limb. After each velocity the patient rested in the intermediate position of the foot or knee for 1 minute. The rest time was extended in the case of a prolonged recovery from claudication pain. The principle of resistance training took place from the lowest velocity (the highest resistance) through to the highest velocity (low resistance, velocity of movement increases: 300°/s), ending again with a high resistance performed at a low velocity of 60°/s.

The NW training took place in a group, while the resistance training was undergone individually, taking place in the Laboratory of Functional Research of the Faculty of Physiotherapy, University of Physical Education in Wroclaw.

*2.3. Statistical Methods.* The distribution and homogeneity of the variance of all analysed parameters obtained by the subjects in each group were examined. Next, mean values, standard deviation, and median were calculated. In order to compare the results obtained in the first and second tests for parameters with a distribution similar to normal, Student's *t*-test was used, whereas when the distribution was not close to normal the Wilcoxon test was applied.

Between the first and the second measurement, participants took part in one of three types of training. In order to compare the effectiveness of the applied form of training,

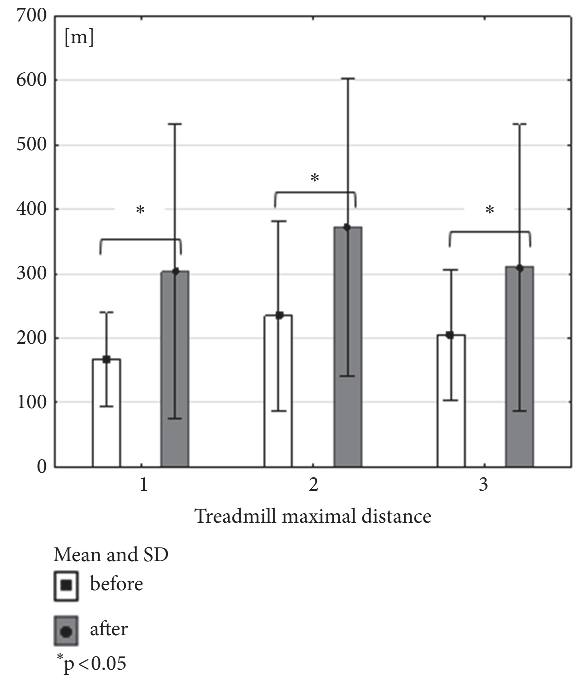


Figure 2: Mean, standard deviation and Wilcoxon coefficient p values calculated between treadmill maximal distance in all groups before and after the training cycle.

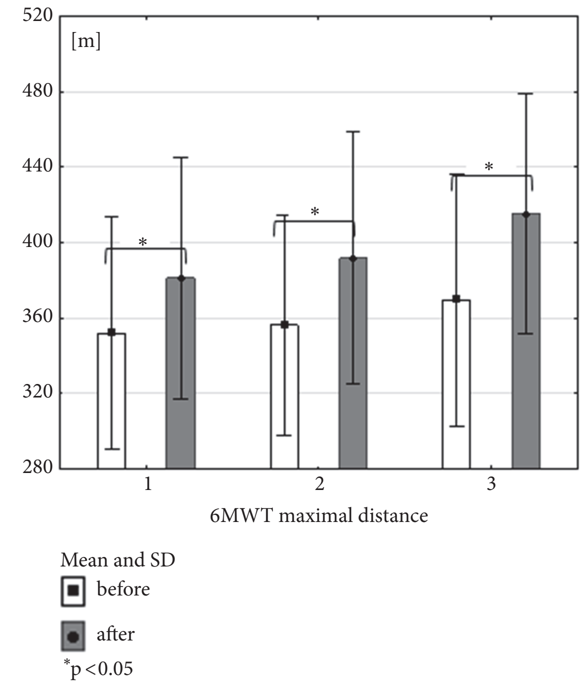


Figure 4: Mean, standard deviation and Wilcoxon coefficient p values calculated between 6MWT maximal distance in all groups before and after the training cycle.

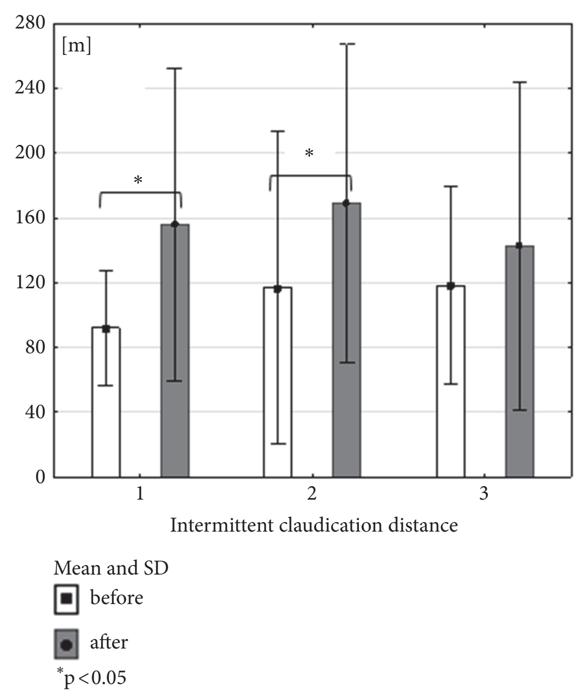


Figure 3: Mean, standard deviation and Wilcoxon coefficient p values calculated between intermittent claudication distance in all groups before and after the training cycle.

an analysis of univariate variance was made in the case of an assumption of the normality of distribution and homogeneity of variance being satisfied. In the absence of normality of distribution, the Kruskal–Wallis test was used. In the case of a lack of homogeneity of variance, despite a near-normal distribution, the Welch test was applied. If the applied analysis showed statistical significance, calculations were continued with the Scheffe post hoc test.

Spearman correlation coefficient values were calculated between walking distance parameters and force-velocity parameters calculated for each of the study groups before and after the training cycle.

Statistical analysis was carried out using Statistica 13.1.

## 3. Results

The results presented below show the values of distance parameters responsible for walking efficiency and values of force-velocity parameters, which describe the level of muscle function acting on the knee and ankle joints.

*3.1. Distance Parameters.* All forms of 3-month exercise training have beneficial influence on maximal distance. Combined training (RES+NW) did not get the significant level in claudication distance. Nordic walking group and treadmill training group had significant influence on claudication distance (Figures 2, 3, and 4). When comparing the groups, no significant differences were recorded, in studies either before or after the training cycle (ANOVA not statistically significant).

*3.2. Force-Velocity Parameters of the Knee Joint.* The results of force-velocity parameters: peak torque (PT [Nm]), total work (TW [J]), and average power (AP [W]) obtained by functional dynamometry tests, typifying the impact of

Table 2: *t*-test coefficient values calculated between force-velocity parameters of knee muscles in all groups before and after the training cycle and results of variance analysis calculated between groups for each of the analyzed parameters.

| Variables KNEE | | GROUP I p | GROUP II p | GROUP III p | ANOVA |
|---|---|---|---|---|---|
| PT ER | 60°/s | 0.26 | 0.28 | 0.84 | ns |
| TW ER | | 0.17 | 0.4 | 0.58 | ns |
| AP ER | | 0.07 | 0.48 | 0.59 | ns |
| PT EL | | 0.61 | 0.17 | 0.96 | ns |
| TW EL | | 0.001∗ | 1 | 0.97 | ns |
| AP EL | | 0.35 | 0.13 | 0.75 | ns |
| PT FR | 60°/s | 0.03∗ | 0.14 | 0.31 | ns |
| TW FR | | 0.02∗ | 0.32 | 0.46 | ns |
| AP FR | | 0.01∗ | 0.05∗ | 0.41 | ns |
| PT FL | | 0.22 | 0.77 | 0.68 | ns |
| TW FL | | 0.22 | 0.73 | 0.54 | ns |
| AP FL | | 0.07 | 0.72 | 0.50 | ns |
| PT ER | 120°/s | 0.16 | 0.43 | 0.61 | ns |
| TW ER | | 0.17 | 0.81 | 0.50 | ns |
| AP ER | | 0.04∗ | 0.29 | 0.42 | ns |
| PT EL | | 0.73 | 0.04∗ | 0.39 | 0.03∗ |
| TW EL | | 0.50 | 0.82 | 0.46 | 0.01∗ |
| AP EL | | 0.33 | 0.17 | 0.41 | 0.01∗ |
| PT FR | 120°/s | 0.02∗ | 0.02∗ | 0.1 | ns |
| TW FR | | 0.02∗ | 0.07 | 0.15 | 0.03∗ |
| AP FR | | 0.01∗ | 0.01∗ | 0.11 | 0.03∗ |
| PT FL | | 0.01∗ | 0.56 | 0.27 | 0.04∗ |
| TW FL | | 0.09 | 0.98 | 0.16 | 0.02∗ |
| AP FL | | 0.04 | 0.73 | 0.17 | 0.02∗ |
| PT ER | 180°/s | 0.81 | 0.72 | 0.3 | 0.01∗ |
| TW ER | | 0.65 | 0.1 | 0.15 | 0.001∗ |
| AP ER | | 0.36 | 0.54 | 0.06 | 0.001∗ |
| PT EL | | 0.02∗ | 0.44 | 0.12 | 0.001∗ |
| TW EL | | 0.08 | 0.69 | 0.10 | 0.001∗ |
| AP EL | | 0.03∗ | 0.52 | 0.02∗ | 0.001∗ |
| PT FR | 180°/s | 0.54 | 0.15 | 0.03∗ | 0.001∗ |
| TW FR | | 0.90 | 0.52 | 0.01∗ | 0.001∗ |
| AP FR | | 0.70 | 0.12 | 0.00∗ | 0.001∗ |
| PT FL | | 0.02∗ | 0.52 | 0.05∗ | 0.001∗ |
| TW FL | | 0.09 | 0.90 | 0.01∗ | 0.001∗ |
| AP FL | | 0.05∗ | 0.55 | 0.01∗ | 0.001∗ |

∗$p<0.05$; ns: results statistical not significant, PT [Nm]: peak torque, TW [J]: total work, AP [W]: average power, E: extensor, F: flexor muscles of the knee joint, R: right, and L: left.

particular types of training on the muscle performance of the knee and ankle joints differently.

As a result of training conducted on the treadmill (Group I), the biggest changes were recorded in the right knee flexors (F) for a velocity of 60°/s and 120°/s in peak torque (PT), total work (TW), and average power (AP) (Table 2).

Nordic walking training improved AP of flexors of the right knee joint for velocities 60°/s and 120°/s and also PT of flexors for a velocity of 120°/s. In the left knee there was only one significant change for extensors in PT parameter for velocity 120°/s (Table 2).

As a result of the combined training (resistance training and Nordic walking) improvement was observed at a velocity of 180°/s in all investigated force-velocity parameters, for both flexors (F) and extensors (E) of the knee joint. There was also changes for knee flexors in both legs at a velocity of 120°/s except one parameter (PT FR) and for knee extensors at this same velocity but observed only in left leg (Table 2).

*3.3. Force-Velocity Parameters of the Ankle Joint.* There were no significant changes recorded in the force-velocity parameters of the dorsal extensor (E) and plantar flexor (F) muscles

Table 3: Wilcoxon coefficient p values calculated between force-velocity parameters of ankle muscles in all groups before and after the training cycle and results of variance analysis calculated between groups for each of the analyzed parameters.

| Variables ANKLE | | GROUP I p | GROUP II p | GROUP III p | ANOVA |
|---|---|---|---|---|---|
| PT ER | 60°/s | 0.99 | 0.53 | 0.19 | ns |
| TW ER | | 0.87 | 0.31 | 0.11 | 0.01* |
| AP ER | | 0.96 | 0.31 | 0.13 | ns |
| PT EL | | 0.72 | 0.35 | 0.22 | ns |
| TW EL | | 0.72 | 0.1 | 0.31 | 0.01* |
| AP EL | | 0.94 | 0.06 | 0.23 | ns |
| PT FR | 60°/s | 0.76 | 0.47 | 0.001* | 0.001* |
| TW FR | | 0.58 | 0.62 | 0.001* | 0.001* |
| AP FR | | 0.54 | 0.78 | 0.001* | 0.001* |
| PT FL | | 0.56 | 0.49 | 0.04* | 0.001* |
| TW FL | | 0.26 | 0.74 | 0.02* | 0.001* |
| AP FL | | 0.31 | 0.78 | 0.01* | 0.001* |
| PT ER | 120°/s | 0.76 | 0.37 | 0.01* | 0.02* |
| TW ER | | 0.8 | 0.59 | 0.03* | 0.001* |
| AP ER | | 0.68 | 0.91 | 0.01* | 0.001* |
| PT EL | | 0.24 | 0.16 | 0.01* | 0.02* |
| TW EL | | 0.54 | 0.31 | 0.01* | 0.001* |
| AP EL | | 0.56 | 0.29 | 0.001* | 0.001* |
| PT FR | 120°/s | 0.8 | 0.73 | 0.001* | 0.001* |
| TW FR | | 0.56 | 0.43 | 0.001* | 0.001* |
| AP FR | | 0.51 | 0.27 | 0.001* | 0.001* |
| PT FL | | 0.53 | 0.28 | 0.001* | 0.001* |
| TW FL | | 0.99 | 0.27 | 0.03* | 0.001* |
| AP FL | | 0.71 | 0.39 | 0.001* | 0.001* |

*$p<0.05$; ns: results statistical not significant, PT [Nm]: peak torque, TW [J]: total work, AP [W]: average power, E: extensor, F: flexor muscles of the ankle joint, R: right, and L: left.

of the ankle joint in response to the treadmill walking training (Group I) and Nordic walking (Group II) (Table 3).

Combined training (Group III) significantly improved the results in all analysed parameters, for both the dorsal extensor (E) and plantar flexor (F) muscles of the left and right ankle joints at a velocity of 120°/s. At a velocity of 60°/s, this change concerned only the plantar flexors (F) of both ankle joints (Table 3).

*3.4. Comparison of Results of Force-Velocity Parameters of the Knee and Ankle Joints.* In analysing the force-velocity results for both flexors and extensors of both joints (knee and ankle) at different velocities, it turned out that following a 3-month training cycle the most significant changes were observed at a velocity of 180°/s for the knee joint and at 120°/s for the ankle joint. No significant changes were reported at 60°/s for the knee joint (Tables 2 and 3).

*3.5. Comparison of Results of Force-Velocity Parameters between the Three Forms of Training.* Post hoc analysis revealed the most significant changes taking place between the results in Group I (TW) and Group III (RES+NW) at a velocity of 180°/s for the knee joint muscles and 120°/s for the ankle joint muscles. Some significant variations were also observed between Group II (NW) and Group III (RES+NW), with knee joint muscles bearing a velocity load of 180°/s while the ankle joint muscles had a velocity of 60°/s and 120°/s (Tables 4 and 5).

*3.6. Correlation between Walking Distance and Force-Velocity Parameters.* Before the exercise rehabilitation program there were no significant relationships between the maximum distance and the distance of claudication obtained in the treadmill test and force-velocity parameters in all examined groups. The exception is one correlation between the maximum distance and PT ER at 120°/s obtained by Group III. Its value indicates moderate correlation strength ($r$=0.4) (Tables 6 and 7).

The maximum distance obtained in 6MWT before the exercise rehabilitation programme correlates with force-velocity parameters mainly in Group III (RES + NW) for extensors and flexors of the knee joint and extensors of the ankle joint. In Group II (NW) no correlations were noted. In Group I (TW) there were maximal distance compounds with left knee flexors mainly at the speed of 120°/s (Table 8).

After 3 months of exercise training, the most relationships between the maximum distance obtained in the test on the treadmill and the force-velocity parameters are observed in

Table 4: Scheffe's post hoc test results showing relationships between results obtained in particular groups (I, TW; II, NW; III, RES + NW) for all analysed parameters of the muscles of the knee joint.

| Variables | | 60°/s | | | 120°/s | | | 180°/s | |
|---|---|---|---|---|---|---|---|---|---|
| KNEE | 1vs2 | 1vs3 | 2vs3 | 1vs2 | 1vs3 | 2vs3 | 1vs2 | 1vs3 | 2vs3 |
| PT ER | ns | ns | ns | ns | ns | ns | ns | 0.01* | ns |
| TW ER | ns | ns | ns | ns | ns | ns | ns | 0.001* | 0.01* |
| AP ER | ns | ns | ns | ns | ns | ns | ns | 0.001* | 0.02* |
| PT EL | ns | ns | ns | ns | 0.03* | ns | ns | 0.001* | ns |
| TW EL | ns | ns | ns | ns | 0.02* | ns | ns | 0.001* | 0.02* |
| AP EL | ns | ns | ns | ns | 0.01* | ns | ns | 0.001* | 0.01* |
| PT FR | ns | ns | ns | ns | ns | ns | ns | 0.001* | 0.04* |
| TW FR | ns | ns | ns | ns | 0.04* | ns | ns | 0.001* | 0.001* |
| AP FR | ns | ns | ns | ns | 0.04* | ns | ns | 0.001* | 0.01* |
| PT FL | ns | ns | ns | ns | ns | ns | ns | 0.001* | ns |
| TW FL | ns | ns | ns | ns | 0.03* | ns | ns | 0.001* | ns |
| AP FL | ns | ns | ns | ns | 0.02* | ns | ns | 0.001* | ns |

* $p < 0.05$; ns: results statistical not significant; PT: peak torque; TW: total work; AP: av. power; E: extension; F: flexion; R: right; L: left.

Table 5: Scheffe's post hoc test results showing relationships between results obtained in particular groups (I, TW; II, NW; III, RES + NW) for all analysed parameters of the muscles of the ankle joint.

| Variables | | 60°/s | | | 120°/s | |
|---|---|---|---|---|---|---|
| ANKLE | 1vs2 | 1vs3 | 2vs3 | 1vs2 | 1vs3 | 2vs3 |
| PT ER | ns | ns | ns | ns | 0.03* | ns |
| TW ER | ns | 0.03* | 0.03* | ns | 0.001* | 0.001* |
| AP ER | ns | ns | ns | ns | 0.001* | 0.001* |
| PT EL | ns | ns | ns | ns | 0.04* | ns |
| TW EL | ns | 0.04* | 0.03* | ns | 0.001* | 0.001* |
| AP EL | ns | ns* | ns | ns | 0.001* | 0.001* |
| PT FR | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |
| TW FR | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |
| AP FR | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |
| PT FL | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |
| TW FL | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |
| AP FL | ns | 0.001* | 0.001* | ns | 0.001* | 0.001* |

* $p < 0.05$; ns: results statistical not significant; PT: peak torque; TW: total work; AP: av. power; E: extension; F: flexion; R: right; L: left.

Group III (RES + NW) for flexors and extensors of the knee joint muscles and extensors of the ankle joint (mainly left) (Table 6). In the case of claudication distance, there are single correlations in three exercise groups which have low to moderate strength (Table 7).

The most relationships of force-velocity parameters are observed in the maximum distance obtained in 6MWT, both in Group III (RES + NW) and in Group II (NW) at the level of moderate and strong correlation strength (Table 8). This indicates that if the lower limbs are stronger the walking distance achieved in 6MWT is longer.

## 4. Discussion

A systematically undertaken physical training is the most effective therapeutic treatment for patients with PAD, showing an advantage over pharmacological treatment and angioplasty [16, 40, 41]. It is also the most cost-effective and long-lasting form of treatment for this group of patients [42, 43].

Despite the proven effectiveness of physical training running for at least 3 months, three times a week, a problem that researchers have highlighted is the participation of patients with PAD in these physical rehabilitation programs. Research by De la Hayel et al. [44], Malagoni et al. [45], and Müller-Büh et al. [46] shows that dropout rate from these training programs is as much as 34–44%. Based on the literature review, the main reasons of resignation are not attractive form of exercises (treadmill walking training, recommended by TASC II and ACC / AHA), lack of motivation, health problems, and being far from the place of residence to the centres in which the rehabilitation programs are dedicated for patients with PAD [47]. Despite this, in our study, the dropout rate from the programme was only 16%. One person resigned from training on the treadmill, 11 people from Nordic walking training, and 3 people from combined

Table 6: Spearman correlation coefficient values calculated between treadmill maximal distance and force-velocity parameters calculated for each of the study groups before and after the training cycle.

| Treadmill maximal distance | | BEFORE GROUP I | | | BEFORE GROUP II | | | BEFORE GROUP III | | | AFTER GROUP I | | | AFTER GROUP II | | | AFTER GROUP III | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VS | | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s |
| PT ER | KNEE | ns | ns | ns | ns | ns | ns | ns | 0.40* | ns | ns | ns | 0.42* | ns | ns | ns | 0.51* | 0.53* | 0.50* |
| TW ER | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.40* | ns | ns | ns | 0.56* | 0.50* | 0.53* |
| AP ER | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.57* | 0.48* | 0.55* |
| PT EL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.47* |
| TW EL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.38* | 0.42* | ns | ns | ns | ns | ns | 0.42* | 0.49* |
| AP EL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.39* | 0.50* |
| PT FR | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.41* | 0.46* |
| TW FR | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.42* | 0.43* | 0.45* |
| AP FR | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.46* | 0.49* | 0.43* |
| PT FL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.54* | 0.42* | 0.57* |
| TW FL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.54* | ns | ns | ns | ns | 0.47* | 0.39* | 0.53* |
| AP FL | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.49* | ns | ns | ns | ns | 0.42* | 0.39* | 0.50* |
| PT ER | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.55* | 0.46* | - | ns | ns | - |
| TW ER | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.45* | ns | - |
| AP ER | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| PT EL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.56* | 0.42* | - |
| TW EL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.57* | 0.51* | - |
| AP EL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.51* | 0.44* | - |
| PT FR | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW FR | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.40* | ns | - |
| AP FR | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| PT FL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW FL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| AP FL | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |

* $p < 0.05$; ns: results statistical not significant; -: no measurement.

Table 7: Spearman correlation coefficient values calculated between intermittent claudication distance and force-velocity parameters calculated for each of the study groups before and after the training cycle.

| Intermittent claudication distance | | BEFORE | | | | | | | | | AFTER | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | GROUP I | | | GROUP II | | | GROUP III | | | GROUP I | | | GROUP II | | | GROUP III | | |
| | VS | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s |
| PT ER | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| TW ER | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.38* | ns | ns |
| AP ER | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.44* | ns | 0.38* |
| PT EL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| TW EL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| AP EL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| PT FR | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| TW FR | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.49* | ns | ns | ns | ns | ns |
| AP FR | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| PT FL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |
| TW FL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.47* | ns | ns | ns | ns | ns | ns | ns |
| AP FL | | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.42* | ns | ns | ns | ns | ns | ns | ns |
| PT ER | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW ER | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | 0.53* | - | ns | ns | - |
| AP ER | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.48* | ns | - | ns | ns | - |
| PT EL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW EL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| AP EL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| PT FR | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW FR | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| AP FR | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| PT FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| TW FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| AP FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |

* $p < 0.05$; ns: results statistical not significant; -: no measurement.

Table 8: Spearman correlation coefficient values calculated between 6MWT maximal distance and force-velocity parameters calculated for each of the study groups before and after the training cycle.

| 6MWT maximal distance | | BEFORE GROUP I | | | BEFORE GROUP II | | | BEFORE GROUP III | | | AFTER GROUP I | | | AFTER GROUP II | | | AFTER GROUP III | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | VS | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s | 60°/s | 120°/s | 180°/s |
| PT ER | KNEE | ns | ns | ns | ns | ns | ns | 0.42* | 0.41* | 0.44* | ns | ns | ns | 0.53* | 0.51* | 0.62* | 0.52* | 0.62* | 0.49* |
| TW ER | | ns | ns | ns | ns | ns | ns | 0.39* | 0.43* | 0.53* | ns | ns | ns | 0.51* | 0.47* | 0.61* | 0.56* | 0.59* | 0.52* |
| AP ER | | ns | ns | ns | ns | ns | ns | 0.48* | 0.39* | 0.52* | ns | ns | ns | 0.51* | 0.50* | 0.53* | 0.57* | 0.57* | 0.51* |
| PT EL | | ns | ns | ns | ns | ns | ns | 0.41* | 0.44* | 0.39* | 0.39* | ns | ns | 0.52* | 0.48* | 0.56* | 0.58* | 0.63* | 0.63* |
| TW EL | | 0.39* | ns | ns | ns | ns | ns | 0.39* | 0.46* | ns | ns | 0.40* | ns | 0.59* | 0.47* | 0.56* | 0.66* | 0.72* | 0.58* |
| AP EL | | ns | ns | ns | ns | ns | ns | 0.42* | 0.48* | ns | ns | ns | ns | 0.52* | ns | 0.48* | 0.59* | 0.65* | 0.54* |
| PT FR | KNEE | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns | 0.63* | 0.65* | 0.72* |
| TW FR | | ns | ns | ns | ns | ns | ns | ns | 0.38* | 0.40* | ns | ns | ns | ns | ns | 0.52* | 0.69* | 0.69* | 0.63* |
| AP FR | | ns | ns | ns | ns | ns | ns | ns | 0.40* | 0.46* | ns | ns | ns | 0.47* | ns | 0.47* | 0.72* | 0.73* | 0.60* |
| PT FL | | ns | 0.42* | ns | ns | ns | ns | ns | 0.51* | ns | ns | 0.46* | ns | 0.54* | ns | 0.52* | 0.68* | 0.60* | 0.53* |
| TW FL | | ns | 0.46* | ns | ns | ns | ns | 0.42* | 0.41* | ns | ns | 0.54* | ns | 0.58* | ns | 0.60* | 0.67* | 0.68* | 0.46* |
| AP FL | | ns | 0.45* | ns | ns | ns | ns | 0.45* | 0.43* | ns | ns | 0.46* | ns | 0.54* | ns | 0.60* | 0.63* | 0.65* | 0.45* |
| PT ER | ANKLE | ns | 0.45* | - | ns | ns | - | 0.39* | ns | - | ns | ns | - | 0.63* | 0.67* | - | ns | 0.43* | - |
| TW ER | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.57* | 0.59* | - | 0.44* | 0.38* | - |
| AP ER | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.61* | 0.54* | - | 0.39* | ns | - |
| PT EL | | ns | ns | - | ns | ns | - | 0.58* | 0.57* | - | ns | 0.40* | - | 0.69* | 0.69* | - | 0.62* | 0.62* | - |
| TW EL | | ns | ns | - | ns | ns | - | 0.54* | 0.55* | - | ns | ns | - | 0.47* | 0.52* | - | 0.63* | 0.57* | - |
| AP EL | | ns | ns | - | ns | ns | - | 0.57* | 0.59* | - | ns | ns | - | 0.57* | 0.53* | - | 0.60* | 0.60* | - |
| PT FR | ANKLE | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.67* | 0.64* | - | ns | ns | - |
| TW FR | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - |
| AP FR | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.51* | 0.48* | - | ns | ns | - |
| PT FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.54* | ns | - | 0.40* | ns | - |
| TW FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.51* | 0.42* | - |
| AP FL | | ns | ns | - | ns | ns | - | ns | ns | - | ns | ns | - | 0.46* | ns | - | ns | ns | - |

* $p < 0.05$; ns: results statistical not significant; -: no measurement.

training (resistance + Nordic walking). The authors observed that outdoor exercises and changing weather conditions were the biggest problem for patients who dropped out from the Nordic walking group, because of deterioration of health status. In the resistance and Nordic walking training this tendency was not found. Impairment of the walking function as a result of chronically occurring claudication pain leads to a significant reduction in the strength and endurance of lower-limb muscles and subsequently to the deterioration of walking skills [1, 48, 49]. This is due not only to the ischaemia of lower-limb muscles but also to the reduced daily physical activity of people with PAD. Introducing resistance training to the standards of therapeutic treatment of people with intermittent claudication seems to be desirable and is confirmed in studies by McDermott et al. [34], McGuigan et al. [35], Parmenter et al. [36], and Wang et al. [37].

Our study suggests that all forms of exercise training have beneficial influence on walking distance. When the force-velocity parameters are taken into account, the combined training (resistance + Nordic walking) caused the most significant changes, comparing to the treadmill training alone and Nordic walking training alone. The most evident effect appears to be the improvement in muscle functions supporting the ankle joint, where peak torque, total work, and average power of left and right lower limbs increased for both the dorsal and plantar flexors at higher velocity of the movement (120°/s). In greater resistance conditions (60°/s), this change occurred only for the flexor muscles of the plantar foot.

Studies by Scott-Okafor et al. [50] confirm that the weakest muscles of the ankle joint in people with intermittent claudication are the dorsal flexors. In comparison to healthy people, the difference in the strength of these muscles is 22% [50]. Furthermore, Chen et al. [51] showed that the torque of dorsal flexor muscles is significantly lower in this group of patients compared to healthy individuals, especially in a situation of developing ischaemic pain. However, what is interesting is that when comparing the torque of both muscle groups in painless and painful walking conditions, it is the flexors of the plantar feet that exhibit significant weakness in response to intermittent claudication [51]. It should be added that the weakness of the muscles supporting the ankle joint can cause an increased risk of falling. Research by Gardner and Montgomery [52] confirms that patients with PAD trip or fall 70% more often than healthy people. It is also important that depending on the speed of the gait the muscles supplying the ankle joint produce 40-60% of the impulsion energy necessary for locomotion [53]. So the resistance training plays significant role in improving walking ability of patients with peripheral arterial disease. In our study, under the impact of combined training, an improvement was achieved in both the dorsal and plantar flexors; however, with greater load, significant change was achieved only in the efficiency of the dorsal flexors of the foot. Presumably, this is due to the physiological superiority of plantar over dorsal flexors in terms of strength; plantar flexors are characterized by a greater muscle mass and number of supplying arteries. Therefore, in this muscle group there is a higher probability of collateral circulation in response to physical training [54], which prevents a reduction in muscle performance of the plantar flexors compared to the smaller and weaker dorsal flexor muscles.

In the literature, the muscles that act on the knee joint have been subjected to a detailed functional analysis under isokinetic conditions, mostly in healthy elderly people and athletes [55, 56]. However, there has been little research on the functional assessment of these muscle groups in patients with chronic diseases [1, 57, 58].

Taking into account changes in the force-velocity parameters of the knee joint, a significant improvement took place mainly in response to the treadmill training and combined training. In the first case, there was improvement only in the right knee flexors at low and medium velocities. This is probably due to the fact that over 60% of respondents had symptoms of intermittent claudication in the right lower limb. In the second case, all analysed force-velocity parameters improved for both flexors and extensors of the knee joint at higher velocity. Studies by McGuigan et al. [35], which showed an increase in the area of muscle fibres types I and II by an average of 25% in response to resistance training, confirm these results. Type I (slow-twitch) fibres are mainly responsible for endurance performance, while type II (fast-twitch) fibres are responsible for high-speed performance, which is why in this study people in Group III performed best with the highest given velocity (180°/s).

One of the most important goals of the rehabilitation of patients with intermittent claudication is to extend their walking distance. In our research, this goal was achieved in response to all the proposed forms of training. Prolongation of the distance of claudication and the maximal distance in response to a 3-month training on a treadmill is unsurprising, given that, as a result of many studies, it has become a recommended form of rehabilitation for patients with intermittent claudication [18]. It should be added that the same form of training, as that of the testing, makes it easier to achieve better results, as observed by Schieb [59].

In recent times, attention has been paid to Nordic walking training by people with PAD, because of similar or even better results being achieved in terms of walking abilities, than training on a treadmill [29–32]. The unconstrained nature of the movement is largely responsible for this, which is similar to the natural walk, in contrast to treadmill training, during which a patient covers the distance at a constant speed, in a nonergonomic position of the body (grabbing the handles for fear of falling). In addition, a great advantage of Nordic walking is training in the open air, providing the patient with more attractions than during the somewhat monotonous training on a treadmill.

In reviewing the literature, it is difficult to find studies which connected endurance and strength training, despite the confirmed benefits of their separate forms, when rehabilitating patients with intermittent claudication. Only in the study by Plitz et al. [60] has it been proposed to combine walking training with prescribed pace, together with strength training performed on the Multiped 303 ergometer. As a result, after 3 months, the speed of walking, the distance of claudication, and the efficiency of the lower-limb muscles assessed in the functional tests all improved [60].

In light of these reports, training that consists of endurance and strength components seems to be a promising form of rehabilitating patients with intermittent claudication. In addition to improvements of the walking distance, which are so important from the daily functioning of patients with PAD point of view, the parameters responsible for strength, endurance, and coordination of lower-limb muscles are also subject to progression. Despite the supervised nature of the combined training, the participants training found it to be attractive with lower drop-out rates comparing to other rehabilitation programs.

## 5. Conclusions

(1) Combined training (resistance and Nordic walking) is the most effective form of exercise training in strengthening the legs and also has beneficial influence on maximal walking distance.

(2) The highest efficiency of combined training (RES +NW), compared to other methods of exercise training, was observed in the force-velocity parameters of the muscles supporting the ankle joint.

(3) Each of the proposed rehabilitation programmes had a positive effect on the walking capacity of patients with intermittent claudication.

(4) The introduction of Nordic walking combined with resistance training should be considered for the therapeutic treatment of patients with intermittent claudication, not only because of the effectiveness of the training, but also in terms of its attractiveness as a form of rehabilitation, preventing dropout from rehabilitation programmes.

## Data Availability

The data (force-velocity parameters and walking parameters) used to support the findings of this study have been deposited in the WROVASC repository (e-mail: zuk@wssk.wroc.pl).

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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*Review Article*

# Frailty and Exercise Training: How to Provide Best Care after Cardiac Surgery or Intervention for Elder Patients with Valvular Heart Disease

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The aim of this literature review was to evaluate existing evidence on exercise-based cardiac rehabilitation (CR) as a treatment option for elderly frail patients with valvular heart disease (VHD). *Pubmed* database was searched for articles between 1980 and January 2018. From 2623 articles screened, 61 on frailty and VHD and 12 on exercise-based training for patients with VHD were included in the analysis. We studied and described frailty assessment in this patient population. Studies reporting results of exercise training in patients after surgical/interventional VHD treatment were analyzed regarding contents and outcomes. The tools for frailty assessment included fried phenotype frailty index and its modifications, multidimensional geriatric assessment, clinical frailty scale, 5-meter walking test, serum albumin levels, and Katz index of activities of daily living. Frailty assessment in CR settings should be based on functional, objective tests and should have similar components as tools for risk assessment (mobility, muscle mass and strength, independence in daily living, cognitive functions, nutrition, and anxiety and depression evaluation). Participating in comprehensive exercise-based CR could improve short- and long-term outcomes (better quality of life, physical and functional capacity) in frail VHD patients. Such CR program should be led by cardiologist, and its content should include (1) exercise training (endurance and strength training to improve muscle mass, strength, balance, and coordination), (2) nutrition counseling, (3) occupational therapy (to improve independency and cognitive function), (4) psychological counseling to ensure psychosocial health, and (5) social worker counseling (to improve independency). Comprehensive CR could help to prevent, restore, and reduce the severity of frailty as well as to improve outcomes for frail VHD patients after surgery or intervention.

## 1. Introduction

Worldwide, the population is aging, and the associated challenges for the healthcare system are significant. There is a clear association between degenerative valve disease, older age, and increasing life expectancy [1, 2]. According to the Euro Heart Survey on Valvular Heart Disease (VHD), patients with diagnosed VHD are often older, with a higher prevalence of other cardiovascular risk factors and comorbidities [2].

Careful monitoring, adequate medication, and perfect surgery or intervention timing is key to a successful treatment of VHD. Due to the shift in patient population, the profile of patients who are referred to cardiac surgeon changed dramatically. The share of surgically treated elderly patients (≥80 years old) increased from 2.6-7% to 9.3-12% in a period of 10 years [3, 4]. Innovation in cardiac surgery techniques [5], advance in anesthesiology, and early postsurgery care led to a lower risk of cardiac surgery in elderly patients [4] and

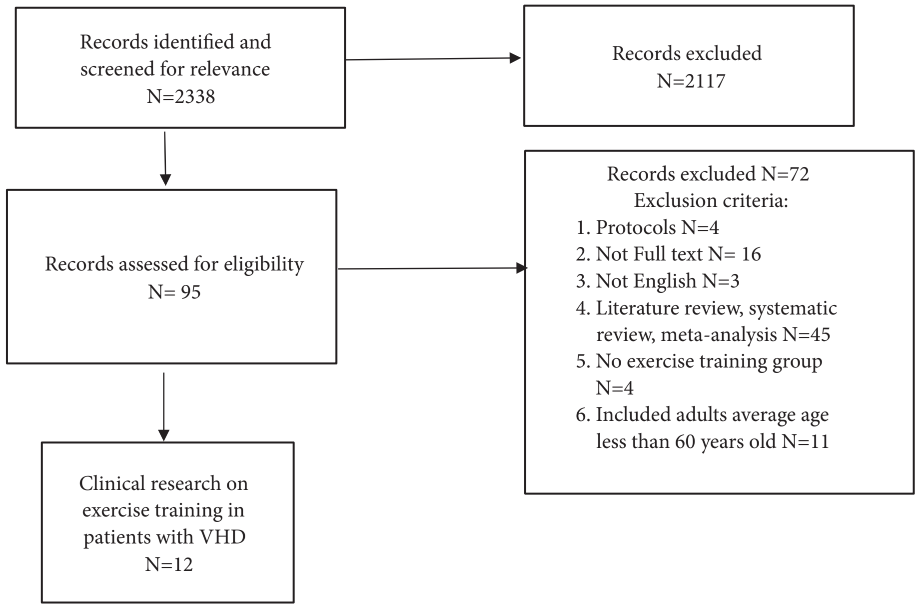


Figure 1: Flowchart of the selection of publications included in literature review related to valve surgery and exercise training.

evidence of improved outcomes with valve surgery or transcatheter aortic valve implantation (TAVI) [6, 7]. However, older patients still have higher mortality and morbidity rates, more frequent complications related to surgery, and longer stay in hospital compared to younger patients [3, 4, 6].

Disease complexity in the elderly raises questions about other risk factors that exist upon well-known and established prognostic factors. Frailty is a common and relevant geriatric syndrome that could be defined as a biological syndrome with reduced reserve and resistance to stressors, resulting from cumulative deficits across multiple physiologic systems and causing vulnerability to adverse outcomes [8]. Most of the studies analyzed frailty before surgery/intervention as prognostic tool for later outcomes [9] and frailty is a reliable prognostic factor for mortality, morbidity, major complications [10–16], functional decline [17], quality of life [18], and risk of delirium after procedure [19, 20]. Frailty status can be changed and its assessment should not only be for prognosis but also lead to “pre-rehabilitation” interventions [21] and clear comprehensive cardiac rehabilitation (CR) recommendations [9, 22]. Physical rehabilitation for frail older people can positively affect physical fitness and this effect may be related to level of frailty in a setting of long-term care [23]. On the other hand, there are no clear recommendations concerning what methods and tools are sensitive enough and could be used to detect existence *and* dynamics of frailty syndrome in this particular patient population.

The aim of this literature review was to evaluate existing evidence on exercise-based cardiac rehabilitation (CR) as a treatment option for elderly frail VHD patients. This literature review aimed to assess the following issues:

(1) Are assessment tools used for frailty screening sensitive enough to show improvement in frailty status after exercise-based CR?

(2) What exercise interventions would be the most beneficial for frail patients?

(3) Would the change of frailty status improve outcomes on levels of disability, functional capacity, and quality of life after surgical/interventional VHD treatment beyond the effects of the surgery/intervention itself?

## 2. Methods

We conducted a literature review of articles published from 1980 to January 2018. Literature search was performed using the PubMed database. Relevant studies were identified using the following key words: valve surgery/TAVI and exercise training, cardiac rehabilitation, moderate aerobic exercise training, high intensity interval training, resistance training, strength training, exercise capacity, prognosis, mortality, frailty, and sarcopenia. Additionally, we manually searched the bibliographies of all included articles.

The search was limited to publications related to adults over 60 years old and published in English (see Figures 1 and 2).

## 3. Results

*3.1. Are Assessment Tools Used for Frailty Screening Sensitive Enough to Show Improvement in Frailty Status after Exercise-Based CR?* In order to answer first research question we describe most often used frailty tools for screening in patients with VHD and compare results with frailty assessment methods used in a setting of CR.

Large variety of methods and instruments are used to describe existence or/and level of frailty for patients with VHD (Table 1). Most of the conducted studies were designed to evaluate various outcomes after surgery or intervention. The results of studies evaluating prevalence of the frailty and

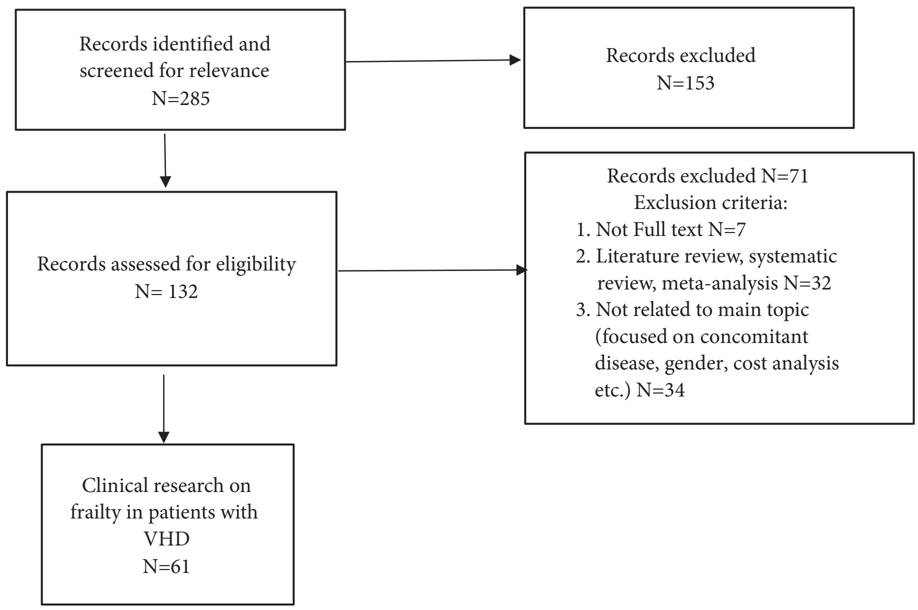


Figure 2: Flowchart of the selection of publications included in literature review related to valve surgery and frailty.

frailty status strongly depended upon used assessment tools and variables measured [24]. Prevalence of frailty varied from 20-26% to 68-82%, according to the scale and the population examined [9, 24]. A systematic review and meta-analysis by Anand et al. evaluated the relationship between preoperative frailty and outcomes following TAVI and demonstrated that the proportion of frail patients varied greatly across the different studies from 5 to 83% [25]. Although frailty has a good predictive value, results of the different studies are inconclusive and/or contradictory even with the same tools and similar populations. Also there is a gap of evidence concerning frailty tools sensitivity in this particular patient population. The most frequently used frailty assessment procedures for patients with VHD are discussed below.

*3.1.1. Fried Phenotype Frailty Index Assessment (FFS).* FFS represents the definition of physical frailty and it is based on the results of the Cardiovascular Health Study and the Women's Health and Aging Studies [8]. It has been widely adopted and consists of five health domains: nutrition (unintentional weight loss), physical exhaustion (CES–D (depression) scale), low energy expenditure (or inactivity status) (Minnesota Leisure Time Activity questionnaire), mobility (5-meter walking test (5MWT)), and muscular strength (dominant hand handgrip strength) [8]. FFS covers all domains of physical frailty and is recommended by the American Geriatrics Society [26]. FFS scale also could be named as frailty index from Cardiovascular Health Study (5-item CHS).

However, the study that validated the FFS was performed with general population. There is no information about VHD patients, and the share of very old individuals included in the study was relatively low (3.6% of patients were 85 years or older) [8]. Moreover, used methods were subjective and based on qualitative manner and could not precisely evaluate cognitive function and level of independence. Enhanced FFS (or 7-item expanded CHS) with additional testing of cognitive function (using Mini Mental State Examination (MMSE)) and depressed mood was implemented [24, 27]. Another example of FFS modification (modified fried frailty criteria) was scale for frailty evaluation that includes similar domains by using different methods to describe malnutrition (hypoalbuminemia) and clearly describe level of independence with Katz index [13, 28–30].

FFS [12, 24, 31–35] and scale modifications are widely used in studies involving VHD patients for frailty screening and unfavorable intervention/surgery outcome prediction. FFS was an accurate frailty assessment tool for prediction of increased hospitalization costs after cardiac surgery [31]. Some authors did not find any relation between frailty (measured by FFS) and mortality, morbidity, or increased length of stay in the hospital [33, 36, 37]. However the studies concluded that frail patients are more often referred to cardiac rehabilitation facilities [33, 36]. In a large study from Arnold et al. (N=2830) the authors demonstrated that frailty measured by FFS was a good predictor for negative short-term outcome (mortality, low quality of life) [32]. Similar results were reported in other studies [34, 35, 38, 39]. Forcillo et al. included high- and extreme-risk patients undergoing TAVI and found that serum albumin, Katz index, and 5MWT were associated with increased risk of adverse outcomes, but only albumin was predictive of 30-day all-cause mortality [28]. In contrast, in two studies from Afilalo et al. (2012 and 2017) the FFS and its modifications were inferior compared to other assessment tools (5MWT alone and EFT) for frailty screening [12, 24]. We failed to find any study that would be designed to evaluate FFS sensitivity for patients with VHD or in which FFS would be used in cardiac rehabilitation settings. According to our analysis, although FFS is a traditional method for frailty syndrome diagnosis and screening, it may be not reasonable for frailty dynamics after comprehensive CR program.

Table 1: Characteristics of reviewed studies on frailty and VHD.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Abramowitz (2016)** [29] | N=805; Age 82.0±8.8, F 321 (39,9%) | TAVI 279 (34.7%) | (1) MFFC (2) BMI | (1) To assess the influence of BMI on the short- and midterm clinical outcome following TAVI. | (1) Obese patients had lower prevalence of frailty. (2) All-cause mortality up to 30 days was 2.9% (10/340) vs 4.5% (12/268) vs 0.5% (1/186) in patients with normal weight, overweight, and obesity, respectively ($p<0.048$). (3) In a multivariable model, overweight and obese patients had similar overall mortality compared to patients with normal weight. |
| **Ad (2016)** [33] | N=167; Age 74.1±6.6, F 41 (25%) | Cardiac surgery 39 (23%) | (1) FFS | (1) Impact of frailty on outcomes of patients undergoing cardiac surgery | (1) Frail patients had longer median ICU stays (54 vs. 28h, $p=0.003$), longer median LOS (8 vs. 5 days, $p<0.001$), greater likelihood of STS-defined complications (54% vs. 32%, $p=0.011$), and discharge to an intermediate-care facility (45% vs. 12%, $p<0.001$) (2) not different from non-frail patients on major outcome, operative mortality, or readmissions. |
| **Afilalo (2010)** [6] | N=131; Age 75.8± 4.4; F 44 (34%) | Open cardiac surgery 60 (46%) | (1) 5MWT | (1) Inhospital post-operative mortality or major morbidity, defined by the STS. | (1) Slow gait speed was an independent predictor of the composite end point after adjusting for the STS risk score (OR: 3.05; 95% CI: 1.23 to 7.54). |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Afilalo (2012)** [12] | N=152;<br>Age 75,9±4,4,<br>F 52 (34%) | Cardiac surgery<br>20%- 46% | (1) FFS<br>(2) 7-item FFS<br>(3) 4-item MSSA<br>(4) 5MWT | (1) The STS composite end point of in-hospital postoperative mortality or major morbidity | (1) The most predictive scale in each domain was 5MWT<br>(2) ≥6 s as a measure of frailty |
| **Afilalo (2016)** [52] | N=15171;<br>Age 71,<br>F 4622 (30.5%). | Cardiac surgery<br>4588 (30,24%) | (1) 5MWT | (1) Operative mortality or within 30 d | (1) Compared with patients in the fastest gait speed tertile, operative mortality was increased for those in the middle tertile (0.83-1.00m/s; OR, 1.77; 95% CI, 1.34-2.34) and slowest tertile.<br>(2) After adjusting gait speed remained independently predictive of operative mortality (OR, 1.11 per 0.1-m/s decrease in gait speed; 95% CI, 1.07-1.16).<br>(3) Gait speed was also predictive of the composite outcome of mortality or major morbidity (OR, 1.03 per 0.1-m/s decrease in gait speed; 95% CI, 1.00-1.05). |
| **Afilalo (2017)** [24] | N=1020;<br>Age 82 (77–86), F 421 (41%) | SAVR, TAVI<br>26-68% | (1) FFS<br>(2) MFFC<br>(3) CHSA<br>(4) SPPB<br>(5) Bern scale<br>(6) Columbia scale<br>(7) EFT | (1)Death from any cause at 12 mo<br>(2) death from any cause at 30 d or worsening and institutionalization<br>(3) new accrued disabilities at 12 mo | (1) EFT was the strongest predictor of death at 1 y (adjusted [OR]: 3.72; 95% [CI]: 2.54 to 5.45).<br>(2) EFT was the strongest predictor of worsening disability at 1 y (adjusted OR: 2.13; 95% CI: 1.57 to 2.87) and death at 30 d (adjusted OR: 3.29; 95% CI: 1.73 to 6.26). |
| **Alfredsson (2016)** [51] | N=8039;<br>Age 84 (79–88)<br>F 4128 (51.4%) | TAVI<br>6100 (75,88%) | (1) 5MWT | (1) all-cause mortality at 30 d | (1) 30-d all-cause mortality rates were 8.4%, 6.6%, and 5.4% for the slowest, slow, and normal walkers, respectively (P<0.001).<br>(2) Each 0.2-m/s decrease corresponded to an 11% increase in 30-d mortality (adjusted OR, 1.11; 95% CI, 1.01–1.22).<br>(3) The slowest walkers had 35% higher 30-d mortality than normal walkers (adjusted OR, 1.35; 95% CI, 1.01–1.80), significantly longer LOS, and a lower probability of being discharged to home. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Arnold (2017)** [32] | N=2830;<br>Age 83.3,<br>F 1284 (45.4%) | TAVI<br>1692 (59.8%) | (1) FFS | (1) death within the first 6 mo after TAVI;<br>(2) very poor QoL at 6 mo;<br>(3) moderate worsening in QoL from baseline to 6 mo | (1) For all models except the 1-year clinical model, frailty was associated with an increase in the odds of a poor outcome of 30% to 40% when added to the existing models;<br>(2) Adding frailty as a syndrome increased the c-indexes by 0.000 to 0.004, with the most important individual components being disability and unintentional weight loss |
| **Assmann (2016)** [19] | N=89;<br>Age 80.4±6,3,<br>F 51 (57%) | TAVI<br>NA | (1) MGA/MGBE | (1) Postprocedural period, mortality in 30 d follow-up | (1) Variables from frailty assessment protectively associated with delirium were MMSE, IADL and gait speed<br>(2) TUG was predictively associated with delirium<br>(3) MMSE was independently associated with delirium.<br>(4) Variables predictively associated with mortality were the summary score Frailty Index (HR 1.66, 95% CI 1.06 to 2.60; p=0.03)<br>(5) Variables from frailty assessment are associated with delirium and mortality |
| **Bagienski (2017)** [20] | N=141;<br>Age 82.0,<br>F 89 (63,1%) | TAVI<br>2,8-90,1% | (1) 5MWT,<br>(2) Elderly mobility scale<br>(3) CSHA,<br>(4 ) Katz index,<br>(5) Grip strength,<br>(6) ISAR | (1) All-cause mortality at 30 d and 12 mo | (1) 30-d and 12-mo all-cause mortality rates were higher in the delirium group (p <0.001).<br>(2) Significantly more patients with delirium were considered as frail before TAVI. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Bogdan (2016)** [59] | N=150;<br>Age 81±6 years<br>F 90 (60%) | TAVI<br>79 (53%) | (1) Low albumin | (1) Correlation between baseline serum albumin and all-cause mortality in TAVI patients.<br>(2) low post-procedural albumin following TAVI. | (1) Mortality was higher in the low albumin group compared with the normal albumin group (35% vs. 19%, p=0.01).<br>(2) Multivariate analysis indicated that low preprocedural albumin (≤40 g/L) was independently associated with a more than twofold increase in 2.1 year all-cause mortality (p=0.01, HR=2.28; 95% CI: 1.174.44).<br>(3) Low postprocedural serum albumin remained a strong parameter correlated with all-cause mortality (HR=2.47; 95% CI: 1.284.78; p<0.01). |
| **Capodanno (2014)** [63] | N=1878<br>NA<br>F 1087 (57,9%) | TAVI<br>459 (24,4%) | (1) Geriatric status scale | (1) 30-d mortality | (1) Frailty OR 2.09, CI (1.30-3.37), p =0.003<br>(2) OBSERVANT risk model did not include frailty as a risk factor |
| **Chauhan (2016)** [38] | N=342;<br>Age 81.85,<br>F 179 (52,3%) | TAVI<br>104 (30%) | (1) MFFC | (1) all-cause mortality<br>(2) total postoperative LOS, discharge disposition and incidence of stroke. | (1) Patients with frailty score of 3/4 or 4/4 had increased all-cause mortality (P = 0.015 and P <0.001) and were more likely to be discharged to an ICU facility (P =0.083 and P = 0.001).<br>(2) 4/4 frail patients had increased post-operative LOS (P = 0.014)<br>(3) Individual components of the frailty score were also independent predictors of all-cause mortality.<br>(4) The HR of mortality increased with each increase in frailty score |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Cockburn (2015)** [64] | N=312; Age 81.2±6.8, F 146 (46,8%) | TAVI NA | (1) General mobility EuroSCORE II (2) Brighton mobility index (3) NYHA (4) Karnofsky performance scale (5) Katz Index (6) CSHA | (1) Assess whether different frailty indices predict outcomes both in the shorter and longer terms | (1) Both univariate and multivariate analyses confirmed poor mobility (EuroSCORE II), as the best predictor of adverse outcome over both the short-term (OR 4.03, 95% CI (1.36–11.96), P50.012 (30 days)) and longer term (OR 2.15, 95% CI (1.33–3.48), P50.002, (2.261.5 years.) (2) Mobility impairment, of either neurological or musculoskeletal etiology, is an appropriate screening measure when considering patients for TAVI. |
| **Codner (2015)** [49] | N=360; Age 82. ± 6.9, F 203 (56.4%) | TAVI NA | (1) 5MWT (2) Katz Index, (3) albumin levels, (4) oxygen therapy, (5) cognitive status, (6) gen. appearance | All-cause mortality during follow-up. | In multivariate analysis frailty (HR 1.89, 95% CI 1.11 to 3.2, p =0.02) was independent predictor for all-cause mortality. |
| **Dahya (2016)** [65] | N=104, Age 81 ± 10, F 50 (48%) | TAVI NA | CT scan – SMI MFFC | (1) Relationship between SMI and LOS | (1) A multivariate model showed SMI as independent predictors of LOS. (2) For every 14-cm2/m2 increase in SMI, there was a 1-d reduction in LOS. (3) None of the standard measures of frailty predicted LOS. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **de Thézy (2017)** [66] | N=49; Age 84.8, F 27 (55.1%) | TAVI 41 (83.67%) | (1) G8 scale (2) CGA | (1) sensitivity and specificity of G8 | (1) G8 had a sensibility of 100% (IC 95% [0.91]), a specificity of 72.7% (IC 95% [0.430.9]), a positive predictive value of 92.6% and a negative prospective value of 100% (IC: 95%). (2) G8 scale could be performed by cardiologists in older patients with AS for identifying patients with a geriatric risk profile in consultation before surgery. |
| **Debonnaire (2015)** [37] | N=511 Age 82 F 317 (62%) | TAVI 98 (21%) | (1) FFS (2) Eye ball test | (1) 1y mortality | (1) Frailty was not associated with the study end point |
| **Eichler (2017)** [41] | N=344; Age 80.9 ± 5.0; F 191 (55,5%) | TAVI 152 (45.8%) | (1) MGA/MGBE | (1) All-cause mortality at 12 mo after TAVI. | (1) MGA/MGBE had no predictive power; its individual components, particularly nutrition (OR 0.83 per 1 pt., CI 0.72–0.95; p=0.006) and mobility (OR 5.12, CI 1.64–16.01; p=0.005) had a prognostic impact. |
| **Esses (2018)** [43] | N= 3088; Age 69.24 ± 13.10, F 1163 (37.7) | SAVR 25,74- 56,19% | (1) modified CSHA (2) RAI (3) 6-mo mortality index by Porock (3) Ganapathi index | (1) 30-d mortality and major postoperative morbidity. | (1) Frailty was a better predictor of mortality than morbidity, and it was not markedly different among any of the 3 indices. (2) Frailty was associated with an increased risk of 30 d mortality and longer LOS. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Forcillo (2017)** [28] | N=361; Age 82; F 167 (43%) | TAVI NA | MFFC | (1) 30-d mortality and to compare the discrimination of 30-d mortality, and to compare its discriminative ability with STS PROM. | (1) For high- and extreme-risk patients undergoing TAVR, serum albumin, Katz Index, and 5MWT were associated with increased risk of adverse outcomes. (2) Only albumin was predictive of 30-day all-cause mortality. |
| **Garg (2017)** [67] | N=152; Age 83.3±6.5, F 64 (42%) | TAVI 76 (50%) | (1) CT scan - PMA | (1) early poor outcome (30 d mortality, stroke, dialysis, and prolonged ventilation | (1) Indexed PMA ([OR] 3.19, [CI] 1.30 to 7.83; p =0.012) and age (OR 1.92, CI 1.87 to 1.98; p = 0.012) predicted early poor outcome. (2) High-resource utilization was observed more frequently in patients with PMA less than the median (73% vs 51%, OR 2.65, CI 1.32 to 5.36; p = 0.006). |
| **Goldfarb (2017)** [31] | N=235 Age 73.0; F 68 (29%) | Cardiac surgery N=91, (38,72%) | FFS or SPPB | (1) The impact of preoperative frailty status on postoperative hospitalization costs | (1) The median cost was $32,742 in frail patients compared with $23,370 in non-frail patients (P < 0.001). (2) Total costs were independently associated with frailty and valve surgery (P < 0.001). (3) This effect persists after adjusting for age, sex, surgery type, and surgical risk score. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Green (2013)** [55] | N=484; Age 84,7, F 224 (46%) | TAVI 351 (72,52%) | (1) 6MWT | (1) association between baseline 6MWT and functional improvement (2) association between baseline 6MWT and mortality. | (1) There were no differences in 30-d outcomes among 6MWTD groups. (2) At 2 y, the rate of death from any cause was 42.5% in those unable to walk, 31.2% in slow walkers, and 28.8% in fast walkers (p = 0.02), driven primarily by differences in noncardiac death. (3) Patients with poor baseline functional status exhibit the greatest improvement in 6MWTD. |
| **Green (2015)** [39] | N=244; Age 86,25, F 1118 (48,3%) | TAVI 110 (45%) | (1) MFFC | (1) Time to death from any cause over 1 y of follow up and poor outcome at 1y | (1) At 30 d, there were no differences in rates of MACCE according to baseline frailty status. (2) At 1 y all-cause mortality rate was 32.7% in the frail group and 15.9% in the non-frail group (log-rank p=0.004). (3) Frailty remained independently associated with an increased odds of poor outcome after TAVI at both 6 mo (OR 2.21, 95% CI 1.09–4.46, p = 0.03) and 1 y (OR 2.40, 95% CI 1.14–5.05, p = 0.02). |
| **Grossman (2017)** [57] | N=426; Age 83.8, F 242 (56,8%) | TAVI 192 (45,07%) | (1) Low albumin | (2) 1-y all-cause mortality. | (1) Participants with low albumin levels had higher mortality (HR) = 3.03, 95% (CI) = 1.66–5.26, P < .001). (2) Participants with low serum albumin and a high STS (HR = 4.55, 95% CI = 2.21–9.38, P < .001) or EuroSCORE-2 (HR = 2.72, 95% CI = 1.48–5.06, P = .001) (3) Serum albumin, as a marker of frailty, can significantly improve the ability of STS and EuroSCORE-2 scores to predict TAVR-related mortality. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Herman (2013)** [68] | N=4270;<br>Age 67,<br>Female 25% | Cardiac surgery 171 (4%) | (1) Katz index<br>(2) independence in ambulation<br>(3) dementia | (1) Composite end point defined as MACCE | (1) Frailty was significant (OR 1.7; 95% CI 1.2-2.5) predictor.<br>(2) The concordance statistic for the MACCE model in a mixed population was 0.764 (95% CL; 0.75-0.79) and had excellent calibration. |
| **Hermiller (2016)** [69] | N=3687;<br>Age 83.3 ± 7.8 F 1707 (46.3%) | TAVI<br>NA | (1) 5MWT<br>(2) grip strength<br>(3) BMI<br>(4) anemia<br>(5) hypoalbuminemia<br>(6) weight loss;<br>(7) Fall | All-cause mortality rate 30 d and 1 y | (1) Albumin levels <3.3 g/dl predicted death at 30 d.<br>(2) Albumin levels <3.3 g/dl, falls in the past 6 months, predicted death at 1 y.<br>(3) This score (Albumin, assisted living, home oxygen, age>85y) showed a 3-fold difference in mortality rates for the low-risk and high-risk subsets at 30 d (3.6% and 10.9%, respectively) and 1 y (albumin, comorbidities, home oxygen, STS>7%) (12.3% and 36.6%, respectively). |
| **Huded (2016)** [36] | N=191<br>Age 82.4 ± 9.2;<br>F 93 (49%) | TAVI<br>N=64, (33,5%) | FFS | (1) 30-d mortality, AE, hospital readmission<br>(2) hospital LOS,<br>(3) Discharge to a rehabilitation facility, | (1) There was no difference in 30-d mortality, major complications, mean hospital LOS, 30-day hospital re-admission, or overall survival between groups.<br>(2) Frailty was independently associated with discharge to a rehabilitation facility (p=0.004). |
| **Kamga (2013)** [70] | N=30;<br>Age 86 ± 3,<br>F 14 (47%) | TAVI<br>NA | (1) The ISAR<br>(2) The SHERPA score | (1) Outcomes 30 d and 1 y | (1) The ISAR score was similar but the SHERPA score was significantly higher in non-survivors (7.8 ±1.6 vs. 4.9 ±2.4; P = 0.001).<br>(2) SHERPA score (>7) and BMI were independent predictors of 1y mortality (P = 0.004). |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Kano (2017)** [50] | N=1256; Age NA F 895 (71,25%) | TAVI 693 (55,17%) | (1) 5MWT | (1) 30 d and 12 mo mortality | (1) The slowest walkers and those unable to walk demonstrated independent associations with increased midterm mortality after adjustment (HR, 1.83, 4.28; 95% CI, 1.03–3.26, 2.22–8.72; P=0.039, <0.001, respectively). (2) Gait speed <0.385 m/sec associated with worse prognosis (HR 2.40; 95% CI, 1.75–5.88; P=0.001). (3) Increased midterm mortality rate in patients with a gait speed of 0.385~0.5 m/sec, or unable to walk as compared with patients with a normal gait speed. |
| **Kleczynski (2017)** [30] | N=101; Age 81.0 F 60.4% | TAVI 6,9-52,5% | (1) Katz index (2) EMS (3) Katz Index (4) CSH (5) 5MWT (6) Hand grip strength (7) ISAR | 12-mo mortality | (1) Associations between frailty indices and 12-mo all-cause mortality were significant, adjusted for logistic EuroSCORE: (1) for 5MWT, 72.38 (15.95-328.44); (2) for EMS, 23.39 (6.89-79.34); (3) for CSHA scale, 53.97 (14.67-198.53); (4) for Katz index, 21.69 (6.89-68.25); (5) for hand grip strength, 51.54 (12.98-204.74); (6) for ISAR scale, 15.94 (2.10-120.74). (2) 5MWT, EMS, or hand grip test may be advocated. |
| **Kobe (2016)** [71] | N=130; Age 83.3 F 65 (50%) | TAVI 71 (55%) | (1) FORECAST | (1) 12-mo mortality | (1) ROC showed that the FORECAST is a valid tool to predict in-hospital mortality (area 0.73). (2) By combining the FORECAST and the STS score, this effect was even higher (area 0.77; P = 0.021). (3) Stratifying the patients according to the FORECAST score showed best survival in the lowest frailty group. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Koifman (2016)** [62] | N=491;<br>Age 83,8<br>F 245 (50%). | TAVI<br>43 (8,75%) | BMI | (1) all-cause mortality at 1 y of follow-up | (1) All-cause mortality at 1 y was higher in the low-BMI group (log-rank p=0.003) with no significant difference among normal and above-normal BMI patients.<br>(2) In a multivariate model, BMI <20 kg/m2 was an independent predictor of mortality (HR=2.45, p=0.01) |
| **Kotajarvi (2017)** [45] | N=103;<br>Age 80.6 years, F 42 (40,1%) | SAVR<br>54 (52,4%) | (1) CSHA | (1) to determine the extent to which surgery affected measures of physical and mental health and QoL,<br>(2) examine how changes in these patient-centered outcomes compared between non-frail and frail study participants. | (1) Frail participants had lower baseline independence and QoL measures;<br>(2) At follow-up, frail participants showed significant improvement in physical function, with physical health scores improving by 50% and 14%. Non-frail subjects did not significantly improve in these measures.<br>(3) Mental health scores also improved to a greater extent in frail participants (3.6 vs < 1 point).<br>(4) Frail participants improved to a greater extent in physical well-being (21.6 vs 7.1 points) and quality of life measures (25.1 vs 8.7 points) |
| **Laure Bureau (2017)** [72] | N=116;<br>Age 86.2 ± 4.2<br>F 116 (49.1%) | TAVI<br>10-58% | MPI score the sum of<br>(1) Katz Index<br>(2) MNA-SF<br>(3) SPMSQ<br>(4) CIRS | All cause of mortality at 1 mo | Mortality rate was significantly different between MPI groups at 6 and 12 mo (p=0.040 and p=0.022). Kaplan Meier survival estimates at 1 y stratified by MPI groups were significantly different (HR=2.83, 95% (CI) 1.38–5.82, p=0.004). Among variables retained to perform logistic regression analysis, Katz index appeared the most relevant (p < 0.001). |
| **Lee (2010)** [15] | N=3826;<br>Age 68,5;<br>F 998 (26%) | Cardiac surgery<br>157 (4.1%) | (1) Katz index<br>(2) independence in ambulation<br>(3) dementia | (1) In-hospital mortality, midterm all-cause mortality and discharge to an institution | (1) Frailty was an independent predictor of in-hospital mortality (OR 1.8, 95% CI 1.1 to 3.0), as well as institutional discharge (OR 6.3, 95% CI 4.2 to 9.4).<br>(2) Frailty was an independent predictor of reduced midterm survival (HR 1.5, 95% CI 1.1 to 2.2). |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Mamane (2016)** [73] | N=208;<br>Age 80.7± 6.8<br>F 114 (55%) | TAVI<br>NA | (1) CT scan – PMA | All-cause mortality | (1) PMA was lower in non-survivors compared with survivors among women (12.9 vs 14.5 cm2; P = 0.047) but not men (21.7 vs 22.4 cm2; P = 0.50).<br>(2) The association between PMA and all-cause mortality in women persisted after adjustment (HR, 0.88 per cm2; 95% CIerval, 0.78-0.99).<br>(3) PMA is a marker of frailty associated with midterm survival in women |
| **Martin (2017)** [74] | N=6339;<br>Age, 81.3;<br>F 2927 (46.2%) | TAVI<br>NA | (1) Katz Index<br>(2) CSHA<br>(3) poor mobility | (1) Internally validate a multivariable TAVI CPM for predicting 30-d mortality in UK-TAVI patients | (1) The final UK-TAVI CPM included 15 risk factors, which included 2 variables associated with frailty.<br>(2) Scale demonstrated strong calibration and moderate discrimination |
| **Metze (2017)** [16] | N=213<br>Age 78<br>F 122 (42,7%) | PMVR<br>97 (45,5%) | (1) FFS | (1) procedural outcomes, short-term functional changes, and long-term clinical outcomes | (1) Mortality at 6 w was significantly higher in frail (8.3%) compared with nonfrail (1.7%) patients (p =0.03). Hazards of death (HR: 3.06; 95% CI: 1.54 to 6.07; p <0.001) and death or heart failure decompensation (HR 2.03; 95% CI 1.22 to 3.39; p. 0.007) were significantly increased in frail patients during long-term follow-up, which did not change relevantly after adjustment<br>(2) PMVR can be performed with equal efficacy and is associated with at least similar short-term functional improvement in frail patients. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
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| **Mok (2016)** [61] | N=460; Age 81 ± 8 F 224 (49%) | TAVI Sarcopenia 293 (64%) Sarcopenic-Obesity 212 (46%) | (1) CT scan – SMM, FM | (1) assess the feasibility of evaluating body composition by CT (2) determine the prevalence of sarcopenia, obesity, sarcopenic obesity; (3) analyze the impact of differing body composition on 30-day and late clinical outcomes. | (1) Sarcopenia predicted cumulative mortality (HR 1.55, 95% confidence interval 1.02 to 2.36, p=0.04). (2) Differences in body composition had no impact on 30-day clinical outcomes after TAVI. |
| **Nemec (2017)** [75] | N=238; Age 82.3 ± 10.0, F 78 (32,33%) | TAVI 53 (34%) sarcopenia, | (1) CT scan - SMI | (1) inter- and postprocedural complications (2) LOS, 30 d and 1-y mortality | (1) SMIs at L3 and T12 significantly correlated with prolonged LOS. (2) SMI3, SMI7 SMI12, SC, and BMI did not show a relationship with perioperative death or complications or 30- day and 1-year mortality rates. (3) VF showed a significant relationship with 30-day and 1-year mortality rates |
| **Okoh (2017)** [34] | N=75; Age 92±2; F 49 (65%) | TAVI 30 (40%) | FFS | (1) all-cause mortality | (1) Significant improvement in overall health status of non-frail patients (mean difference: 11.03, P=0.032). (2) Unadjusted 30-day and 2-year mortality rates were higher in the frail group than the non-frail group (14% vs. 2% P = 0.059; 31% vs. 9% P = 0.018). (3) Kaplan-Meier estimated all-cause mortality to be significantly higher in the frail group (log-rank test; P = 0.042). (4) Frailty status was independently associated with increased mortality (hazard ratio: 1.84, 95% C.I: 1.06–3.17; P=0.028) after TAVI. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Paknikar (2016)** [76] | N=295; Age 74,68, F 102 (34,5%) | SAVR/TAVI NA | (1) CT scan - TPA | (1) To evaluate the use of sarcopenia as a frailty assessment tool | (1) 2 y survival was 85.7% in patients with sarcopenia, compared with 93.8% in patients without sarcopenia (P = .02). (2) Independent predictors of late survival included TPA (HR, 0.47; P = .02). (3) Male sex (OR, 0.52; P = .04) and TPA (OR, 0.6; P = .001) were predictive of high resource utilization. (4) A separate analysis by treatment group found that TPA predicted high resource utilization after SAVR (OR, 0.4; P<.001), but not after TAVI (P = .66) |
| **Puls (2014)** [77] | N=300; Age 82±5 years F 198 (66%) | TAVI 144 (48%) | (1) Katz Index | (1) all-cause mortality | (1) Early mortality was significantly higher in frail persons (5.5% vs. 1.3%, p=0.04 for immediate procedural mortality; 17% vs. 5.8%, p=0.002 for 30-day mortality; and 23% vs. 6.4%, p<0.0001 for procedural mortality). (2) In contrast, the Katz Index <6 was identified as a significant independent predictor of long-term all-cause mortality by multivariate analysis (HR 2.67 [95% CI: 1.7-4.3], p<0.0001). |
| **Rodés-Cabau (2010)** [78] | N=339; Age 81±8; F 187 (55,2%) | TAVI 85 (25.1) | Eye ball test | (1) Procedural and 30-d outcomes | (1) Patients with either porcelain aorta (18%) or frailty (25%) exhibited acute outcomes similar to the rest of the study population |
| **Rodés-Cabau (2012)** [79] | N=339; Age 81±8; F 187 (55,2%) | TAVI; 85 (25.1) | Eye ball test | (1) the occurrence of mortality (yes/no) | (1) At a mean follow-up 188 patients (55.5%) had died. (2) The predictors of late mortality were frailty (HR: 1.52, 95% CI: 1.07 to 2.17). |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Rodrigues (2017)** [46] | N=221; Age 71, F 76 (34,3%) | Cardiac surgery; Pre-frailty 144 (65,15%) | (1) CSHA | (1) main outcomes after cardiovascular surgery in pre-frail patients compared with non-frail patients. | (1) Pre-frail patients showed a longer mechanical ventilation time (193 ± 37 vs. 29 ± 7 hours; p<0.05), LOS at ICU (5 ± 1 vs. 3 ± 1 days; p < 0.05) and total time of hospitalization (12 ± 5 vs. 9 ± 3 days; p < 0.05). (2) In addition, the pre-frail group had a higher number of AE with an increased risk for development stroke (OR: 2.139, 95% CI: 0.622–7.351, p = 0.001; HR: 2.763, 95%CI: 1.206–6.331, p = 0.0001) and in-hospital death (OR: 1.809, 95% CI: 1.286–2.546, p = 0.001; HR: 1.830, 95% CI: 1.476–2.269, p = 0.0001). (3) higher number of pre-frail patients required homecare services (46.5% vs. 0%; p < 0.05). |
| **Rodríguez-Pascual (2016)** [35] | N=606; Age 83,95, F 355 (58%) | TAVI/SAVR 299 (49.3%) | (1) FFS | (1) all-cause mortality during the follow-up | (1) The HR (95% CI) of mortality among frail versus non-frail patients was 1.83 (1.33–2.51). (2) frailty criteria were considered separately; mortality was also higher among patients with slow gait speed [1.52 (1.05–2.19)] or low physical activity [1.35 (1.00–1.85)]. |
| **Ryomoto (2017)** [80] | N=85; Age 78 ± 6, F 57 (67%) | AVR 8 (9,4%) | (1) FIM | (1) whether the preoperative FIM is useful for decision making for a strategy in the era of TAVI | (1) The preoperative motor FIM score was significantly lower in the compromised group (45 ± 24) than in the unaffected group (85 ± 9, p =<0.01). (2) The duration of postoperative intubation, ICU stay, and postoperative hospitalization were significantly longer in the compromised group than in the unaffected group (48 ± 67 vs 16 ± 12 h, p<0.01; 6.7 ± 5.3 vs 3.4 ± 2.0 days, p<0.01; 34 ± 27 vs 23 ± 11 days, p = 0.02, respectively). |
| **Saji (2016)** [81] | N=232; Age 80.1 ± 8.7 F 132 (57%) | TAVR; 77 (33,2%) | (1) CT scan - PMA (2) 5MWT | (1) all-cause mortality at 30 d and 6 mo. | (1) After adjustment for multiple confounding factors, the normalized PMA tertile was independently associated with mortality at 6 mo (adjusted HR 1.53, 95%, CI 1.06 to 2.21). (2) Kaplan-Meier analysis showed that tertile 3 had higher mortality rates than tertile 1 at 6 m (14% and 31%, respectively, p =0.029). (3) PMA is an independent predictor of mortality after TAVI; 5MWT combined with normalized PMA showed greater discrimination ability than alone. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Saji** **(2017)** [27] | N=155;<br>Age 85 F 99 (65) | TAVI<br>NA | (1) SPPB<br>(2) MFFC<br>(3) PARTNER scale<br>(4) Frailty index (Japan)<br>(5) CSHA<br>(6) 5MWT | (1) all-cause unplanned readmission following TAVI | (1) Frailty markers other than MFFC were independently associated with unplanned readmission.<br>(2) The analysis found that the SPPB, the PARTNER frailty scale, the frailty index, CSHA and 5MWT were independently associated with unplanned readmission even after adjustment in the multivariate analysis. |
| **Schoenenberger** **(2013)** [17] | N=119;<br>Age 83.4+4.6 years;<br>F 66 (55.5%) | TAVI<br>59 (49.6%) | (1) MGA/MGBE | (1) Functional decline over 6 mo | (1) The frailty index strongly predicted functional decline in univariable (OR per 1 point increase 1.57, 95% CI: 1.20–2.05, P = 0.001) and bivariable analyses (OR: 1.56, 95% CI: 1.20–2.04, P = 0.001 controlled for EuroSCORE; OR: 1.53, 95% CI: 1.17–2.02, P = 0.002 controlled for STS score).<br>(2) Overall predictive performance was best for the frailty index [Nagelkerke's R2 (NR2) 0.135] and low for the EuroSCORE (NR2 0.015) and STS score (NR2 0.034).<br>(3) In univariable analyses, all components of the frailty index contributed to the prediction of functional decline. |
| **Seiffert** **(2014)** [44] | N=845;<br>Age 80.9 ± 6.5<br>F 432 (51.1%) | TAVI<br>16 (4.6) | (1) CSHA | (1) to determine the additional value of indicators of frailty for postoperative survival in the elderly patient sample in the last step | (1) BMI, eGFR, hemoglobin, pulmonary hypertension, mean transvalvular gradient and LV ejection fraction at baseline were most strongly associated with mortality and entered the risk prediction algorithm [C -statistic 0.66, 95 % confidence interval (CI) 0.61–0.70, calibration v2 -statistic = 6.51; P = 0.69].<br>(2) Frailty increased the C -statistic to 0.71, 95 % CI 0.65–0.76.<br>(3) Frailty was strongly related to outcome and increased the discriminatory ability of the risk algorithm. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Shimura (2017)** [47] | N=1215;<br>Age 84.4 ± 5.0,<br>F 854 (70,2%) | TAVI<br>Moderately frail<br>122 (10.0%)<br>Severely frail<br>48 (4.0%) | (1) CSHA<br>(2) BMI<br>(3) Albumin,<br>(4) 5MWT<br>(5) Hand grip. | The 30-d mortality and in-hospital mortality | (1) Cumulative 1-y mortality increased with increasing CSHA stage (7.2%, 8.6%. 15.7%, 16.9%, 44.1%, p<0.001).<br>(2) In a Cox regression multivariate analysis, the CSHA (per 1 category increase) was an independent predictive factor of increased late cumulative mortality risk (HR: 1.28; 95% CI: 1.10-1.49; p<0.001). |
| **Stortecky (2012)** [14] | N=100;<br>Age 83.7± 4.6 F 60 (60.0%) | TAVI<br>49 (49.0%) | (1) MGA/MGBE | (1) outcomes at 30 day and 1 year | (1) Associations of cognitive impairment (odds ratio [OR]: 2.98, 95% confidence interval [CI]: 1.07 to 8.31), malnutrition (OR: 6.72, 95% CI: 2.04 to 22.17), mobility impairment (OR: 6.65, 95% CI: 2.15 to 20.52), limitations in basic ADL (OR: 3.63, 95% CI: 1.29 to 10.23), and frailty index (OR: 3.68, 95% CI: 1.21 to 11.19) with 1-year mortality were similar compared with STS score (OR: 5.47, 95% CI: 1.48 to 20.22) and EuroSCORE (OR: 4.02, 95% CI: 0.86 to 18.70).<br>(2) Similar results were found for 30-day mortality and MACCE. |
| **Sunderman (2011)** [82] | N=400<br>Age 80.3 ±4<br>F 206 (51,5%) | Cardiac surgery<br>Moderately frail<br>170<br>Severely frail 31 | (1) CAF | (1) correlation of Frailty score to 30-d mortality. | (1) There were low-to-moderate albeit significant correlations of Frailty score with STS score and EuroSCORE ( $p < 0.05$).<br>(2) There was also a significant correlation between Frailty score and observed 30-day mortality ( $p < 0.05$).<br>(3) The comprehensive assessment of frailty is an additional tool to evaluate elderly patients adequately before cardiac surgical interventions. |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Sündermann (2011)** [11] | N=400;<br>Age 80.1 ± 4 years,<br>F 206 (51,5%) | Cardiac surgery 114 (55,33% ) | CAF | (1) 1 y all-cause mortality | (1) Patients who died within 1 y had a median frailty score of 16 [5;33] compared to 11 [3;33] to the 1 y survivors (P = 0.001).<br>(2) 1 y mortality within each CAF subgroup shows a significantly higher mortality rate among patients in the "severely frail" compared to less frail groups.<br>(3) Higher frailty group had a LOS at the ICU.<br>(4) The CAF score facilitates prediction of mid-term outcome of high-risk elderly patients |
| **Yamamoto (2015)** [58] | N=777;<br>Age 83,9,<br>F 400 (51,48%) | TAVI<br>56 (7,2%) | BMI | (1) The 30- d mortality | (1) Kaplan-Meier curves indicated no significant differences in cumulative 30-d and 1-y survival.<br>(2) BMI <20 was not associated with increased early or midterm mortality. |
| **Yamamoto (2017)** [58] | N=1215;<br>Age 84.4 ± 5.0,<br>F 854 (70.3%) | TAVI<br>284, (23,3%) | (1) Low albumin | (1) all-cause mortality after TAVI | (1) cumulative all-cause, cardiovascular, and noncardiovascular mortality rates were significantly higher in the low albumin group than in the normal albumin group (log-rank test, p <0.001, p = 0.0021, and p <0.001, respectively).<br>(2) Poorer prognosis of the low albumin group in terms of cumulative all-cause and non-cardiovascular mortality was retained (p = 0.038, and p = 0.0068, respectively) |

Table 1: Continued.

| Publication (year) | Sample size (N) Patient population (Age, Female N (%)) | Intervention Frail sample N (%) | Tool for frailty assessment | Primary end point | Main results/Conclusions |
|---|---|---|---|---|---|
| **Zuckerman (2017)** [83] | N=82;<br>Age 71,6<br>F 24, 29% | Cardiac surgery<br>NA | (1) CT scan - PMA | (1) postoperative LOS defined as the number of days from index procedure to hospital discharge | (1) Low PMA was correlated with lower handgrip strength and SPPB scores indicative of physical frailty.<br>(2) Postoperative LOS correlated with PMA (R=L0.47, p =0.004), LMA (R=−0.41, p=0.01), and TMA (R= −0.29, p=0.03).<br>(3) After adjustment PMA remained significantly associated with LOS ($\beta$= −2.35, 95% CI −4.48 to −0.22).<br>(4) The combination of low PMA and handgrip strength, indicative of sarcopenia, yielded the greatest incremental value in predicting LOS. |

*Intervention.* TAVI: Transcatheter Aortic Valve Implantation, SAVR: survival aortic valve replacement, PMWR: percutaneous mitral valve repair.
*Frailty Assessment.* FFS: Fried phenotype frailty index, SPPB: Short Physical Performance Battery, 5MWT: 5-meter walking test, CSHA: *Canadian Study of Health and Aging,* ISAR: Identification of Seniors at Risk, MMSA: MacArthur Study of Successful Aging, EMS: Elderly Mobility Scale, EFT: Essential Frailty Toolset, MFFC: Modified Fried Frailty Criteria, BMI: body mass index, SHERPA: Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie, CGA: comprehensive geriatric assessment, MPI: Multidimensional Prognostic Index, UK-TAVI CPM: UK TAVI clinical prediction models, RAI: risk analysis index, SMI: skeletal muscle index, 6MWT: six-minute walking test, CAF: comprehensive assessment of frailty, PMA: psoas muscle area, SMM: skeletal muscle mass, FM: fat mass, TPA: total psoas area, LMA: lumbar muscle area, TMA: thoracic muscle area, VF: visceral fat, SC: subcutaneous tissue area, FIM: functional independence measure, MGA/MGBE: *Multidimensional Geriatric Assessment*/Modified Geriatric Baseline examination, *MMSE:* Mini Mental State Examination, *TUG:* Time Up and Go, *IDAL:* instrumental activities in daily living, FORECAST: Frailty predicts death One yeaR after Elective CArdiac Surgery Test.
*Outcomes.* AE: Adverse events, LOS: length of stay, STS: Society of Thoracic Surgery, QoL: quality of life, NYHA: the New York Heart Association, MACCE: major adverse cardiac and cerebrovascular events.
*Results.* OR: odds ratio, HR: hazard ratio, CI: confidence interval, NA: not available, ICU: intensive care unit, eGFR: estimated glomerular filtration ratio.

*3.1.2. Multidimensional Geriatric Assessment (MGA) or Modified Geriatric Baseline Examination (MGBE).* Stortecky et al. and Schoenenberger et al. showed MGA/MGBE to be a good predictor of mortality and major adverse cardiovascular and cerebral events (MACCE) [14] as well as functional decline or death [17] after TAVI. This tool describes frailty by results of MMSE, Mini Nutritional Assessment (MNA), Katz index, independence in instrumental activities in daily living (IADL), Time Up and Go (TUG), and a subjective mobility disability (defined as a decreased frequency of walking 200 m and/or of climbing stairs). This tool was used in several studies and resulted in good predictive value [14, 17, 19]. It has all necessary elements for frailty assessment: mobility (TUG and subjective mobility evaluation), nutrition (MNA), cognitive functions (MMSE), and independence (ADL, IADL).

In addition, Eichler et al. showed that this instrument could be used in CR settings, although there were no changes in Katz index and IADL results after 3-4 weeks of inpatient CR for patients after TAVI [40]. As a result of the comprehensive rehabilitation program, the proportion of frail patients was significantly reduced by 9% (from 36.9% to 27.9%). The overall frailty index decreased by 0.4 points, driven by the significant changes of the single parameters cognition (MMSE), nutrition (MNA), and subjective mobility disability and mobility (TUG). On the other hand, it was small (N=136), short (observation for 3-4 weeks), observational type study without control group or randomization.

However, other authors have not confirmed the predictive value of this instrument and found that it only partly predicted unfavorable outcome after TAVI (nutrition and mobility) [41]. More studies with VHD patients and MGA should be done in order to receive higher level evidence, but its possibility of evaluating most of complex frailty syndrome components looks promising not only in screening but also in frailty dynamics after CR.

*3.1.3. Canadian Study of Health and Aging (CSHA) Scale or Clinical Frailty Scale or Rockwood Scale.* CSHA scale is a multidomain approach that defines frailty as a proportion of accumulated health deficits [9, 26]. In the Canadian Study of Health and Aging, authors worked with 3 approaches: (1) developing a rules-based definition of frailty, (2) creating a method of counting a patient's clinical deficits, and (3) proposing the clinical frailty scale, a measure of frailty based on clinical judgment [42]. The seven-point scale is displayed in an easily visualized form including objective clinical judgment and subjective patient assessment [26]. It is a validated instrument for diagnosing physical frailty and easy to use [9, 42, 43]. Seiffert et al. used the Rockwood scale in the Bonn group (N=347/847 patients) undergoing TAVI and found frailty to be significantly related to 1-year mortality [26, 44]. Other authors also used this scale and reported significant results related to quality of life, poor physical and mental function, physical well-being [45], and poor outcomes even in pre-frail patients [46]. Shimura et al. compared it with other well-known frailty markers and concluded that CSHA predicted late mortality in an elderly TAVR patient cohort better than 5MWT, body mass index (BMI), and handgrip strength [47]. We did not find any study that would use CSHA scale to evaluate frailty dynamics after CR for patients with VHD. What is more, CSHA did not show superiority compare to other frailty tools (such as 5MWT or handgrip test) in other reviewed studies [24, 30]. On the other hand, CHSA scale is based upon patients level of disability, level of independence, that could be a link to other tools used in rehabilitation settings such as Barthel index (BI) or functional independence measure (FIM). Systematic review and meta-analysis performed by Ribeiro et al. [48] showed that frail patients after TAVI or surgical aortic valve replacement improved significantly according to BI or FIM results, compared before and after CR. What is more, recently published call of action regarding frailty in CR offered to use CSHA scale as possible frailty measure [9].

*3.1.4. 5-Meter Walking Test.* One of the requirements for frailty assessment (especially for screening) is simplicity and ability to assess frailty in a very short period of time. One of the most evaluated frailty assessments is the 5-meter (15 feet ~ 4,5 meters) walking test which can be used as part of other scales (FFS) or as stand-alone evaluation [13, 20, 24, 27, 30, 47, 49–51]. This test results could be evaluated in different manner: (1) measuring time taken for 5-meter walk in seconds and (2) measuring gait speed in meters per second. Different authors offer different cutoff values to describe frail patients that vary from 5 to 7 seconds according to gender and body composition [6, 8]. Gait speed is an independent predictor of adverse outcomes after cardiac surgery, with each 0.1-m/s decrease conferring an 11% relative increase in mortality [52]. The slowest walkers (6-10 or more seconds) had 35% higher 30-day mortality than normal walkers (adjusted OR, 1.35; 95% CI, 1.01–1.80) [51]. Kano et al. described stepwise incremental increased risk of mortality after TAVI in patients with the slowest gait speed (<0.5 m/sec) or who were unable to walk compared to patients with a normal gait speed [50]. Studies that compared several frailty assessment tools also demonstrated 5MWT superiority among other more complex ways to evaluate frailty in VHD population [27, 53]. This test is validated in large trials, has good predictive value for patients undergoing cardiac surgery, and is superior to other instruments [12, 52]. Although it seems logical to use this 5MWT in cardiac rehabilitation, as it is recommended by AHA guidelines [54], none of the reviewed studies in CR setting chose this test. All of the mentioned studies regarding exercise training for patients with VHD evaluated six-minute walking test to show improvement in physical capacity, but this test failed to show predictive value in frailty screening before the procedure [55]. Future studies will be needed to evaluate 5MWT sensitivity in a setting of CR.

*3.1.5. Serum Albumin Levels.* Pre-procedural albumin levels (as single measurement or as part of other indexes) have been demonstrated to have significant predictive value [47, 56–58]. Hypoalbuminemia (<3.5 g/dL) was associated with poor prognosis, highlighted by the increase in noncardiovascular mortality in elderly TAVI patients [58]. Grossman et al. showed that even higher pre-procedural albumin (< 4 g/dL) can significantly improve the ability of the Society of Thoracic Surgeons (STS) and EuroSCORE II scores to predict TAVR-related mortality [57]. In addition Bogdan et al. showed that low post-procedural (4 days after procedure) serum albumin remained a strong parameter correlated with all-cause mortality (HR=2.47; 95% CI: 1.284.78; p<0.01) [59]. Forcillo et al. analyzed whether MFFC predicted 30-day mortality after TAVI. The results demonstrated that although all MFFC components were associated with increased risk of adverse outcomes, only albumin (<3.5 g/dL) was predictive of 30-day all-cause mortality [28]. Eichler et al. focused on nutrition assessment but used another instrument, validated MNA scale [41]. Moreover, one of the components of the successful frailty risk score for the elderly undergoing aortic valve replacement (EFT) is low pre-procedural albumin level [24].

Albumin level seems to have higher prediction value and could be a good screening instrument for frailty. What is more, serum albumin levels can be linked to lower muscle mass in elderly [60]. Albumin as nutrition measure could be connected with low body mass index (BMI) and sarcopenia. Mok et al. showed that higher BMI in TAVI patients was associated with higher skeletal muscle mass [61]. However, 46% of these cases were sarcopenic obesity that was significantly higher than the 4% to 12% in the general population [61]. These results could give an impression that muscle mass is more important than whole body mass. Shimura et al. showed significant relation between lower BMI and higher level of frailty [47]. The results from Koifman et al. confirmed that BMI <20 kg/m2 should be considered as a frailty marker during the screening process of severe aortic stenosis TAVI patients as it is associated with higher mortality [62]. Albumin levels should be taken in to account during comprehensive CR program, which is the role of dietician counseling, helping to reach healthy body mass not only through healthy diet but also through increasing muscle mass.

*3.1.6. Katz Index of Activities of Daily Living.* The Katz index is used for functional assessment of dependency in elderly individuals in the six functions: feeding, bathing, dressing, transferring, toileting, and urinary continence [95]. It provides objective data on a patient's independency in daily activities [26]. Frailty usually overlaps with disability; hence some authors use the same instruments for disability measurement while others use it for frailty assessment [32, 69]. Earlier studies incorporated Katz index in the frailty assessment and demonstrated that it is an independent risk factor for in-hospital mortality and institutional discharge in patients after cardiac surgery [15, 26, 96]. Therefore, a more pragmatic approach in defining frailty, commonly called the social domain, often includes an ADL assessment [26]. Puls et al. identified a Katz index <6 as a powerful independent predictor of immediate-, short-, and long-term all-cause mortality in TAVI patients [26, 77]. Most of the review studies included Katz index as part of frailty assessment and demonstrated it to produce good prediction values [17, 49, 68, 69, 72]. Recently published American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) guidelines recommend the Katz index as one of the frailty assessment instruments for risk prediction before cardiac surgery [97, 98]. On the other hand, other authors did not detect Katz index as good predictor for long- and short-term outcomes; in those studies it was inferior to mobility and nutrition measures [30, 41, 64]. Although usage of Katz index looks promising, we failed to find any study in CR with VHD patients that would test individuals with KI before and after CR program. Eichler et al. used IADL and basic DAL [40]; other authors successfully used BI or FIM to evaluate frailty, disability, or patient independence [85, 99].

*3.2. What Exercise Interventions Would Be the Most Beneficial for Frail Patients?* In order to answer the second research question, we analyzed 12 studies published in English since 1980 on topic of VHD and exercise training with elderly (Table 2). All analyzed studies demonstrated benefit of exercise training in patients after surgical/interventional VHD treatment. Although the evaluated exercise-based CR programs were differently structured, the patient population included and the primary endpoints examined were similar and focused on the results of 6-minute walking test and cardiopulmonary stress test (peak $VO_2$). 6 studies were conducted in inpatient facilities and 6 studies analyzed the results of outpatient programs only. In 8 studies the program started early (< 1 month) after surgery or intervention. Other studies included patients after ≥1 month of surgery or intervention. In all reviewed publications specified documented adverse events were not related to exercise [91, 93, 100].

Although recently published studies concentrate on disabled, comorbid high-risk elderly patients, all authors demonstrated that exercise training is safe and effective in improving functional and physical capacity [40, 84, 85, 87, 89, 93], quality of life [40, 84], and independence in daily life activities [48, 84, 85, 87, 93]. Exercise training type, method, length, and intensity differed among the studies and did not allow clear recommendations concerning how exactly this patient group should be treated.

Only two randomized controlled trials (RCT) were performed with patients aged 60 years or older [91, 92]. Low sample size pilot study on exercise training after TAVI, with combined endurance and resistance training, showed significant improvements in exercise capacity, muscular strength in different muscles groups, and quality of life compared with usual care [91]. In this study, 13 TAVI patients participated in an eight-week outpatient CR, starting 2-3 months after intervention. Resistance training was added in the second week of the program and performed in 2 of the 3 weekly workouts. It included 5 different exercises starting with 1 set with 10 repetitions at 30% 1 repetition maximum (1-RM) and was gradually increased to 3 sets with 15 repetitions at 50% to 60% 1-RM. Sbilitiz et al. showed that CR group compared with control had a beneficial effect on VO2 peak at 4 months (24.8 mL/kg/min versus 22.5 mL/kg/min, p=0.045) but mental health and other measures of exercise capacity and self-reported outcomes was not affected [92]. Exercise training in this study was initiated 1 month after surgery, comprising 3 weekly exercise sessions for 12 weeks. The

Table 2: Characteristics of reviewed studies on VHD and exercise training.

| Author (Year) | Study group Patient characteristics | CR variety CR length Intervention | Primary endpoint | Main results and adverse events | Conclusion |
|---|---|---|---|---|---|
| Zanettini (2014) [84] | N=60;<br>None;<br>Age 83.5;<br>Female 53%;<br>TAVI<br>CD - mentioned;<br>Time to CR - 10,6 ± 3.4 d. | CR inpatient;<br>Length 18.3 ± 5.6 days;<br>Intervention: 6d/w<br>(1) Intensity according to clinical condition, 6MWT, disability<br>(2) In pts with mild disability interval or steady-state aerobic training and callisthenics was used. | (1) to determine the in-hospital and mid-term outcomes of these patients. | AE: NA<br>6MWT at discharge was significantly higher and corresponded to the 64%± 23% of the predicted vs. 49%± 21% in the admission test. | Most patients showed significant improvement in functional status, QoL, and autonomy, which remained stable in the majority of subjects during mid-term follow-up. |
| Russo (2014) [85] | N=158;<br>TAVI = 78;<br>SAVR = 80;<br>Age 82.1;<br>Female 60%;<br>TAVI, SAVR;<br>Time to CR - 13,7 ± 11.7 d | CR inpatient;<br>Length 2 w;<br>Intervention:<br>70% predicted max HR, RPE 3 sets of exercises, 6 d/w: 30 min of respiratory workout, aerobic session on a cycle and 30 min of callisthenic exercises.<br>Aerobic session 10 min⟶30min | (1) The safety and efficacy of a structured, exercise-based CR program | AE: none<br>All enhanced autonomy;<br>6MWT did not significantly differ (272.7±108 vs. 294.2±101 m, p. 0.42), neither peak-VO2 12.5±3.6 vs. 13.9± 2.7 ml/kg/min, p. 0.16. | CR is feasible, safe and effective in octogenarian patients after TAVI as well as after traditional surgery. CR rehabilitation programme enhances independence, mobility and functional capacity and should be highly encouraged |
| Pardaens (2014) [86] | N=145;<br>VHD, risk, type of surgery;<br>Age 64;<br>Female 48,9%;<br>AVR, MVR;<br>CD - mentioned;<br>Time to CR - 43±22 d | CR outpatient;<br>Length 12-20 weeks;<br>Intervention: 2-3/w for 60 min. Aerobic training, an intensity of the HR at AT combined with RPE. Strengthening exercises (15 minutes) at 60% of 1-RM for 2 sets of 15 to 20 repetitions. | (1) difference in exercise capacity early after VHD surgery<br>(2) whether the functional improvement after training was affected by risk or type of surgery | AE: NA<br>(1) Higher risk had a worse postoperative exercise capacity, higher VE/VCO2<br>(2) Exercise training - significant improvement in WL, peak VO2, AT, and 6MWD in each risk group ($p < 0.01$).<br>(3) Significant decrease in the VE/VCO2 in the medium- and high-risk patient groups ($p < 0.05$). | (1) Exercise capacity after VHD surgery is related to the preoperative risk and to the type of surgery.<br>(2) Similar benefit from exercise training can be obtained, independent of the preoperative risk class or the type of surgery. (3) ET should be offered to all patients after valvular surgery, regardless of their EuroSCORE risk or type of surgery |

Table 2: Continued.

| Author (Year) | Study group Patient characteristics | CR variety<br>CR length<br>Intervention | Primary endpoint | Main results and adverse events | Conclusion |
|---|---|---|---|---|---|
| Fauchere (2014) [87] | N=112;<br>TAVI vs SAVR;<br>Age 79;<br>Female 60%;<br>TAVI, SAVR;<br>CD - mentioned;<br>Early phase CR. | CR inpatient;<br>Length 3 weeks;<br>Intervention:<br>Training 2–3/d., 6 d./w. of supervised gymnastics, aerobic and respiratory workout sessions.<br>Low/medium intensity (RPE). | (1) improvement during the CD in FIM-score, HADS-score and 6-MWT | AE: NA<br>(1) 6-MWT in TAVI and SAVR patients (84.2 m ± 68.7 m vs. 82.8 m ± 65.1 m; p = 0.92) (2) total FIM score in TAVI and SAVR patients (9.9 ± 6.1 vs 12.2 ± 10.9; p=0.34). | (1) Patients in TAVI group were older and sicker than SAVR<br>(2) Both patient groups did benefit in the same way from a post-acute in-patient rehabilitation program. |
| Baldasseroni (2016) [88] | N=160;<br>Performance >15 vs. <15%;<br>Age 80;<br>Female 29,4%;<br>CABG, HVS, CABG+HVS, ACS;<br>CD - mentioned;<br>Time to CR - 12 ± 10 d. | CR outpatient;<br>Length 4 weeks;<br>Intervention:<br>5d/w aerobic training program at an 60–70% of VO2 peak, RPE 11–13.<br>Progressive increase in resistance on the basis of RPE, reevaluated weekly. | (1) effects of an exercise-based CR program on exercise tolerance and muscle strength (2) the independent predictors of changes in physical performance | AE: none<br>Physical performance improved (VO2 peak, 10.9%; 6MWT, 11.0%; peak torque, 11.5%).<br>higher baseline values predicting less improvement (VO2 peak: OR=0.86, 95% (CI)=0.77–0.97; 6MWT: OR= 0.99, 95% CI=0.99–1.00; peak torque: OR=0.96, 95% CI=0.94–0.98). | (1) An exercise-based CR program was associated with improvement in all domains of physical performance even in older adults after an acute coronary event or cardiac surgical intervention, particularly in those with poorer baseline performance. |

Table 2: Continued.

| Author (Year) | Study group Patient characteristics | CR variety<br>CR length<br>Intervention | Primary endpoint | Main results and adverse events | Conclusion |
|---|---|---|---|---|---|
| Voller (2015) [89] | N=442;<br>TAVI = 76;<br>SAVR = 366;<br>Age 69.94;<br>Female 38%;<br>TAVI, SAVR;<br>CD - mentioned;<br>Early phase CR. | CR inpatient;<br>Length 3 weeks;<br>Intervention: 4-5/w.<br>Aerobic exercise depending on the initial exercise intensity, outdoor walking, gymnastics and resistance training of the lower extremities | (1) the effect of CR on in patients after TAVI in comparison to patients after sAVR | AE: NA<br>(1) 6-MWT and exercise capacity significantly increased in both groups (p<0,05).<br>(2) After adjustment, changes were not significantly different between SAVR and TAVI, with the exception of 6-MWT (p. 0.004). | (1) Patients after TAVI benefit from CR despite their older age and comorbidities. (2) CR is a helpful tool to maintain independency for daily life activities and participation in socio-cultural life. |
| Savage (2015) [90] | N=576;<br>HVS vs CABG vs CABG+HVS;<br>Age 64.9;<br>Female 22%;<br>CABG, HVS;<br>CD - mentioned. | CR outpatient;<br>Length 12-20 weeks;<br>Intervention:<br>Aerobic training at 70- 85% of peak HR and/or RPE 12-14 for 45-60 min. Resistance training 1 set of 10 rep. | (1) If patients after HVD benefit similarly CR as CABG. | AE: NA<br>(1) Peak VO2 increased 19.5% from 17.4±4.4 to 20.8±5.5 mL/O2/kg/min (p<0.0001). (2) | CABG and VHD patients experienced similar improvements in strength, and self-reported physical function and depression scores.<br>Improvements in peak VO2 were similar between all groups |
| Pressler (2016) [91] | N=30;<br>Intervention = 13;<br>Control = 14;<br>Age 81;<br>Female 44%;<br>TAVI;<br>CD - mentioned;<br>Time to CR 83 ± 34d | CR outpatient;<br>Length 8 weeks;<br>Intervention:<br>2-3/w 20min at 40%VO2 peak ⟶ 45 min at 70%VO2 peak by 8 week.<br>(2) Resistance training in 2nd w 2/w at 30% 1-RM ⟶ 3 sets with 15 rep. at 50-60% 1-RM. | (1) difference in change in VO2 peak from baseline<br>(2) Change in muscular strength, 6MWT, NYHA, QoL | AE: 3, not related<br>(1) Significant changes in favor of Int. were observed for Peak VO2 (group difference, 3.7 mL/min per kg), muscular strength, components of QoL and 6MWT. | In patients after TAVI, ET appears safe and highly effective with respect to improvements in exercise capacity, muscular strength, and quality of life. |

Table 2: Continued.

| Author (Year) | Study group Patient characteristics | CR variety CR length Intervention | Primary endpoint | Main results and adverse events | Conclusion |
|---|---|---|---|---|---|
| Sibilitz (2016) [92] | N=147; Intervention = 72; Control = 75; Age 62; Female 24%; Valve surgery; CD - mentioned; Time to CR - 1 mo | CR outpatient/home based; Length 12 w; Intervention: 3/w. (1) supervised training (69%) or (2) home-based training (31%). Intensity according to RPE increasing up to 12 w. The strength exercises; (2) cont. group not allowed to | (1) Improved physical capacity (VO2 peak) (2) Improved mental health. | AE: Int.:13pts vs cont. 3pts, not related (1) CR compared with cont. had a beneficial effect on VO2 peak at 4 months (24.8 mL/kg/min vs 22.5 mL/kg/min, p=0.045); (2) did not affect SF-36 MC at 6 mo (53.7 vs 55.2 points, p=0.40); | CR after HVD surgery significantly improves VO2 peak at 4 months but has no effect on mental health and other measures of exercise capacity and self-reported outcomes. |
| Genta (2017) [93] | N=135; TAVI vs SAVR; Age 80; Female 63%; TAVI, SAVR; CD - mentioned; Early phase CR. | CR inpatient; Length 4 w; Intervention: (1) 2/d. 30-min cycling/treadmill 6 d./w., starting at min⟶up to 14 RPE (2) OR 2/d. 30 min of walking along the 6MWT and pedal exerciser (0W) (3) 40-min 1/d respiratory exercise. (4) early mobilization | (1) Improved BI (2) Decreased risk of falls (3) Improved functional capacity | AE: 9pts (not related) (1) BI improved for all p<0,05 (from 73±23, to 90±16) (2) MFS decreased to all p<0,05 (from 30±21, to 25±17) (3) 6MWT improved for all p<0,05 (from 193 ±87, to 292±103) | (1) Intensive CR after TAVI is safe, well tolerated, and leads to a net improvement in disability, risk of falls, and exercise capacity, similar to that observed in less disabled SAVR patients. |

Table 2: Continued.

| Author (Year) | Study group Patient characteristics | CR variety CR length Intervention | Primary endpoint | Main results and adverse events | Conclusion |
|---|---|---|---|---|---|
| Pollman (2017) [94] | N=168; None; Age 63; Female 16%; HVS, TAVI; CD - mentioned. | CR outpatient; Length 12 w; Intervention: 2/w 90 min and aerobic interval training at 60-80% VO2 peak; resistance training with 3 sets of 15 rep of 60% 1RM | (1) the effect of CR after VHD surgery on VO2 peak, long term morbidity, mortality | AE: none (1) VO2 peak improved by 16% from 21.6 to 24.8 mL/kg/min ( $P < 0.0001$) and 6MWT by 13% from 349 to 393 m ($P = 0.0016$). | CR after VHD surgery improved exercise capacity and was associated with reduced morbidity. Elderly were less likely to attend or complete CR and deserve special attention |
| Eichler (2017) [40] | N=136; None; Age 80.6; Female 52,5%; TAVI; CD - mentioned; Time to CR - 17.7±9,9 d. | CR inpatient; Length 3 Intervention: 5d/w 30 min the continuous/interval Patients (> 1.0 W/kg) strength training at 30–50% 1RM Outdoor walking, gymnastics, aqua gymnastics and spinal gymnastics in groups | (1) effect of a multicomponent inpatient CR after TAVI (2) predictors for the change in physical capacity, QoL. | AE: NA (1) 6MWD - 56.3 - 65.3m (2) max WL increased by 8.0 - 14.9 wat ($p<0.001$). (2) Higher cognition, nutrition and autonomy positively influenced the physical scale of SF-12. (3) baseline values of SF-12 had an inverse impact on the change during CR. | CR can improve functional capacity as well as QoL and reduce frailty in patients after TAVI. |

*Intervention.* AVR: aortic valve replacement, MVR: mitral valve replacement, **PTMC:** Percutaneous Trans Mitral Comm**issurotomy**, TAVI: Transcatheter Aortic Valve Implantation, CABG: coronary artery bypass graft, HVS: heart valve surgery, ACS: acute coronary syndrome.
*Patients and Study Characteristics.* CR: cardiac rehabilitation, RPE: rate of perceived exertion, CD: comorbidities, HR: heart rate, 1-RM: 1 repetition maximum.
*Results.* AE: adverse events, WL: workload, CV: cardiovascular, AT: anaerobic threshold, QoL: quality of life, ET: exercise training, MFS: Morse fall scale, HR: hazard ratio, CI: confidence interval, OR: odds ratio, NYHA: New York Heart Association, 6MWT: six-minute walking test.

program consisted of graduated cardiovascular training and strength exercises.

None of these studies assessed level of patients frailty before and after exercise training program; on the other hand, it did show that structured training program could improve older patient physical capacity [91, 92]. What is more, Sbilitiz et al. did not find improvement in patients' mental health which could be seen as a one component of complex frailty syndrome. It is interesting that latter study had special structured psychosocial education that cover relevant topics: changed body-image and self-image, recovery from major surgery, and dependency on relatives and medical issues, but did not receive positive results [92].

Only one study, conducted by Eichler et al., evaluated the effect of a multicomponent inpatient CR on frailty in patients after TAVI [40]. It is important to mention that the CR included patient education, diet counseling, psychological support, and risk factor management as well as individualized training components. Exercise training performed was mainly aerobic such as cycle-ergometer training and Nordic walking. Patients with a higher exercise capacity (> 1.0 W/kg) conducted additional strength training at 30–50% 1-RM. For frailty assessment, frailty index by Schoenberg et al. was used. As a result of the rehabilitation the proportion of frail patients was significantly reduced by 9% (from 36.9% to 27.9%). The overall frailty index decreased by 0.4 points, driven by the significant changes of the single parameters cognition (MMSE), nutrition (MNA), and subjective mobility disability and mobility (TUG). Although frailty index could be reversed during cardiac rehabilitation, it did not show a prognostic impact itself [40]. On the other hand, it was observational type study, did not have control group, and was not designed as randomized control trial.

Russo et al. showed that early cardiac rehabilitation enhances independence evaluated with Barthel index, mobility, and functional capacity for patients after surgical or interventional aortic stenosis treatment. The exercise training consisted of aerobic training and calisthenics [85]. Systematic review and meta-analysis performed by Ribeiro et al. [48] showed that patients after TAVI or surgical aortic valve replacement achieve similar benefits from cardiac rehabilitation. Frailty components analyzed in this review were independently measured by Barthel index or functional independence measure (FIM), which improved significantly in both groups. The cardiac rehabilitation programs included exercise endurance training (cycle or treadmill), resistance training, and/or inspiratory muscle training.

Summarizing of existing evidence on exercise training for patients with VHD would show that exercise program should be individualized and intensity should be measured by RPE with beginning of 40-60% of maximal VO2. All analyzed training protocols included aerobic training component implemented through various activities (Nordic walking, bicycle ergometer, gymnastics, etc.) and in 9 of them additional strength training was performed starting form the second or third week of exercise training, measuring intensity with 1 repetition maximum method. Inpatient CR program length varied from 2 to 4 weeks, while the duration of the outpatient programs was 12-24 weeks.

*3.3. Would the Change of Frailty Status Improve Outcomes on Levels of Disability, Functional Capacity, and Quality of Life after Surgical/Interventional VHD Treatment beyond the Effects of the Surgery/Intervention Itself?* According to recent studies, in 23-32,8% of cases functional capacity of TAVI patients did not improve or even deteriorate in a period of 6-12 months after intervention [101–104]. If we put aside certain procedure technique, surgeon experience, risk-benefit ratio evaluation, and careful patient selection, individualized care or CR in inpatient/outpatient setting could outweigh unwelcome complications. Older VHD patients constitute a sensitive group that requires more specific comprehensive cardiac rehabilitation programs and they return to casual life could be more difficult [4, 105].

After analyzing the reviewed studies, we could not directly answer to the third research question. Two studies that were designed as RCT did not evaluated frailty or its components [91, 92], and study that was designed to evaluate exercise training impact on frailty did not have control group [40]. On the other hand, all reviewed studies show positive impact of CR and did not register any adverse event or clinical deterioration linked to exercise training program.

Participation in CR improves outcomes of patients with cardiovascular disease [106] and may be specifically beneficial for patients with frailty syndrome; however, cardiac rehabilitation facility remains unused.

## 4. Discussion

The results of this review highlight the importance of frailty syndrome in patients with VHD. Screening for frailty as a high-risk factor is well implemented in Heart team decision making for high-risk patients with aortic stenosis. However, there is gap of evidence considering frailty in CR settings. This literature review was designed to seek for answers of several research questions: Are assessment tools used for frailty screening sensitive enough to show improvement in frailty status after exercise-based CR? What exercise interventions would be the most beneficial for frail patients? Would the change of frailty status improve outcomes on levels of disability, functional capacity, and quality of life after surgical/interventional VHD treatment beyond the effects of the surgery/intervention itself?

First of all, our analysis revealed several different methods used for frailty assessment and evaluation. The analysis of these frailty tools was difficult because (1) a huge variety of instruments were used, (2) the same instruments were chosen to evaluate disability or cognitive functions in some studies and frailty in others, (3) the same instruments were named differently in separate studies, (4) authors were using validated scales but chose to analyze components separately, (5) authors created and offered new risk scores for frailty assessment that has not been implemented in other studies, and (6) some studies described subjective frailty evaluation manner "eye-ball test" [78, 79], while others used objective, quantitative or semiquantitative tests to evaluate all possible deficits.

It is clear that the prevalence of frailty plays an important role for patients with VHD: recently updated AHA VHD and

ESC guidelines emphasize the frailty issue as an important factor for Heart team decision making in patients with aortic stenosis [97, 107]. In 2014, the AHA guidelines recommended the use of Katz Index of independence of daily living and the 5-meter gait speed test, and this recommendation was left in 2017 [54, 107]. Frailty as worse outcome predictor is already mentioned in ESC guidelines in 2012, but still without clarification of how exactly frailty should be measured and evaluated [108]. ESC 2016 guidelines indicate that frailty assessment should not be subjective and criticize the "eyeball test" [97]. According to cited studies frailty could be measured with complex evaluation of the patient that includes Katz index of independence of daily living, cognitive function evaluation, nutrition assessment, and patient functional capacity (TUG) [97].

Existing literature confirms frailty predictive value for higher complications rate, longer length of hospital stay, and mortality and morbidity after cardiac surgery or interventional treatment [9, 97]. On the other hand, most of the studies describe frailty assessment before procedure. Frailty status is dynamic and can transit over time. In most cases people become more frail while aging, but in up to 20% of the population frailty criteria also can disappear over time [109, 110]. Study that analyzed community living elderly persons showed that, of the 754 participants, 434 (57.6%) had at least 1 transition between any 2 of the 3 frailty states during 54 months. Transitions to states of greater frailty were more common (rates up to 43.3%) than transitions to states of lesser frailty (rates up to 23.0%) [109, 110]. A small study that was performed by Forman et al. showed significant worsening of frailty level (measured by CSHA, 5MWT, and MMMSE) and functional capacity in 10 weeks for patients that are waiting for TAVI [111]. This dynamics shows that even short-term (3-4 weeks) CR could be effective for these patients.

Vigorito et al. recently published a call for action on frailty in CR and offer mainly two instruments for frailty assessment in this specific field: Edmonton frailty scale (EFS) and clinical frailty scale from the CSHA study. The EFS could be used as a comprehensive instrument that has been validated in elderly patients after acute coronary syndromes [9]. It also includes two clinical performance items interrogating cognition (clock test) and functional performance (TUG) [9]. However, some EFS questions are developed for screening more than for effect evaluation (e.g., hospitalizations per year, functional independence, social support, and medication usage) and would not be sensitive to show results of comprehensive CR. Also we did not find any study with VHD patients where frailty would be measured with EFS. Clinical frailty scale from the CSHA is popular and looks effective for screening in this patient population [20, 35, 44]. It is easy-to-use standardized tool based on subjective evaluation of frailty; however, it lacks psychosocial factors [9, 26]. Moreover, studies that compare different frailty tools (including CSHA frailty scale) did not show its superiority to other instruments for frailty screening and outcomes prediction [24, 27, 30].

Our analysis revealed the six most used tools for frailty in VHD population: 3 scales (fried frailty scale and its modifications, multidimensional geriatric assessment, and clinical frailty scale from the CSHA study) and 3 single measures (5-meter walking test, Katz index, and serum albumin levels). Together with existing guidelines and expert opinions we believe that simple and fast-performed single test would not show comprehensive CR effect on a frail patient. An instrument of frailty assessment in CR should have the various components included in different risk assessment scores (mobility, independence in daily living, cognitive functions, nutrition, muscle mass and strength, and anxiety and depression evaluation). We did not find enough studies performed in CR with frail patients to find out which of all the mentioned tools is the best and most sensitive for frailty syndrome and its dynamics after CR program. Future studies are needed to build new evidence in this field of research.

Second research question aim was to find an ideal exercise training-based CR program for frail patient with VHD. It is known that exercise-based comprehensive CR is based on strong evidence and is a well-recognized treatment for patients with different cardiovascular diseases [112, 113]. Physical rehabilitation for frail older people can positively affect functional and physical capacity and this effect may be related to the level of frailty [23]. Physical activity recommendations and supervised exercise programs can be useful for frailty prevention, to improve physical and functional capacity (gait speed, TUG, and SPPB), survival, and quality of life as well as to decrease prevalence of anxiety and depression and risk of falls in community-dwelling frail older people [114–117]. According to recent published systematic review, interventions for pre-frail and frail older adults should include multicomponent exercises, including in particular resistance training, as well as aerobic, balance, and flexibility tasks [117]. A study that included older patients soon after CABG demonstrated that additional resistance training and special balance training improved functional capacity (6-MWD, TUG time) significantly more than aerobic training alone [118]. Exercise training-based cardiac rehabilitation could be a treatment option for frail VHD patients. EAPC Cardiac Rehabilitation Section raised awareness and importance of frailty topic in the field of CR [9].

However, literature data in exercise training and CR in VHD patients is scare [100]. According to a published Cochrane meta-analysis, exercise training is beneficial and provides short-term improvement; however, it was assessed by only two studies included in this meta-analysis, and both of them were performed in a young-middle aged sample [100]. Our literature review showed that different exercise training programs with VHD elderly patients after surgery/intervention were safe and effective in improving functional and physical capacity [40, 84, 85, 87, 89, 93], quality of life [40, 84], and independence in daily life activities [48, 84, 85, 87, 93]. Studies with frail patients demonstrated that exercise-based programs increased gait speed and improved balance and performance in activities of daily life or SPPB [9]. A systematic review on exercise-based CR for patients after aortic stenosis surgical/interventional treatment demonstrated that a short-term (2-6 weeks) program could improve Barthel index, FIM, 6MWT, and anxiety and depression [48]. Eichler et al. demonstrated that participating in comprehensive CR results in frailty index decrease by 0.4 points, driven by the significant changes of single parameters such as cognition (MMSE), nutrition (MNA), and subjective mobility disability and mobility (TUG). In addition, several studies showed improvement in frailty and physical and functional capacity in frail patients, although baseline evaluation before surgery/intervention demonstrated lower results in the frail patient group [18].

All reviewed studies had an aerobic component of exercise training that was fulfilled in different ways, and 9 of 12 reviewed studies had an additional strength-training component. All described exercise programs were individualized according to the patient capability and described careful exercise intensity dosage according to rate of perceived exertion. We believe that ideal CR for VHD patients should be supervised by a cardiologist, and its content should include (1) exercise training (endurance and strength training to improve muscle mass, strength, balance, and coordination and to avoid falls), (2) nutrition counseling (to improve healthy body mass), (3) occupational therapy (to improve independency and cognitive function), (4) psychological counseling to ensure psychosocial health, and (5) social worker counseling (to improve independency). To improve outcomes of these patients CR services need to be optimally utilized and the protocols modified to cater for frail patients and to monitor their progress over the course of the treatment [106].

## 5. Limitations

Our literature review has several limitations and weaknesses. First of all, it was not designed as a meta-analysis or systematic review, so results of our study have lower evidence level. We searched only one database and used informal and subjective methods for studies inclusion and quality check. A quality assessment of the included studies would have strengthened our study.

What is more, we failed to find concrete and practical answers for research questions that were raised in the beginning of the study. We could only provide existing situation and try to find possible goals for future studies.

## 6. Conclusions

Frailty assessment in CR settings should be based on functional, objective tests and should have similar components as tools for risk assessment (mobility, muscle mass and strength, independence in daily living, cognitive functions, nutrition, and anxiety and depression evaluation). Participating in comprehensive exercise-based CR could improve short- and long-term outcomes in frail VHD patient. Comprehensive CR not only should include exercise training, psychological interventions, and improvement in nutrition but also could prevent, restore, and reduce the severity of frailty as well as improving outcomes for frail VHD patients.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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*Review Article*

# Aging and Thermoregulatory Control: The Clinical Implications of Exercising under Heat Stress in Older Individuals

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Climate change is predicted to bring about a greater variability in weather patterns with an increase in extreme weather events such as sustained heat waves. This change may have a direct impact on population health since heat waves can exceed the physiological limit of compensability of vulnerable individuals. Indeed, many clinical reports suggest that individuals over the age of 60 years are consistently the most vulnerable, experiencing significantly greater adverse heat-related health outcomes than any other age cohort during environmental heat exposure. There is now evidence that aging is associated with an attenuated physiological ability to dissipate heat and that the risk of heat-related illness in these individuals is elevated, particularly when performing physical activity in the heat. The purpose of this review is to discuss mechanisms of thermoregulatory control and the factors that may increase the risk of heat-related illness in older individuals. An understanding of the mechanisms responsible for impaired thermoregulation in this population is of particular importance, given the current and projected increase in frequency and intensity of heat waves, as well as the promotion of regular exercise as a means of improving health-related quality of life and morbidity and mortality. As such, the clinical implications of this work in this population will be discussed.

## 1. Introduction

In the context of climate change, global surface temperatures are rising and the frequency, duration, and intensity of heat waves are projected to increase in the coming decades [1]. In countries like Australia, heat waves have been identified as being responsible for more deaths than all other types of natural disasters combined [2]. Around the world, over the past 20 years heat waves have led to extremely high levels of excess morbidity and mortality [3–5]. A classic example, and perhaps the most severe, is the 2003 Western European heat wave where an estimated 13,700 people died in France as a result of the increase in temperature [6]. In light of these events, climate change clearly poses a global threat of considerable magnitude for human health, the incidence of which is projected to increase especially in vulnerable populations.

Elderly individuals, particularly those who are over the age of 60 years, are one of the most vulnerable populations during environmental heat exposure, experiencing significantly greater adverse heat-related health outcomes than any other age cohort [7, 8]. Indeed, there is now evidence showing that older individuals have impaired thermoregulatory control [9–12] and that the risk of heat-related illness in these individuals is elevated, particularly when performing physical activity in the heat [13, 14]. Although regular physical activity leads to a reduction in health-related morbidity and mortality, individuals who do not have regular access to temperature-controlled exercise training facilities (i.e., gymnasiums) and/or in-home air-conditioning are therefore more likely restricted to performing physical activity outside of formal exercise training programs, which can take place under a range of environmental conditions, including outdoors in a warm environment (particularly in the summer months). Whilst current guidelines provide a general overview of the risk of exertional heat-related illness for younger individuals and athletic populations [15, 16], there are no public health recommendations for performing physical activity in the heat specifically for older individuals. In this brief review, we describe the normal thermoregulatory mechanisms and how these may be altered in older individuals. Additionally, the clinical relevance of this work is discussed; this is particularly relevant given that climate change, coupled with an aging population, is exposing an increasingly greater number of individuals, including those with chronic heart and lung disease, to the risks of heat-related morbidity and mortality.

## 2. Thermoregulatory Control

Humans maintain a relatively stable core body temperature of ~37°C despite being exposed to a wide variety of environmental conditions. Maintaining core body temperature within a safe, narrow range (i.e., between 35 and 39°C) ensures that metabolic reactions within the human body occur at a near-optimal level when possible [17]. When humans are exposed to heat stress (i.e., elevated environmental temperatures, physical activity, or a combination of both), the thermoregulatory system engages a number of physiological mechanisms to maintain heat balance. That is, the internal heat produced by cellular respiration (metabolic heat production [$H_{prod}$]) is balanced out by the rate of heat that is lost from the skin surface to the surrounding environment through a combination of dry (conduction, convection, and radiation) and evaporative heat exchange (Figure 1, Panel (a)) [18, 19]. Increases in metabolic and muscular activity cause a rise in $H_{prod}$ which is due to the inefficiency of the metabolic reactions required to provide energy to the working muscles [20]. Muscular contraction is extremely inefficient with approximately 80% of the energy generated produced as heat [21]. As such, the change in core body temperature secondary to the additional heat energy stored inside the body provides thermal afferent impulses to the central nervous system [22], which subsequently sends efferent signals to appropriate effector organs to initiate sustained increases in sweating and skin blood flow (SkBF) ensuring that core body temperature is maintained within safe limits.

In accordance with the fundamental heat balance theory [18], core body temperature will continue to rise if heat imbalance persists, whereby sweating and SkBF responses are not able to facilitate the required rate of heat loss during environmental and/or physical activity-induced heat stress (Figure 1, Panel (b)) [13]. Extended periods of heat stress can increase the likelihood of heat-related illness (particularly in older individuals) [13]. Major heat-related conditions, including heat stroke which is characterized as a severe elevation in body temperature that causes body tissue and central nervous system dysfunction [23, 24], all result from insufficient heat loss from the body.

In recent years, the changes in thermoregulatory control with aging have received some attention [13, 25–27]. These changes have been attributed to a combination of factors including alterations in sweating and SkBF (detailed below). Aside from these well-documented age-related changes, alterations in cardiovascular function with comorbid disease such as heart and lung disease can also contribute to altered thermoregulatory control in the older individual, particularly during exercise. Therefore, to maintain heat balance an optimally functioning thermoregulatory system is essential for humans to respond appropriately to environmental and/or physical activity-induced thermal challenges.

## 3. Age-Related Changes in Sweating

In humans, the thermoregulatory response with the greatest capacity for heat loss during environmental heat exposure and physical activity is the evaporation of sweat [29]. Under conditions permitting complete evaporation (i.e., when the maximal evaporative potential within a given environment does not limit an individual's ability to achieve heat balance), evaporation is the primary mechanism for heat loss [29, 30], with just one gram of sweat liberating 2426 J of heat energy upon evaporation [31]. To date, evidence suggests that older individuals exhibit alterations in sweating during heat stress compared to younger, gender-matched individuals [7, 11, 12, 27, 32–35]. A common finding amongst studies is that older individuals demonstrate a delayed core temperature onset threshold for sweating and a reduction in evaporative heat loss (due to a lower overall sweat rate) compared to their younger healthy counterparts. These age-related decrements in sweating do not appear to be due to a reduction in the number of activated sweat glands, but rather to a reduction in the amount of sweat produced per gland, as shown by studies in which sweat glands were pharmacologically stimulated [35, 36]. The decrease in sweat gland output with aging may reflect age-related changes in sweat glands themselves (sweat gland atrophy) or a decrease in cholinergic sensitivity [37]. Moreover, additional findings indicate that regional differences in sweat gland function exist between older and younger groups [38]. Indeed, greater age-related effects have been commonly reported for sweat gland function on the forehead and limbs when compared to sweat glands located on the trunk. In light of these findings, it has been suggested that sweat gland function may decline in a peripheral-to-central direction as skin ages [27].

With respect to examining sweating responses during exercise in the heat, Kenney and Anderson [39] demonstrated that local sweat rate was less in older individuals than their younger counterparts during exercise at a relative intensity (40% of maximal oxygen uptake) in the heat. Tankersley et al. [40] and Inbar et al. [14] demonstrated that local and whole-body sweat rate was lower in older individuals compared to younger individuals during exercise at 65% and 50% of maximal oxygen uptake, respectively, in a hot (30°C and 41°C, respectively) environment. The attenuated evaporative heat loss capacity found in older individuals results in greater heat energy stored inside the body which can cause core body temperature to rise to potentially dangerous levels. Whilst these findings [14, 39, 40] support the above evidence in that the capacity to produce sweat during heat stress decreases with advancing age, it must be noted that differences in biophysical properties (body mass and surface area, and absolute external work load) associated with $H_{prod}$ were not controlled in these studies.

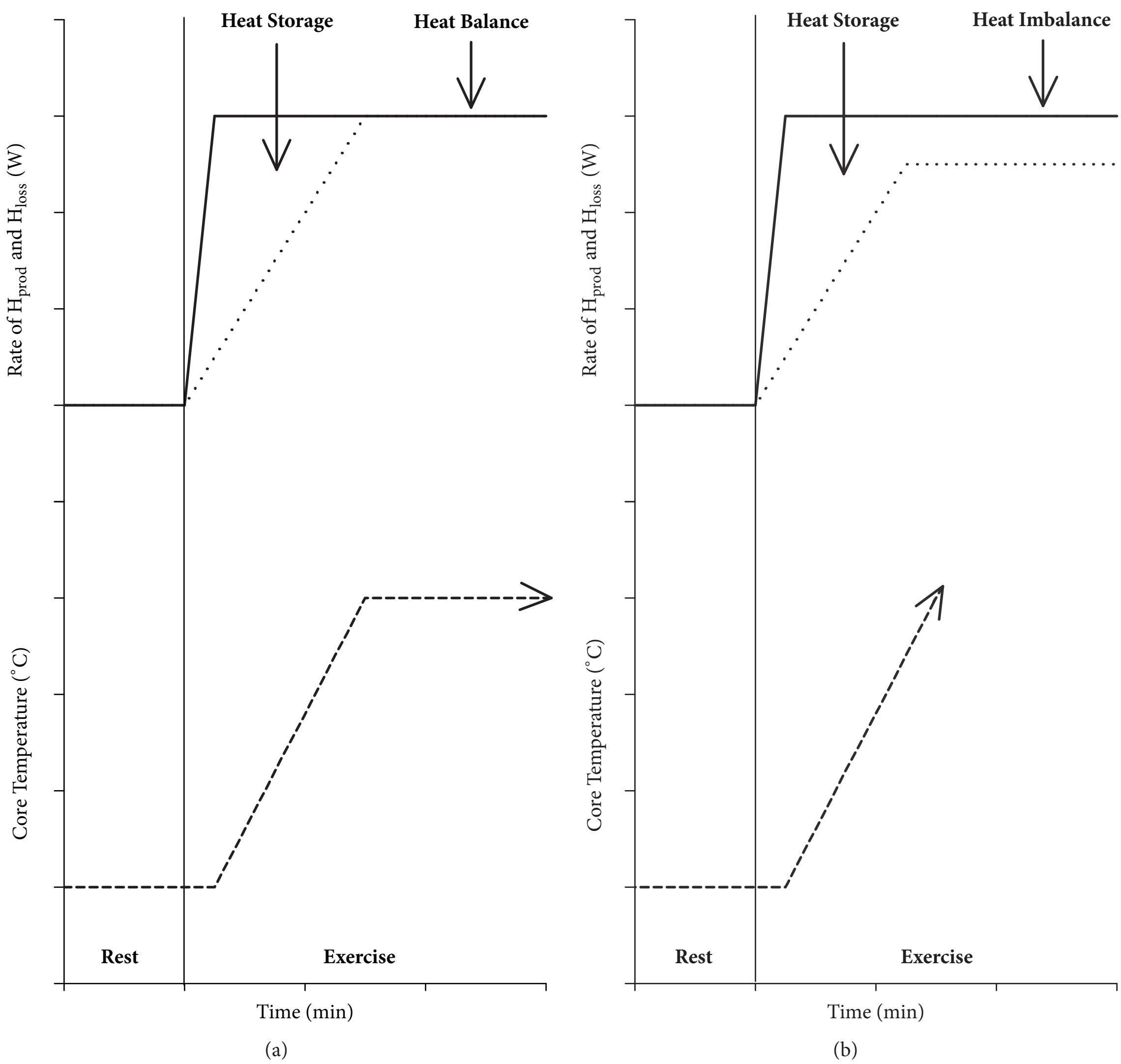


FIGURE 1: **(a)** At rest, the rate of $H_{prod}$ (solid line) is balanced out by the rate of $H_{loss}$ (dotted line), a combination of evaporative and dry heat exchange. At the onset of exercise, $H_{prod}$ rapidly rises reaching a steady state within 5 min. Due to the delay in the onset of $H_{loss}$ responses, $H_{loss}$ does not immediately balance the rate of $H_{prod}$ resulting in net heat storage. The additional heat energy stored inside the body initiates increases in sweating and skin blood flow to increase $H_{loss}$ and achieve heat balance to prevent a continuing rise in core temperature (dashed line). **(b)** When heat balance cannot be achieved, core temperature will continue to rise to potentially dangerous limits and not plateau, due to limited $H_{loss}$ capacity; the rate of $H_{loss}$ required to achieve heat balance is greater than the maximum capacity for heat dissipation. $H_{prod}$: metabolic heat production; $H_{loss}$: net heat loss.

Recent studies have shown that biophysical differences can independently influence sweating responses, particularly during exercise [29, 41–44]. For example, an individual with a small body surface area would require a greater amount of sweat to be produced per unit body surface area to achieve the same absolute rate of evaporation compared with an individual with a larger body surface area. This is consistent with the findings of Cramer and Jay [41], who demonstrated that local sweat rate was significantly higher in individuals with a smaller body surface area (~1.8 $m^2$) compared with individuals with a larger body surface area (~2.1 $m^2$) during exercise at any given fixed rate of evaporative requirement and thus $H_{prod}$. Hence, it is difficult to determine whether the aforementioned findings are due to aging *per se* [14, 39, 40] or can be purely ascribed to between-group biophysical differences associated with $H_{prod}$. In this regard, given the clear independent influence of biophysical properties on thermoregulatory control, future studies should look to perform a more comprehensive examination of thermoregulatory-induced sweating during exercise in this vulnerable population, whereby all between-group differences in biophysical factors have been accounted for (i.e., $H_{prod}$ and body mass and surface area).

## 4. Age-Related Changes in Skin Blood Flow

In addition to evaporative heat loss, the ability to adjust cutaneous vasomotor tone provides an effective means of managing a thermal load by redistributing cardiac output to modulate SkBF [45]. Indeed, this allows for the convective transfer of heat content within the circulatory system from the core to the periphery. These responses enable the distribution of internal heat content amongst various tissues in the body, as well as potentially raising skin temperature to facilitate increases in dry heat loss or minimise the rate of dry heat gain when the gradient for dry heat exchange is reversed (provided that the ambient temperature was greater than skin temperature) at a given ambient temperature. Therefore, the thermoregulatory-induced redistribution of blood flow to the skin is seen as a fundamental thermoregulatory response [46]. A common finding amongst studies that have examined thermoregulation in healthy aging to date is that older individuals demonstrate impaired heat-induced rises in SkBF compared to their younger counterparts [10, 11, 25, 26, 47–49]. Whilst aging does not appear to independently influence the onset threshold for cutaneous vasodilation (and accompanying changes in SkBF) [13], studies have consistently shown that older individuals exhibit attenuated increases in SkBF for a given change in core temperature, as well as lower time-dependant changes in SkBF compared to younger individuals [10, 11, 25, 26, 47–49]. This impaired cutaneous vascular response to heat stress reported in the aforementioned studies is observed even when older and younger individuals are matched for aerobic fitness, acclimation, and hydration status, suggesting that this is a primary function of human aging.

Whilst passive heat exposure stimulates increases in SkBF, it must be acknowledged that the combination of heat stress and exercise can further challenge the human cardiovascular system [50]. As such, the maintenance of blood pressure and skeletal muscle perfusion, in the face of increases in SkBF to meet thermoregulatory demands, necessitates an increase in cardiac output and redistribution of blood flow from inactive regions including the renal and splanchnic circulations [46]. In light of this, the combined independent demands from the skin, active skeletal muscle (both locomotor and respiratory), and blood pressure regulation will likely exceed available cardiac output [45]. In keeping with this suggestion, previous work has demonstrated that SkBF plateaus at ~60% of its maximum during exercise in the heat in healthy young individuals [51]. This is likely the result of a baroreceptor reflex-mediated control of SkBF imposed by exercise-induced metabolic demands to redistribute blood flow away from the cutaneous circulation to maintain optimal skeletal muscle and cerebral perfusion and blood pressure regulation [52]. If SkBF was to continue rising unabated during exercise, blood pressure would potentially fall which may then lead to a catastrophic perfusion failure of vascular beds. With such changes evident in apparently healthy young individuals, it may be argued that cardiovascular and thermal strain would be exacerbated to a greater extent in older individuals when exercising in a hot environment. The fact that SkBF responses during exercise in the heat are diminished to a much greater extent in older individuals compared to younger individuals, thereby negatively affecting heat content distribution and possibly even heat loss capacity in this population, lends some support to this suggestion [25].

Over the past several years, a number of researchers have examined the mechanisms underlying age-related impairments in cutaneous vasomotor control [9, 10, 13, 26, 38, 53–60]. From these investigations, it has been recognised that impairments in the mechanisms mediating cutaneous vasomotor control occur at multiple sites along the efferent arm of the sympathetic nervous system. These impairments include reductions in sympathetic cholinergic cotransmitter release, alterations in downstream signalling for vascular endothelial function, and attenuation in heat stress-induced sympathetic neural drive. Furthermore, it is important to note that age-related alterations in cardiovascular function and fluid status can also contribute to impaired SkBF responses during heat stress in older individuals. These age-related factors are discussed in greater detail below.

Thermoregulatory-induced rises in SkBF are primarily mediated by a sympathetic cholinergic active vasodilator system [61, 62]. Active cutaneous vasodilation is mediated through the release of acetylcholine and unknown cotransmitters, which facilitate cutaneous vasodilation through NO-dependant mechanisms [61, 62]. Studies have shown that older individuals exhibit an impaired vasodilatory response to hyperthermia and can be attributed to decreased sensitivity of the active vasodilator system [60, 63]. This decreased sensitivity of the active vasodilator system results in reduced cotransmitter signalling and, thus, attenuated NO-dependent cutaneous vasodilation. Hence, compared to younger individuals, older individuals predominately rely on compromised nitric oxide- (NO-) dependant cutaneous vasodilation to increase SkBF in response to environmental heat exposure and/or physical activity [54, 56, 57]. Furthermore, increases in skin and core body temperature elicit robust increases in skin sympathetic nerve activity in young healthy individuals [64]. However, when compared to young individuals, Stanhewicz et al. [58] not only demonstrated that older individuals exhibit less sympathetic outflow to the skin during passive heat stress, but also have an attenuated vasodilator response for a given increase in skin sympathetic nerve activity. These findings are consistent with that of Grassi et al. [53] who showed that skin sympathetic nerve activity modulation from mild changes in ambient temperature (±8°C) is markedly reduced in older individuals. Since increases in skin sympathetic nerve activity are thought to drive cutaneous vasodilator responses, overall these studies suggest that differences in sympathetic activity may contribute to the altered SkBF response observed in older individuals during heat stress.

Previous studies have also examined the cardiovascular response to heat stress. Findings from these studies have shown that capillary density in aged skin is reduced [65, 66] and that age-related reductions in SkBF are secondary to less cardiac output and blood flow redistribution from inactive visceral areas such as the renal and splanchnic circulations [26]. Minson et al. [26] demonstrated that smaller heat-induced rises in cardiac output were primarily due to a lower stroke volume, since the older individuals were able to increase their heart rate to a similar extent as the young individuals during passive heat stress. Similarly, Gagnon et al. [59] demonstrated that older individuals exhibit a lower cardiac output during passive heat stress compared to younger individuals. However, these authors reported that the Frank-Starling relation appropriately shifts during passive heat stress in older individuals, resulting in maintained stroke volume despite reductions in cardiac filling pressures and that the lower cardiac output observed was primarily mediated by a blunted heat-induced chronotropic response [59]. At present, the explanation for the differing findings between Minson et al. [26] and Gagnon et al. [59] is unclear; however, it may be that methodological differences between studies were responsible, as previously discussed [59].

In addition to the above, it has previously been proposed that less cardiac output and blood flow redistribution during heat stress may be due to age-related changes in fluid status [49, 67, 68]. Indeed, studies have shown that older individuals exhibit decrements in thirst sensation [69, 70], and renal sodium- and water-conserving capabilities decline with advancing age [71]. As such, these findings suggest that the capacity to accommodate large increases in intravascular blood volume and that the amount of blood available to circulate through the cutaneous vasculature are limited in older individuals compared to their younger counterparts. Taken together, this would imply that older individuals have an impaired ability to redistribute internal heat content amongst various tissues in the body and that internal heat storage is concentrated more toward the body core during heat stress.

## 5. Thermoregulation, Fitness, and Aging

Common practice for studies isolating the independent effect of a particular physiological factor (e.g., age) on thermoregulation during exercise is to match groups for peak oxygen uptake ($\dot{V}O_{2peak}$) and/or prescribe exercise using relative workloads [14, 25, 39, 40, 48, 72]. The rationale to use such a protocol is based on the original findings of Saltin and Hermansen [73], who demonstrated that exercise at the same $\%\dot{V}O_{2peak}$ yielded similar core body temperature responses in young healthy individuals, irrespective of aerobic capacity. Later in 1989, Greenhaff [74] also reported smaller changes in core body temperature during exercise at a fixed absolute intensity in young fit ($\dot{V}O_{2peak}$: 60-65 ml/min/kg) compared to unfit ($\dot{V}O_{2peak}$: 40-45 ml/min/kg) individuals. Similar findings were further observed by Fritzche and Coyle [75] and Gant et al. [76] during exercise at a fixed $\%\dot{V}O_{2peak}$ in a similar climate (~23°C). Collectively, these findings have led to the long-held notion that interindividual variability in core body temperature regulation during exercise is eliminated when the exercise intensity is expressed as a $\%\dot{V}O_{2peak}$ [77].

Over the last 15 years, there has been a paradigmatic shift from the concept that core body temperature is driven according to $\%\dot{V}O_{2peak}$, to an appreciation that the use of a fixed $\%\dot{V}O_{2peak}$ protocol leads to different rates of $H_{prod}$ between independent groups who are not matched for absolute $\dot{V}O_{2peak}$ [41, 42]. Accordingly, the participant group with the higher $\dot{V}O_{2peak}$ generates a greater level of $H_{prod}$ during exercise at a fixed $\%\dot{V}O_{2peak}$. As such, a greater rate of net heat loss is required to offset the greater rate of $H_{prod}$ elicited by the experimental protocol [29]. Consistent with this suggestion is that greater sweat rates are commonly reported with increasing levels of fitness when exercise is prescribed at a fixed $\%\dot{V}O_{2peak}$ [40, 78–80]. As such, previous studies that used a $\%\dot{V}O_{2peak}$ approach might have incorrectly ascribed differences in thermoregulation to the physiological factor that was thought to be isolated/under investigation (e.g., age) [14, 25, 39, 40, 48, 72], when different rates of $H_{prod}$ and, thus, requirements for heat loss may instead have been accountable.

In accordance with this theory, Jay et al. [42] examined the change in core body temperature during exercise at a fixed $\%\dot{V}O_{2peak}$ and at a fixed absolute exercise intensity (and thus requirement for heat loss) in fit ($\dot{V}O_{2peak}$: ~60 ml/kg/min) and unfit ($\dot{V}O_{2peak}$: ~40 ml/kg/min) men matched for age (~22 y) and body mass (~78 kg). These authors demonstrated that the changes in core body temperature and sweat rates were greater in the fit group compared to the unfit group during exercise at 60% $\dot{V}O_{2peak}$. In contrast, the changes in core body temperature and sweat rates were similar between groups during exercise at a fixed absolute exercise intensity (despite large differences in the relative exercise intensity). These findings support those of a classic study by Nielsen [81] who demonstrated that changes in core body temperature were determined by the absolute exercise intensity (and thus $H_{prod}$), irrespective of aerobic fitness. Therefore, these findings suggest that the individual level of fitness may not influence one's ability to regulate changes in core body temperature during exercise.

It must be acknowledged that the findings of Jay et al. [42] can only be applicable to younger individuals who likely exhibit no physiological impairment in their ability to regulate changes core temperature. Given that there is evidence suggesting that older individuals exhibit impaired thermoregulation during exercise compared to their younger counterparts [14, 25, 39, 40, 48, 72], it must be noted that these studies used a $\%\dot{V}O_{2peak}$ protocol. Therefore, it is difficult to determine whether the reported findings in these studies are due to aging *per se* [14, 25, 39, 40, 48, 72] or are simply ascribed to differences in the absolute $H_{prod}$ and heat loss requirements, secondary to the use of a $\%\dot{V}O_{2peak}$ protocol. In this regard, it is surprising that no study to date has used a similar experimental protocol as that described by Jay et al. [42] to elucidate the true independent influence of age and fitness on thermoregulatory responses during exercise. Hence, we believe that this is an area that requires further examination.

## 6. Clinical Implications of Age-Related Decrements in Thermoregulatory Control

In the preceding sections we have clearly identified that elderly individuals exhibit diminished sweating and SkBF responses during environment and/or physical activity-induced heat stress compared to their younger counterparts. As such, elderly individuals are likely limited in their ability to manage a thermal load secondary to a lower evaporative heat loss capacity and/or impairments in internal heat distribution. Based on the available evidence, we suspect that a lower sweat output per gland for a given level of cholinergic stimulation [35–37], as well as impaired intrinsic vasodilator pathways combined with a reduced cardiac reserve [25, 26, 65, 66], may contribute to this response in these individuals.

An important challenge for this field of research, and perhaps the most imperative, is to avoid older individuals from becoming discouraged from partaking in regular exercise [82]. Indeed, the health benefits associated with exercise still far outweigh the consequences of not performing exercise purely as a means to escape the potentially detrimental effects of hot weather [82]. Whilst current public health guidelines provide information on recommended levels of physical activity with associated long- and short-term beneficial outcomes, there are no recommendations regarding the levels of physical activity specifically for older individuals that can be safely performed in the heat (i.e., the summer months and bouts of hot weather) [15, 16]. Therefore, we believe there is urgent need for the development of public health recommendations for performing physical activity in the heat for older individuals, as well as future studies for developing strategies that enable older individuals' to optimally regulate their body temperature whilst performing routine physical activity.

In regard to strategies that may mitigate harmful elevations in heat strain, regular exercise training is known to improve several physiological parameters critical to thermoregulation. Indeed, exercise training has proven effective in improving cardiac [83, 84], autonomic [85], and vascular endothelial function and accompanying changes in blood flow distribution in older healthy individuals [86, 87]. As such, one may speculate that whilst exercise training is not only important for improving clinical health outcomes and preventing the onset of chronic disease [88], regular exercise training may also be important for maintaining and/or preventing the age-related decline in thermoregulatory control. In keeping with this suggestion are the findings of Inoue et al. [36] who demonstrated that regular exercise training slows the age-related decline in heat loss effector function, whereby sweat gland output in response to cholinergic stimulation is greater in fit older individuals compared to unfit older individuals. Moreover, plasma volume expansion with exercise training may allow for a larger heat-induced rise in cardiac output to facilitate a greater redistribution of blood flow to the skin and optimize heat content distribution amongst peripheral tissues [89]. Indeed, additional findings from Thomas et al. [90] and Okazaki et al. [48] showed that the core body temperature onset threshold for SkBF and sweating was improved in older men following both aerobic and resistance exercise training. From a thermoregulatory, these findings suggest that exercise training may improve thermoregulatory control, by augmenting heat-induced SkBF and sweating responses and thus potential internal heat distribution and evaporative heat loss capacity in older individuals.

Similar to regular exercise training, studies have reported that consecutive days (typically >6 days) of passive heat exposure (above 40°C for a minimum of 60 min) resulted in physiological adaptation to heat stress in older individuals [11, 36, 91, 92]. Physiological changes observed in these studies for older individuals included a lower core temperature onset threshold for sweating and SkBF, enhanced sweating and SkBF for a given absolute core body temperature, and reduced core body temperatures. In keeping with these findings, Best et al. [93] demonstrated that the reduction in resting core body temperature and increased SkBF and sweat production following 6 consecutive days of heat acclimation (60 min, 40% relative humidity) in older cyclists were similar to that observed in younger cyclists. These findings suggest that even older individuals who are habitually active can achieve similar physiological adaptations during consecutive bouts of heat stress as younger individuals. Whilst the above findings highlight the beneficial effect of acclimation on thermoregulatory control, Kohara et al. [94] recently reported that the age-related decline in vascular endothelial function, as evidenced by lower brachial artery pulse wave velocity, is attenuated in individuals who undertake a hot (>41°C) water bath compared to those who undertake a warm (<40°C) water bath more than 5 times per week (over four years). Moreover, a large cohort study (n = 2327) demonstrated that repeated whole-body heat exposure is associated with a marked reduction (~5 fold) in fatal cardiovascular and all-mortality events in men aged 42-60 years [95].

In addition to the above, it has previously been hypothesised that dietary supplements such as folic acid and nitrate (beetroot juice) and the use of electric fans might be beneficial in protecting against heat-related strain in those with thermoregulatory dysfunction [96]. Although theoretical at this time point, future studies are needed to examine the implications of these strategies directly in vulnerable populations. Indeed, this information would be invaluable given that climate change is predicted to bring about a greater variability in weather patterns with an increase in extreme weather events such as sustained heat waves [3, 97–99]. This, combined with the rising costs of electrical energy, which could make affordable electronic cooling devices (air-conditioning units) inaccessible to low-income individuals [3, 100, 101], could have a direct impact on population health since heat waves and/or bouts of hot weather can potentially exceed the physiological limit of compensability of vulnerable individuals, particularly the elderly.

## 7. Comorbid Disease and Thermoregulatory Control

Impaired thermoregulatory responses should be considered in older individuals as they may contribute to heat-related illness and, therefore, adversely impact upon health outcomes during everyday activities, including exercise, particularly during bouts of hot weather. Indeed, identifying potential thermoregulatory dysfunction during exercise in older individuals is important for a variety of reasons. There is now evidence that regular physical activity in this population increases exercise capacity and health-related quality of life and improves morbidity and mortality [15, 16]. However, with potentially suboptimal heat management capabilities, older individuals may become discouraged or even prevented, from participating in regular exercise, resulting in an increased risk

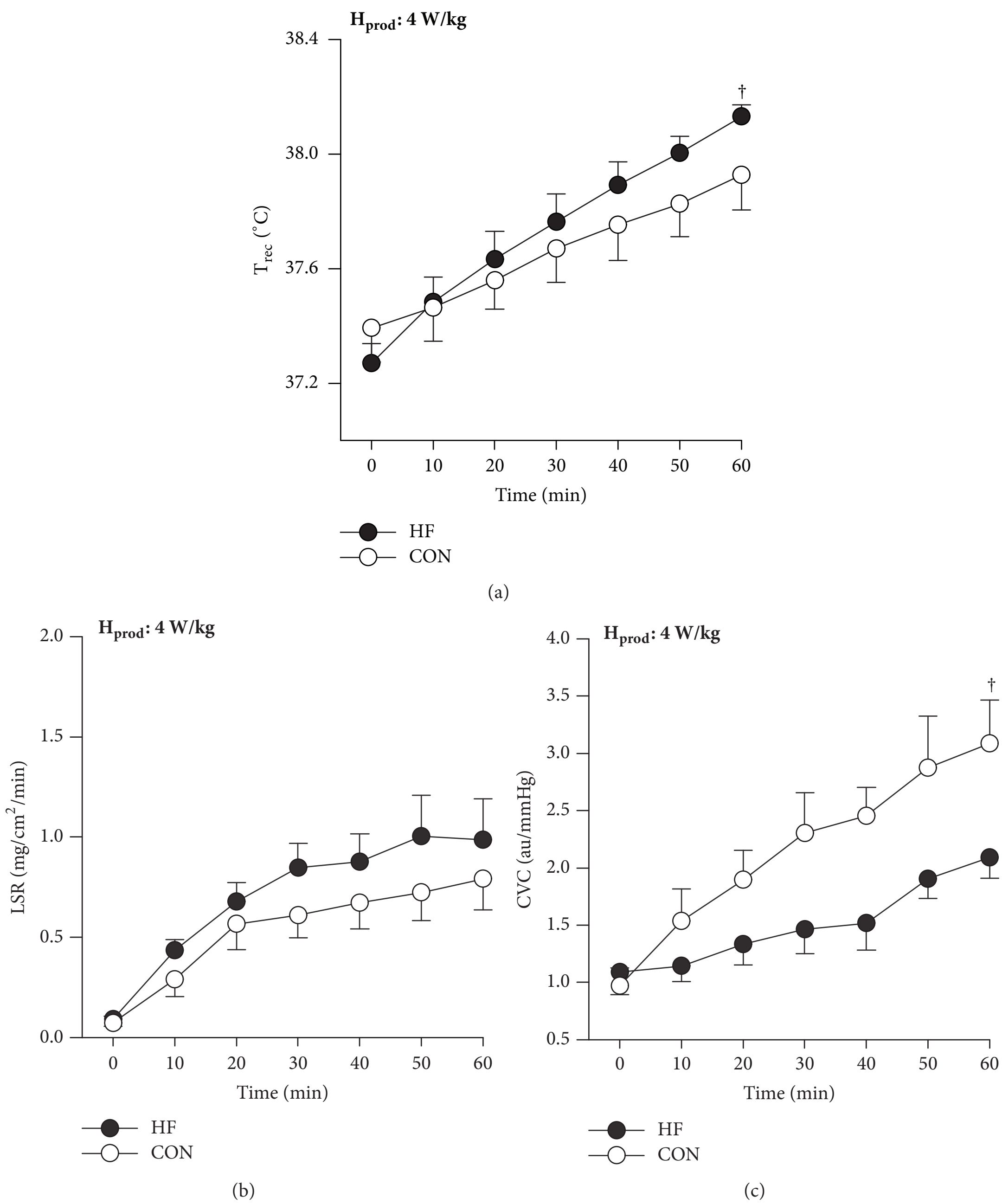


Figure 2: $T_{rec}$ (a), CVC (b), and LSR (c) values recorded at 10-min intervals during the submaximal cycling test. $H_{prod}$: metabolic heat production; $T_{rec}$: rectal temperature; CVC: cutaneous vascular conductance; LSR: local sweat rate. Data are mean ± standard error of the mean. †Significant group-time interaction, $p < 0.05$. Figure adapted from Balmain et al. [28].

of developing chronic heart and lung disease and hence a poorer health-related quality of life.

Risks for heat-related illness are compounded for people with cardiovascular disease. Notably, we have recently demonstrated that thermoregulatory responses in individuals with heart failure differ from age-matched (~61 yr) healthy controls during exercise in a warm environment [28, 96, 102]. When exercising at the same rate of $H_{prod}$ in a warm environment (30°C), we found that heart failure patients have a greater rise in core temperature compared to healthy controls (Figure 2, Panel (a)). Although sweating responses were preserved in heart failure (Figure 2, Panel (b)), cutaneous vascular conductance was greatly attenuated (due to a lower rise in SkBF) in these patients relative to healthy controls (Figure 2, Panel (c)). As such, patients with heart failure have a greater susceptibility to heat strain (greater rise in core body temperature) for a given combination of activity and climate compared to their age-matched healthy counterparts, secondary to poorer circulation to the periphery [96]. Therefore, our results suggest that thermoregulatory dysfunction and the associated risk of heat-related illness are compounded for people with heart failure.

It is important to note that studies examining thermoregulatory control in heart failure to date have included patients who continued with standard therapy [28, 51, 102–107]. Beta-blockade is a standard, first-line therapy for heart failure, which may possibly contribute to the lower rise in SkBF in these patients, particularly since younger individuals taking beta-blockers exhibit attenuated SkBF responses during exercise in the heat [108]. Moreover, diuretics may also influence thermoregulation. In healthy individuals, the use of diuretics has been associated with attenuated SkBF responses secondary to a reduction in plasma volume [109]. As such, patients with heart failure taking diuretics may impair thermoregulatory control during periods of heat stress. The fact that fluid status is also a fine balance in heart failure may predispose these patients to heat-related illness, should they become dehydrated, particularly during an exercise challenge [96].

Similar to individuals with heart failure, a number of clinical reports suggest that individuals with chronic lung disease, including asthma and chronic obstructive pulmonary disease, may be particularly vulnerable to heat-related illness during environmental heat exposure [110–113]. In addition, Jehn et al. [114] recently demonstrated that exposure to heat stress is associated with worse symptoms and a reduction in physical activity levels in individuals with pulmonary arterial hypertension. Whilst it appears that individuals with chronic lung disease are at a greater risk of heat-related morbidity and mortality, there is no evidence to date suggesting whether this is due to physiological impairments in the regulation of body temperature as a result of chronic conditions or simply can be ascribed to changes in air quality that typically accompany bouts of hot weather [115, 116]. Hence, we believe that thermoregulation in the context of chronic lung disease is an area that requires further examination.

## 8. Conclusion

Recent observations clearly show that older individuals are susceptible to heat-related illness during environmental and/or physical activity-induced heat stress. This increased susceptibility appears to be mediated by diminished heat-induced increases in sweating and SkBF responses. Based on this evidence, aging is clearly associated with an attenuated physiological ability to dissipate heat. It is also important to note that with an aging population and the projected consequences of global warming, a greater number of individuals, including those individuals with chronic heart and lung disease, will be exposed to the risks of heat-related morbidity and mortality in the coming decades. Hence, scope exists for further studies examining mechanisms of temperature regulation in the elderly to optimize the management of these vulnerable individuals when exposed to heat stress. Indeed, participation in physical activity is likely to be enhanced if environmental heat stress does not pose a significant barrier or safety concern for such individuals.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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*Research Article*

# Gender Perspective on Older People's Exercise Preferences and Motivators in the Context of Falls Prevention: A Qualitative Study

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*Background.* Several factors have previously been identified to positively influence the uptake and adherence for fall prevention exercise programmes. There is, however, a lack of studies investigating if men and women differ in their views and preferences for fall prevention exercises. *Aim.* To explore exercise preferences and motivators of older community-dwelling women and men in the context of falls prevention from a gender perspective. *Methods.* Workshops including multistage focus group discussions were conducted with 18 older community-dwelling people with and without history of falls. Participants were purposively selected and divided into two groups. Each group met on six occasions over a period of five months. Participatory and Appreciative Action and Reflection methodology was used to guide the discussions. A qualitative content analysis approach was used in the analysis. *Results.* Older participants had many diverse preferences and confirmed that individually tailored exercise, in terms of mode, intensity, challenge, and social context, is important. Moreover, important factors for exercise adherence and maintenance included the experience of individual confirmation; different spirit lifters to increase enjoyment; and personal tricks to maintain exercise routines. The individual differences within genders were more diverse than the differences between women and men. *Conclusion.* Exercise interventions to prevent falls should be individually tailored, based on the specific needs and preferences of the older participant, and do not appear to require gender specific approaches. To increase adherence, intrinsic motivation for exercise may be encouraged by competence enhancing confirmations, energizing spirit lifters, and practical tips for exercise maintenance. The study provides an awareness about women's and men's preferences for fall prevention exercises, and this information could be used as guidance in designing inclusive exercise interventions.

## 1. Introduction

Globally, accidental falls are a major public health problem and the second leading cause of unintentional injury deaths worldwide. Each year 37.3 million falls require medical attention, and adults older than 65 years of age suffer the greatest number of fatal falls [1]. At least one-third of community-dwelling people aged 65 years and above fall every year, and the incidence increases with advancing age and fragility level [2]. In Sweden, falls are the most common cause of injury in old age that leads to deaths, hospitalizations, and visits to emergency services. In the age group over 80 years, nine out of ten injuries are caused by a fall [3]. As the proportion of older people is rising globally, the individual and societal costs associated with falls will increase. The prevention of falls is therefore an urgent public health challenge.

Intervention programmes that focus on balance combined with muscle strength in the lower limbs are effective in addressing risk and rate of falling [4, 5]. Despite this, many older people are reluctant to adopt fall prevention exercise due to factors such as underestimation of falls risk, poor self-efficacy, fear of falling, or stigma associated with exercise for older people [6]. According to a systematic review, only 64% accepted the invitation to join the exercise programme and 19% then dropped out when they learned what the intervention entailed [7]. Moreover, around 77% of the participants in fall prevention exercise studies are women [8]. Instead of participation in exercise, many older people choose individual coping strategies, tailored to their particular circumstances, to avoid future falls, or simply discontinue activities that would involve a risk of falling [9]. Poor adherence is associated with low education (< high school), living in a disadvantaged neighbourhood, being obese, having fair/poor self-rated health and having problems with walking or using a walking aid, and a history of falls [10, 11].

Several factors have been identified that positively influence the uptake and adherence for fall prevention exercise programmes, including facilitators such as support from professionals or family, social interaction, perceived benefits, a supportive exercise context, feelings of commitment, and having fun. However, there is still a lack of studies investigating preferences for specific programme characteristics that may attract older people by making exercise interesting, challenging, and enjoyable [12]. Additionally, in previous studies investigating preferences, more than 75% of the participants have been women and very few studies have investigated if men and women differ in their views and preferences for fall prevention exercises [12]. Unconscious preunderstandings and expectations of how older men and women would prefer to exercise may lead to unnecessary gender bias [13]. In order to identify factors that attract both older women and men to fall prevention exercise programmes, as well as increasing the awareness and knowledge among professionals who deliver these exercise programmes, there is a need to identify if older women and men differ in their views and preferences about exercising. The aim of this study was, therefore, to explore exercise preferences and motivators of older community-dwelling women and men in the context of falls prevention, from a gender perspective.

## 2. Methods

This study is based on workshops including multistage focus group discussions [14] held with older people as part of a larger participatory action research project, aiming to develop an evidence-based, cocreated, fall prevention digital exercise programme [15]. The checklist from the 32-item COREQ (consolidated criteria for reporting qualitative research) [16] was used when designing and reporting the study. The study was approved by the Regional Ethical Review Board (Dnr. 2012-170-31M).

*2.1. Participants and Recruitment.* Participants were recruited from seven senior citizen organisations. Thirty-eight older adults volunteered to be contacted by telephone and interviewed to inform a purposive sample consisting of community-dwelling women and men of at least 70 years of age. Sampling aimed to achieve a heterogeneous group with respect to exercise habits, living conditions, and experiences of falls, with 30% having a fall in the previous 12 months (reflecting population epidemiology). Eighteen participants (10 women and 8 men) were finally included in the study; one woman chose to end her participation after four meetings. The mean age of the participants was 74.6 ± 3.5 years. The majority of the participants were former white-collar workers and, in general, have self-reported being moderately physically active. Two couples were deliberately involved in the project. Four participants lived alone and 14 lived with partners (Table 1).

The participating researchers formed a cross-disciplinary group from the disciplines physiotherapy, informatics, exercise physiology, and computing sciences. The group included experts in e-health, falls prevention, and gender research. All researchers were women. None of the researchers had any preexisting relationship with the participants and they all introduced themselves and their role in the project at the beginning of the process.

Prior to the first meeting, the participants were divided, by the researchers, into two separate groups with similar disposition regarding age, background, and gender. One of the married couples was placed in each group. Before the first focus group discussion, the participants signed a written informed consent.

*2.2. Data Collection.* Data was collected through six workshops including multistage focus group discussions [14] with each group. Each workshop was held at a community centre and lasted for 2.5 hours, including a short refreshment break. All focus group discussions were conducted in a positive atmosphere inspired by Participatory and Appreciative Action and Reflection (PAAR) methodology [17]. The PAAR methodology is a form of Appreciative Inquiry, meaning that it focuses on positive experiences rather than problems. According to this methodology the focus group discussions aimed to understand the root causes of the older participant's positive experiences of and preferences for exercises. The focus was on accomplishments, strengths, and understanding the causes of success, so that these causes could be better understood and augmented. In this way the discussions were not preoccupied by problem solving or by changing negative behavior. This appreciative form of inquiry aims to create an open, positive, and encouraging climate during the discussions.

In order to stimulate the discussions within the group, a range of facilitating techniques and methods were used. The participants were asked, for example, in between the workshops to document their everyday life in different ways in order to stimulate and trigger thoughts about what inspired them to exercise and to be active. One method used for this was Photovoice, a process by which people can identify, represent, and enhance their thoughts through photographs [18]. Another example was to bring pictures from newspapers, reflecting their attitudes towards exercising and moving their body. During other sessions practical activities (e.g., strength and balance exercises) were conducted and the participants were asked to actively reflect over the exercises

Table 1: Characteristics of the participants.

| Code | Age | Focus group | Partner or living alone | White/Blue Collar | Falls last 12 months Yes/No | Physical activity level based on IPAQ |
|---|---|---|---|---|---|---|
| **W1** | 74 | 1 | Partner | White | Yes | Moderate |
| **W2** | 70 | 1 | Partner | White | No | Moderate |
| **W3** | 73 | 1 | Partner | Blue | No | Moderate |
| **W4** | 71 | 1 | Partner | White | No | Moderate |
| **W5*** | 76 | 1 | Living alone | Blue | No | Moderate |
| **W6** | 75 | 2 | Living alone | White | No | Moderate |
| **W7** | 80 | 2 | Living alone | Blue | Yes | Low |
| **W8** | 74 | 2 | Partner | White | No | Moderate |
| **W9** | 71 | 2 | Partner | White | Yes | High |
| **W10** | 70 | 2 | Partner | White | No | Low |
| **M1** | 72 | 1 | Partner | White | Yes | Low |
| **M2** | 80 | 1 | Living alone | White | No | Moderate |
| **M3** | 78 | 1 | Partner | White | Yes | High |
| **M4** | 76 | 1 | Partner | White | No | Moderate |
| **M5** | 70 | 2 | Partner | White | No | Moderate |
| **M6** | 79 | 2 | Partner | White | No | Moderate |
| **M7** | 75 | 2 | Partner | White | No | Low |
| **M8** | 79 | 2 | Partner | White | Yes | Moderate |

W: woman; M: man; IPAQ: International Physical Activity Questionnaire. White collar worker examples: office worker, police officer, nurse, and teacher; blue collar worker examples: taxi driver, shop keeper. The level of physical activity was self-reported as low, moderate, or high based on how much time had been spent being active the previous week, and how strenuous it had been. Examples of activities performed: cycling, swimming, water-aerobics, walks, table tennis, and weight lifting. *Dropped out after four focus group discussions.

and to describe their views and feelings. Sometimes more detailed questions were posed and visualisations of different views were placed around the room. The participants were asked to move to the place that represented their view and were encouraged to explain and discuss their choices. Another facilitating technique used was short descriptions of five fictional characters (personas) representing different motivational profiles [19]. These personas were constructed based on data from the first sessions and the participants rated how well the descriptions defined themselves and the way they preferred to do exercises. The participants were later asked to create their own persona description, by combining sentences from the predefined examples. With the purpose of clarifying and separating differences in the participants reasoning, smaller gender divided discussion groups were organized during the fourth and fifth workshop. The main activities of each workshops have been presented elsewhere [15, 20].

Between five and six of the researchers attended each workshop, except workshop three when only two researchers participated (PP and LLO). Two of the authors (BBK and AMW) had extensive previous experience from participatory action research and they were primarily responsible for facilitating the discussions, assisted by the other authors present. After each session the researchers discussed and reflected on the results and the process. Based on these reflections the purpose of the next meeting was planned. In the beginning of each new meeting the researchers summarized and presented result from the last workshop to get feedback, and then the aim of the current meeting was outlined.

*2.3. Analysis.* All focus group discussions were digitally recorded and transcribed verbatim. As recommended when trying to identify similarities and differences in material, qualitative content analysis was used to analyse data and explore women's and men's reasoning about their experiences and preferences in relation to exercises [21]. An inductive content analysis approach was used since very few previous studies have investigated if men and women differ in their views and preferences for fall prevention exercises. Thus the categories were derived from the interviews and not on the basis of previous knowledge or theories [22]. Two of the authors (PP and MS) read the transcripts independently to get an overall understanding of the participants exercise preferences. The text was then transferred to the data program Open Code 4.01 [23], where meaning units related to the aim were identified and labelled with codes. The codes were organized into preliminary subcategories and categories by two of the authors (PP and MS). The categories were continuously negotiated and the texts reread within the author group until consensus was reached to ensure trustworthiness. The categories and subcategories were in addition presented and discussed at two seminars for PhD students and senior researchers at the University. In the end of this process the results were summarized and presented to the

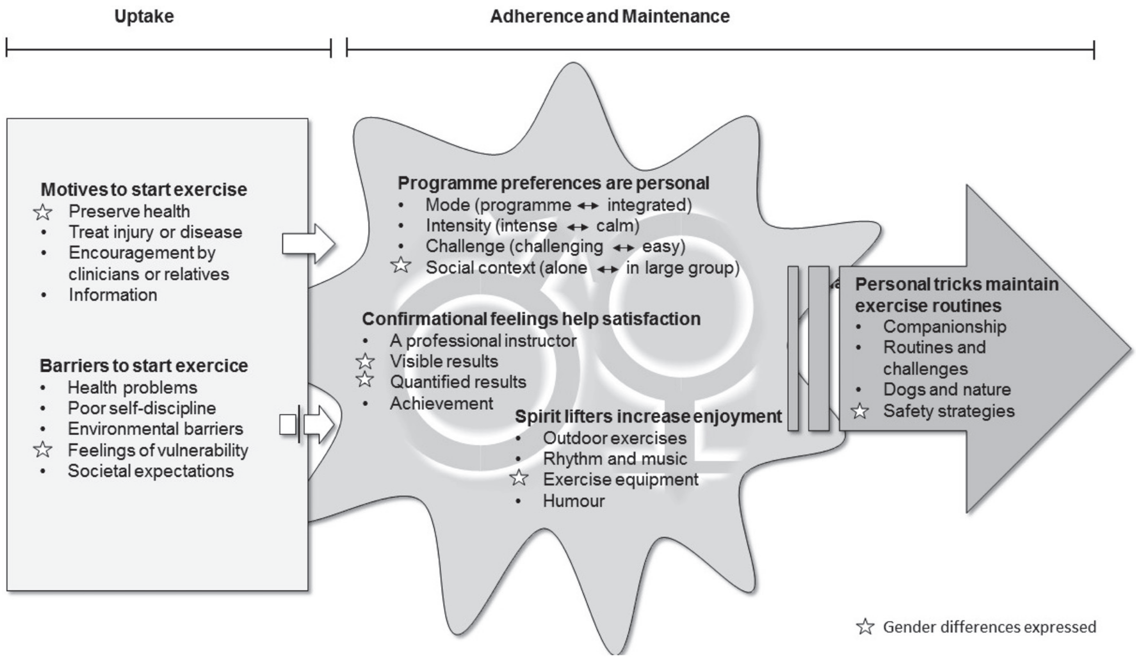


Figure 1: Overview of the categories related to uptake, adherence, and maintenance.

participants. Preliminary results were included in the thesis of one of the authors (PP) [20].

## 3. Results

The participants gave many examples of physical activities they liked to perform, such as walking, cycling, working outdoors, gymnastics, water aerobics, skiing, dancing, Nordic walking, table tennis, and Qigong. They expressed many motives, as well as barriers, for starting to do exercise in the context of falls prevention. Based on their experiences, they voiced many opinions regarding how different exercise properties influence and enhance motivation and they gave examples of "tricks" to facilitate maintenance. In the majority of these opinions no clear gender separation pattern was seen. The individual differences within genders were more diverse than the differences between women and men. The results are presented in six categories with subcategories. Two categories were related to *uptake* and four categories concerned *adherence and maintenance*. An overview of the categories and subcategories is illustrated in Figure 1. Quotations within the text are annotated with participant number and the sex of the participant (W or M).

*3.1. Uptake.* Several factors important for uptake were mentioned in the focus group discussions. Some of them were predominantly expressed as *motivators* and others as *barriers* to starting exercise.

*3.1.1. Motivators and Barriers to Starting Exercise.* The motives for starting to exercise, discussed within the groups, were preserving health; treating injury or disease; encouragement by clinicians or relatives; and information. Common barriers were health problems; poor self-discipline; environmental barriers; feelings of vulnerability; and societal expectations.

Keeping healthy was a major motivator for both men and women. However, there were differences in how men and women expressed their reasons for this. Women talked about preserving health as a necessity in order to manage their responsibilities in their everyday life "*I just have to keep on going myself, so It's just that I need to exercise for my survival*" (W2), whereas men talked more in terms of keeping fit *"You notice that you have to do certain things to... keep fit"* (M1). An injury or disease that could improve by continuous exercise (such as being diagnosed with osteoporosis, sustaining fractures, having a rupture of the Achilles tendon, or suffering from heart disease) was mentioned by both sexes as a motivator for starting to exercise. On the other hand, commonly occurring health problems, such as arthritis and pain, were also major barriers for exercising and sometimes the participants needed to adapt their activities to their health situation.

Professional advice from a doctor or other health personnel was seen as a driving force for starting to do exercises. For some this was also linked to expectations of what it means to be a good patient, as expressed by one of the men in the study "*When you know that you have done what you promised to do, you feel satisfaction in not misbehaving*" (M5). Relatives' influence, for example, persuasion of a spouse or a wish to do certain activities with grandchildren, was also a motivator for being physically active in the context of falls prevention that was frequently mentioned by both women and men. While information in the media inspired some of the participants to exercise: *"I have started to do an exercise programme that works on strength. I saw it on a TV-show"* (W9), other participants said that such information only stayed in their memory for a short time period and seldom resulted in long-term changes.

A common barrier, articulated by both women and men, was poor self-discipline, even though they knew they felt better once they got started *"You have to overcome certain thresholds in order to get out and exercise"* (M4). Environmental barriers, such as the weather, icy or snowy roads, were also common and even though many of the participants liked exercising outdoors, they felt they were less active during the winter. Feelings of being vulnerable or fragile were also expressed as barriers to physical activity by both men and women. However, experience of fractures and fear of falling were particularly experienced as a barrier among the women and caused them to be more cautious in their activities. *"Of course if you have suffered fractures a few times you are very scared after that"* (W9). The men did not generally speak about fear or vulnerability, but many of them noticed that they had started to avoid doing heavy tasks, if possible, as this often led to pain or discomfort in the body for days afterwards. Other examples of situations where feelings of vulnerability or embarrassment could pose a barrier for taking part in exercises were when an exercise group was too small or predominantly one gender, such as being the only man in a group *"I thought I would do it… but I, I dared not* (laughs), *I'd be alone. But then a few men showed up and eventually I dared to pull myself down into the water"* (M1).

The participants expressed different views regarding society's perception of older people. Opinions emerged that older people were often illustrated in media as passive individuals, which may affect older people's views of what is expected of them. "*Well, it is not easy to find any pictures in newspapers illustrating active older people doing gymnastics and such. There is almost nothing!*" (W9). In contrast, other participants expressed the view that older people nowadays are seen as active and that they have more opportunities and resources than older people in former generations.

*3.2. Adherence and Maintenance.* The categories summarizing factors of importance for adherence and maintenance that emerged in the analysis of the focus group discussions were as follows: *programme preferences are personal; confirmational feelings help satisfaction; spirit lifters increase enjoyment;* and *personal tricks maintain exercise routines.*

*3.2.1. Programme Preferences Are Personal.* Above all the older participants expressed that the exercises need to be adapted to the individual in order to stimulate adherence. When it comes to how the older participants preferred to do their training, in terms of *mode*, *intensity*, *challenge*, and *social context*, no general or gender specific patterns were discerned. Instead the discussions pointed to great variation between individuals, and sometimes even within an individual, depending on the situation.

Regarding exercise mode, diverse preferences for exercise to be either conducted as a programme on specific occasions, or integrated in everyday activities were expressed. Those who were more accustomed to exercising seemed to prefer training programmes, while the more inexperienced felt that integrated exercise was preferable.

The preferred degree of intensity also varied between individuals with no gender pattern; some did not like to sweat, while others thought exercising was not worthwhile if they did not feel tired and sweaty afterwards. What was emphasized was the importance of being able to hold an exercise tempo of one's own. Not being able to keep up or being prevented from exerting effort in their own style and tempo could be frustrating. "*But, we* (with husband) *can almost not walk together* (laughs)*… you must have your own pace… if one of you is faster, and one is… well…."* (W3).

Many of the participants took part in group training and did not seem to worry about the level of challenge, e.g., not being able to keep up or perform all the elements correctly. However, they felt that the instructors should emphasize that if someone is not capable of performing a specific exercise, it is acceptable to choose an alternative exercise, as long as one continues to be active. One man even expressed that it may be motivating to see that there are more challenging levels to strive for, even if you currently cannot perform them. "*But I think it may actually be stimulating when you can see that there are different levels of challenges" (M4).*

Some of the participants liked to work out alone while others preferred to exercise together with others. However, such preferences regarding the social context could vary depending on the activity in focus. When exercising in a group setting, a moderate group size composed of peers of the same age was preferred and the social aspect were emphasized as an important motivator. *"I think that the social aspect is very important in group training… because you usually attend at specific sessions and you meet the same people. Then you start to talk to each other and you learn to know each other… that's fun" (W4).* No obvious gender pattern in preferences for the social context when exercising emerged during the focus group discussions. However, in the personas descriptions constructed by the participants to describe their own motivation profile, women were more prone than men to choose sentences representing a social component to describe themselves, such as "*I am social*", "*I like to exercise together*", or "*I prefer to work out in a group*".

*3.2.2. Confirmational Feelings Help Satisfaction.* Confirmation of the effectiveness and efficiency of an exercise were important motivational drivers for both sexes. *"You want your efforts to pay off"* (W3). Confirmation could be perceived in different ways: from a *professional instructor*; through *visible results*; by *quantified results*, or merely by the feeling of *achievement*.

To have a professional and encouraging instructor was considered very important. The participants appreciated having an expert to trust and ask for advice. Their encouragement and praise could be very stimulating. Participants expressed that they felt more inspired by an instructor of the same age, someone they could identify with, while the sex of the instructor did not matter at all. "*Yeah, but… the closer to one's own age, I think that gives more*" (M3).

Both women and men liked to achieve a secondary goal through their training which meant that they often integrated training with everyday activities to get a visible results, such as working in the garden, cleaning their home, or going out for a walk with a clear purpose in mind. One man expressed that he did not want to "*…fool around doing peculiar exercises*". "*With my age… I do not want to just stand and… I prefer to pay attention to my everyday life and then try to integrate my exercises*" (M2). However, a pattern emerged in the participants' personas descriptions suggesting gender differences. It was more common for men to choose expressions representing visible and practical secondary goals, such as "*I want to see a concrete result with benefits*", "*I weave my exercises into everyday activities*", or "*I like working in the garden or my home*".

Many of the participants expressed that quantifying the results of their training was motivating. They wanted to keep track of their performance and see objective outcomes. Some of them used instruments for counting steps and calorie expenditure, or tracking walking or cycling routes etc., and this was perceived as stimulating. Men tended to express more fascination with opportunities to quantify their performance, as this conversation between two men illustrates "*… And then I start to walk again and it's activated, it measures my speed, and how far I've walked and how many calories I have been spent*" (M5). "*Interesting!*" (M7 comments). "*Yes, fun!*" (M5). However, there were also women who expressed interest in these kinds of devices. Contrastingly, there were also people who seemed to be totally disinterested in measuring their performance and were perfectly happy just knowing that they accomplished the task. One woman described how she had an exercise bike that could record several things but she was not interested in using these features "*I am not doing anything* (to record)*… I sit and cycle for half an hour, and am fine with that*" (W4).

The participants expressed that an inner feeling of achievement was important for adherence to exercise. They associated the pleasant sense of relaxation in the body afterwards, and the pure satisfaction in managing to work out, with an intrinsic motivation for continuing to exercise. "*Well… when you know you have done something, and you can take a shower and sit down in the armchair with a good conscience* " (M5) or "*You experience the same thing when doing exercises, -relaxation… when you are active, and feel that you actually manage to be active*" (W5).

*3.2.3. Spirit Lifters Increase Enjoyment.* The focus group discussions revealed the importance of spirit lifters, in an exercise context, i.e., dimensions that could contribute to enjoyment and motivate older participants to continue to be active. These included *outdoor exercises; rhythm and music; exercise equipment*; and *humor*.

Outdoor activities were frequently highlighted as very motivating. Both women and men liked the idea of exercising outdoors. "*I like to be out there… perhaps because I have been sitting inside all… well quite a few years now… it's great to be able to be outdoors*" (W3). Many of the participants engaged in outdoor activities all year around, and some clearly expressed a dislike for exercises indoors. "*I had a gym card when I was employed… I went a few times but I do not get the point… biking indoors when you can bike outdoors and get fresh air?*" (M5). Many of the examples from the participants' outdoor activities referred to taking a walk, cycling, or cross-country skiing. However, at the beginning of the project strength and balance exercises were still mainly performed indoors and only a few participants could imagine doing these kinds of exercises outdoors. During the course of the study though, some of the participants became inspired by the discussions and started to add balance exercises during their regular walks. These participants could later on give examples of suitable ways to do this, which opened the eyes of the other participants to these possibilities.

Another spirit lifter discussed was the use of rhythm and music, which were perceived as engaging and thought of as providing a pleasant atmosphere. "*Yes, music, I like music! Absolutely! For me music is very important when exercising. I know that everyone does not like it, but I think the music means a lot*" (W6). Although the participants generally liked music during their exercises, they highlighted that the music had to be tailored to the participants' age, and the rhythm had to be in line with the exercises performed. Otherwise, the music became frustrating. "*Well, when I do water aerobics… it is often disco music… very rhythmic and the girls* (instructors) *are too darn good and move in time. But they are not in the water…and when I'm not able to do the movements…I become frustrated*" (M8).

The use of exercise equipment was considered effective and a motivating element in an exercise context. However, women often noted that they did not want to buy equipment to use in their own homes; it was better if they got tips on how to use things already available in a household. "*Not to buy a lot of things… I believe it is better to take what you have at hand*" (W1). Men on the other hand preferred specific equipment "*Yes, but those things can sometimes fit … have a better grip and such… it's fun with the real stuff*" (M1). The participants themselves also commented that the use of equipment might be gender related. Furthermore, the participants explained how the use of exercise equipment could contribute in the creation of a social exercise context. For example, both men and women liked to walk with poles and to meet peers who did the same, as this created a feeling of belonging to a group. "*It's nice when you walk with poles, when you go out for an ordinary walk, and you meet unknown people you just walk on, but with poles, then you say hello, it's like you belong to a group in a sense. I think that feels nice*" (M1).

Humor was emphasized as an important source of inspiration. The participants expressed that it should be joyful to exercise. Humor could involve having an instructor joking and teasing, or just giving yourself a chance to enjoy. An exercise session full of laughter and happiness could create a lingering contentment afterwards. "*Something I think is often overlooked is the importance of humor. I think it's very important that you get to laugh*" (M2).

*3.2.4. Personal Tricks Maintain Exercise Routines.* Several tricks or strategies were mentioned by participants to maintain their exercise routines and to prevent lapses and relapses. These tricks involved *companionship*; *routines and challenges*; *dogs and nature*; and *safety strategies*.

Friends or spouses could push each other "*When you are alone, then you have to put in an active effort to get going… it will be easier to find arguments against …-it looks like bad* *weather out there! or whatever*" (M1). Having company was also inspiring, "*So... well, she is the one who is pushing. And I think it is much, much nicer if we're together compared to if I am going out alone*" (M4).

The participants gave examples of having routines, such as specific tracks they walked, which helped them to exercise regularly. To set goals, as well as to start with one that felt achievable, was also proposed as a powerful way to get over the threshold when it felt difficult to start, because, once started, it was often easy to continue. "*It may feel tough in the beginning, but if I think, -Nah, but today I will just take a trip up to the road. Then suddenly, it feels pretty good after all, and I walk on and continue for about a full hour. And that feels great, although there were setbacks when I began*" (W9). A competitive element could also be an incentive for both men and women, but the vast majority created challenges solely for themselves. Other participants emphasized that they did not like competitive elements, "*That you are challenging yourself... I think that is just a pain... Then it becomes a must-do that should be avoided... I have done enough of that in my life*" (M4).

Dogs were mentioned as great helpers to maintenance exercise. "*Yes, we've had a dog, and I miss it immensely, for it was the best exercise help I ever had*" (M7). Several of the participants had a dog and felt this kept them active and provided some company. Some of the participants had even taken it upon themselves to go out with someone else's dog, just to get exercise. "*Therefore, I have an extra dog that I go out with... then I have to go out... and then I feel good*" (W3). Even without a dog the pure experience of nature itself could also be an incentive to go for walks. Feeling the freedom, enjoy listening to the birds, and getting fresh air were described as addictive.

Some participants, mainly women, expressed that a fear of falling could inhibit their activity. But they also gave examples of safety strategies they developed in order to feel more secure and thus gave them the confidence to continue their physical activities. One example discussed was walking with poles, to have support on slippery surfaces. Another example was to bring the mobile phone to be able to call someone if and accident should occur. "*Just that using a mobile phone... I always take it with me when I go out for a walk, even though I will not be long, especially if I you are somewhere where no one knows where you are*" (W6).

## 4. Discussion

These multistage focus group discussions aimed to improve our understanding of the preferences community-dwelling older women and men have regarding exercise in the context of preventing falls. Older participants had many diverse preferences and confirmed that individually tailored exercise programmes, in terms of mode, intensity, challenge, and social context, are important. Moreover, important factors for exercise adherence and maintenance included the experience of individual confirmation; different spirit lifters to increase enjoyment; and personal tricks to prevent lapses and relapses. It is interesting to note that no clear gender separation pattern was seen in the majority of these factors (Figure 1).

It may seem obvious that older people, just like younger people, have very different opinions on how they prefer to perform their exercises. But all too often, older adults seem to be considered as a homogenous group and recommended the same kind of training regardless of needs or preferences. Studies from Sweden have, as an example, shown that walking is by far the most suggested physical activity for older people getting exercise prescriptions in health care settings [24], although it is known that brisk walking will actually increase the fall risk in those with a history of falls [25]. Previous studies have also shown that when the prescribed exercises are not tailored to the individual, and seniors with varying degrees of physical capacity are expected to exercise together, they are frustrated and may drop out [26]. Our results emphasize the importance of taking the experiences and desires of the older individual into account when fall preventive exercises are planned and prescribed.

Previous research indicates that women are more likely to take part in exercise activities to prevent falls [8]; in light of our results that is not due to substantial differences in exercise preferences among women and men. However, a recent literature review suggests that both women and men see women as more receptive to and in more need of fall prevention messages [12]. This may be due to societal norms. Our understanding of gender derives from a social constructionist perspective that gender is created in social relations and dependent on time and context [27]. This means that humans, as social beings, shape themselves in relation to prevailing norms in society for how to be a man or a woman and this is referred to as "doing gender" [28]. According to the norms, men should be independent, self-reliant, strong, tough, and willing to take risks [29]. Physical strength, competition, and risk-taking are all characteristics in "hegemonic masculinity" [30]. These masculinity characteristics often preferred among younger men could have been deemphasized with ageing and a changed life situation among the men in this study. The men were retired, some were widowers, and others were carers for relatives. These circumstances may have contributed to the many similarities in preferences expressed by men and women in this study.

Some differences between men's and women's preferences for exercises were expressed in this study; for example, women talked about preserving health, whereas men wanted to keep fit; men preferred exercise equipment in training; men were more prone to emphasize the importance of quantified results as well as having visible secondary goals; women stressed the social component; and the women, but not men, expressed fear of falling as a barrier for exercise. The gendered patterns revealed in this study are not surprising, since they reflect the social gender norm. Nevertheless, these gender differences may be important for professionals to address when "marketing" exercises to prevent falls, in order to attract both men and women.

An understanding of how to support motivation in a specific situation requires an understanding of how activities and contexts are experienced by the older person. The Self-Determination Theory (SDT) is a social cognition model that addresses the process through which a person acquires motivation for initiating a new health-related behavior and maintains it over time [31]. According to SDT, maintenance of behaviors over time requires that the person internalizes the behavior in order to develop an intrinsic motivation. In this process of internalization the reinforcement of three innate psychological needs: autonomy, competence, and relatedness, is critical [32, 33]. For behaviors to be successfully changed and maintained individuals must come to personally endorse their importance and make an autonomous, intentional, and volitional decision to change. The person must also feel competent and confident enough to change. Finally, relatedness feelings of being included and cared for by others in the relevant context are important [32, 33]. These three innate needs are clearly reflected in the categories summarizing how the focus group participants described factors important for adherence and maintenance. By relating the results of this study to the support of psychological needs, we can gain an increased understanding of how to apply key motivating elements in fall prevention exercises for older people.

*4.1. Uptake.* The motives for starting to do exercises (uptake) expressed by the participants in this study were mainly framed in terms of inherently satisfying goals such as to preserve health and to treat injury or disease, which means the participants valued exercise highly and identified with the behavior. A focus on such intrinsic goals (e.g., being healthy) as opposed to extrinsic goals (e.g., being physically attractive) is believed to increase maintenance over time [32]. Receiving support and receiving adequate information were also cited as important factors for taking up exercise to prevent falls. All these motives are in accordance with previously reported preferences for falls prevention exercises [12] as well as for falls prevention programmes in general [6, 34].

The barriers cited as reasons for not participating in exercises were also consistent with previous studies, e.g., health problems or environmental barriers [12] and poor self-discipline and lack of motivation [26, 35]. However, in our previous review, an anxiety about not being able to keep up with demanding exercises was noticed in many articles [12]. In the present study the participants did not seem to worry about performing correctly at all times, as long as they felt assured by the instructor that doing as good as they could was good enough. On the other hand, feelings of vulnerability, such as fear of falling, or being the only man in a group, were expressed as barriers by the participants. According to the SDT one way to help individuals integrate and internalize a behavior is to support exploration of resistances and barriers and help in the identification of possible solutions [32].

*4.2. Adherence and Maintenance.* Based on the results of this study an individually tailored exercise program seems crucial to stimulate adherence and maintenance, which is in accordance with several previous studies [26, 35–38]. Support for the importance of individualization can also be found in the SDT, which suggests that autonomy and self-determination are supported when opportunities for reflection and choices are allowed. A strong sense of autonomy will, in turn, contribute to internalization of values and skills for change, leading to increased intrinsic motivation and consequently also improved exercise adherence [32, 33].

Those participants who were more accustomed to exercise seemed to prefer training programmes, while the more inexperienced felt that an integrated exercise, into their daily life activities, suited them better. These results seem to conform well with the results of a previous study, who described their moderately active participants as “functional exercisers” who favored activities perceived as purposeful and practical, often unplanned and low in intensity [39]. Such integrated exercises, where balance and strength training are integrated in activities of everyday routines, have been proven effective in protecting older high risk people from falling and in improving and maintaining their functional capacity [40]. It may be a promising alternative to traditional exercise programmes for many older people who are not used to exercising or who do not want to exercise in a group. Earlier studies have suggested that low intensity exercises may facilitate participation [6]. However, the participants in this group expressed preferences for both “calm” and “intense” exercise, again reminding us of the need to consider individual preferences.

The importance of social interaction, and group adherence, is often found to be an important factor to enhance participation in exercise among older people [6, 12]. According to the SDT social interaction will naturally contribute to feelings of relatedness, which is important for intrinsic motivation to develop [33]. Social interaction was emphasized as important by some in this study, in particular by women in their own persona descriptions, while some of the participants preferred to exercise alone. Similar findings have been found in a previous study from the UK, in which more women than men were likely to attend group sessions [41]. In another study comparing exercise habits in older people in Sweden and Ireland, the Swedish participants tended to have a higher regard for solitary exercise in comparison to older persons from Ireland, where physical activity was often seen as a means to socialize [39].

To receive confirmation of being able to exercise and that one’s efforts actually give results was expressed as a very important element in an inspiring exercise context. Confirmation could be seen through visible results of practical activities, by assessment and evaluation of performance, or simply by feelings of achievement. Confirmation could also be obtained through feedback from a professional instructor who offers help to find the optimal exercise and conveys knowledge and confidence that the exercises performed are safe and effective. The characteristics of the instructor may play a role in influencing participants’ attendance to exercise classes [42] and advisory support has previously been raised as important to strengthen participants’ self-efficacy [43]. According to Bandura, the experience of mastery is the most important factor determining a person’s self-efficacy, and in general people with high self-efficacy are more determined and persist longer than those with low self-efficacy [44]. In a particular activity confirmation may contribute to feelings of mastery or competence, which, according to the SDT, is important for successful behavior change [32, 33].

The participants in this study gave several examples of elements in the exercise they thought of as spirit lifters. These elements had the ability to provide energy and joy to the training and bring feelings of both vitality and relatedness. Outdoor activities were such spirit lifters. Recurrent preferences for outdoor exercises among Swedish seniors of all lifestyle categories have previously been reported [39, 45]. The importance of being outdoors and in contact with nature has been reported to enhance energy and induce greater vitality even when controlling for factors such as social interaction [46]. Maybe being outdoors could also contribute to important feelings of relatedness to the nature. Other spirit lifters mentioned by the participants were rhythm and music, exercise equipment, and humor. We believe all these elements may contribute to feelings of relatedness by creating a social context and building a bond between participants. However, feelings of relatedness were also seen in those who exercised alone. One example of this was how the use of walking poles created a sense of belongingness to a group of pole-walkers.

*4.3. Methodological Considerations.* A strength of this study was the design with multistage focus group discussions [14], which gave rich data through the process of meeting with community-dwelling participants on several occasions. The participants had the opportunity to reflect upon their exercise preferences, both during the focus group discussions and in between the sessions. It was sometimes difficult to know if the participants talked about physical activity in general, or about falls prevention in particular. However, all participants were aware that the study focused on exercise in the context of preventing falls and this was emphasized by the researchers during the discussions.

Another strength was the use of the PAAR methodology [17]. By encouraging informants to express themselves in a positive way, it has the potential to generate rich data about perceptions, feelings, experiences, motives, and attitudes. On the other hand, this appreciative approach may potentially result in an underestimation of negative thoughts and experiences, which might also be of importance. We believe that the appreciative approach of the PAAR methodology contributed to the friendly and positive atmosphere during the workshops. The attendance rate at all workshops was very high and the participants expressed that they liked coming to the meetings.

Yet another strength in this study was the sampling strategy, which gave variation in history of falls and experience of exercise in both men and women in each group. However, the transferability of the findings may be limited because most of the participants were retired white-collar workers, were in general well educated, and were mainly resource-rich with previous occupational experiences. Class differences in our study group were minor, which could have contributed to the similarity in exercise preferences. It should also be noted that participants in our study had enrolled in a fall preventive study with focus on exercising and thus shared a motivation for exercise. In this respect a similar interest may had a stronger influence than gender on the results.

The researchers involved were from different fields of expertise, physiotherapy, informatics, exercise physiology, and computing sciences, which enhanced both data collection and analysis [47]. The researchers brought experience from different methods and facilitating techniques that were applied during the workshops. The mix of methods helped the participants share their thoughts and contribute in various ways, which greatly enriched the data collection. Moreover, the author's diverse preunderstandings regarding falls prevention, balance and strength exercises, motivation for exercise, and gender research complemented each other and helped deepen the discussions within the author group, and thus the interpretation and analysis of the data.

The cultural context of the study could affect the generalizability of the results. As norms for how to be a man and a woman differ by age and cultural context, analysis of gender in older men and women needs to consider the wider context of norms for "being old" in the respective time and culture. In Sweden, older people are encouraged to stay active in order to avoid ill health. Investigations using accelerometers have shown that 49% between 65 and 75 years are physically active with a moderate or high intensity for at least 30 minutes during an average day, with very small gender differences [45]. The project was carried out in Umeå, Northern Sweden (latitude 63°N), where snow and icy roads are common in the winter period of November to April. Nature/forest is easily accessible, both in terms of walkability and of "legal rights" to walk everywhere/of public access. The results may thus not be generalizable to countries where the cultural norm of exercise, the gender norm, and attitudes to outdoor activities in old age differ.

## 5. Conclusions

Older people's preferences for exercise programmes are personal, and the individual differences are greater than the differences between men and women. Individually tailored exercise, in terms of mode, intensity, challenge, and social context, is important. In order to enhance uptake, adherence, and maintenance in fall prevention exercise professionals need to *see* the individual older person and apply autonomy-supportive approaches to encourage growth of intrinsic motivation. Besides individually tailored exercises such approaches should, according to older men and women, provide confirmational feelings, different spirit lifters to increase enjoyment, and personal tricks to maintain exercise routines. The study provides an awareness about women's and men's preferences for fall prevention exercises and this information could be used as guidance in designing individual tailored interventions that are inclusive, hence providing uptake and adherence for both sexes.

## Data Availability

The interview data used to support the findings of this study are restricted by the Regional Ethical Review Board Umeå, Sweden, in order to protect patient privacy. Data are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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*Research Article*

# Predicting the Future Need of Walking Device or Assistance by Moderate to Vigorous Physical Activity: A 2-Year Prospective Study of Women Aged 75 Years and Above

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*Objective*. To examine the association between daily moderate to vigorous physical activity (MVPA) and the change in mobility function among community-dwelling Japanese women aged 75 years and above. *Methods*. This prospective study included 330 older women aged 75 years and above who could walk without a walking device or assistance. MVPA and light-intensity physical activity (LPA) were assessed using an accelerometer for seven consecutive days. MVPA was defined as an activity with an intensity of >3 metabolic equivalents. The study outcome was a change in mobility function, defined as the need of walking device or assistance, during the two-year period. *Results*. The results of the logistic regression analysis showed that MVPA was inversely associated with a decline in mobility function after controlling for LPA and potential confounders (adjusted odds ratio (OR) = 0.93 per 1 min/d, 95% confidence interval (CI) = 0.88–0.99; $P = 0.017$), whereas LPA was not when adjusted for MVPA and confounders (adjusted OR = 0.99 per 1 min/d, 95% CI = 0.96–1.01; $P = 0.245$). The receiver operating characteristics analysis identified a 7.9 min/d of MVPA as the cut-off value. *Conclusions*. The results of this study suggest the importance of promoting daily MVPA for preventing mobility limitation in older women aged 75 years and above.

## 1. Introduction

Declined mobility function results in disability, mortality, and increased healthcare costs in old age [1]. In particular, the early detection and prevention of declining mobility function are important among older women aged 75 years and above because of a higher prevalence of physical frailty compared to younger elderly or men [2]. Additionally, risk of incident of disability is higher in older women compared to men [3].

Physical activity (PA) is a modifiable risk factor associated with the onset of slow gait and disability in old age [4], and the causal relationship of increased PA with reduced risk of mobility limitation has been demonstrated in older people through randomized controlled trial [5]. Therefore, promoting PA is a key intervention to maintain mobility function in old age. However, despite the importance of PA, there is a lack of evidence regarding the relationship between PA and mobility function in older people aged 75 years and above [6].

Moderate to vigorous PA (MVPA), generally defined as an activity with an intensity of >3 metabolic equivalents (METs) such as brisk walking and aerobics [7], has favorable effects on muscle mass [8, 9], falling [10], and mortality [11] in older people. A recent prospective study demonstrated that higher-intensity exercise is associated with fewer disabilities, whereas duration of exercise was not after adjusting for exercise duration [12], suggesting that MVPA may contribute to preserving mobility function in old age. However, this study assessed PA using a questionnaire and also did not consider the influences of potential confounding factors such as muscle strength or depression. Painful joint is another factor that affects PA in older individuals [13]. Therefore, objective measurement of MVPA and adjustment of confounders are needed for evidence regarding the favorable effects of MVPA in old age.

We previously reported the inverse relationship between objectively measured MVPA and slow gait in community-dwelling older women, and a significant relationship was observed even when adjusted for potential confounders [6]. Another recent study on subjects aged 65 years and above also reported that objectively measured moderate-intensity PA is an independent factor of physical performance parameters [14]. However, due to the cross-sectional design, the relationship of MVPA with a change in mobility function was not examined by these studies. Therefore, the present study aimed to examine (1) the relationship between objectively measured MVPA and the future need of walking device or assistance and (2) the cut-off value of MVPA to predict this study outcome in Japanese community-dwelling older women by a prospective design.

## 2. Methods

*2.1. Study Population and Design.* This is a prospective cohort study performed as part of a cohort study conducted in our laboratory at the Graduate School of Medicine, Nagoya University, Japan. The inclusion criterion of the main cohort study was community-dwelling older people aged 75 years and above. Exclusion criterion was those who were not able to access a health checkup at Nagoya University Daiko Campus from their homes. The volunteer participants were recruited from senior citizen's clubs in Nagoya city and registered to the Research of Health Promotion at Nagoya University. The registered participants were invited for a health examination via mail every two years, and all of them provided written informed consent to participate in the study. The present study included older women aged 75 years and above who participated in the health examination in 2012 or 2013 and could walk independently without any walking devices. Participants who were lost to follow-up were also excluded. The study protocol was approved by the Ethics Committee of the School of Health Sciences at Nagoya University (approval number 2012-0131). Two years after the baseline survey was conducted, each participant was further monitored to assess the need for a walking device or assistance in daily living.

*2.2. Study Outcome.* The study outcome was a change in mobility function, which was assessed by follow-up survey of the main cohort study or through telephonic interviews. The study outcome was defined as either the inability to walk without a walking device in daily life or the inability to go out alone because of a health or physical problem. In general, a mobility limitation is defined according to difficulty in walking a certain distance (e.g., 400 m or one-fourth of a mile) or climbing stairs without resting [15]. However, study participants in our study were aged 75 years and above who might have decreased cognitive or executive function. Therefore, we avoided asking the distance that they could walk because it was not likely to be reliable.

*2.3. Measurement of Physical Activity.* To avoid seasonal effects, PA was measured in autumn (September to November) using a uniaxial accelerometer (Kenz Lifecorder, Suzuken Co., Ltd., Nagoya, Japan). The device records step counts and intensity of PA. The intensity of PA was categorized into 11 levels (0, 0.5, 1-9) based on the recorded acceleration pattern.

A previous study that assessed the relationship between the accelerometer levels and METs determined using objectively measured oxygen consumption during walking on a treadmill revealed that an accelerometer level >4 corresponded to >3 METs [16]. Taking this result, PA with an accelerometer level >4 from this device has been widely used to categorize MVPA in both middle-aged and older adults [17–19]. An intensity level of 0 meant no movement and that of 0.5 signified slight body or arm movement, such as deskwork. Therefore, PA with an accelerometer level of 1 to 3 was defined as light-intensity PA (LPA).

Participants were instructed to wear the accelerometers around the waist for seven consecutive days, except during bathing, swimming, and sleeping. Additionally, participants were instructed to continue their normal activities of daily living during the measurement period and were blinded to their PA.

A valid day for analysis was defined as 10 or more h/d of monitor wear [20]. The wear time was determined by subtracting the nonwear time (an interval of at least 20 consecutive minutes of zero activity intensity) from 24 h [20]. The mean durations of MVPA and LPA per day were calculated using five or more valid days [21]. Data from participants with four or less valid days were regarded as missing data.

*2.4. Demographic Characteristics.* Data on age and comorbidities of each participant were collected using a self-administered questionnaire. Body mass index was calculated as body weight (kg) divided by the square of height (m). The number of prescribed medications was counted for each participant by checking their prescriptions. Self-reported pain in the back or leg was also assessed as "none," "rarely," "sometimes," or "always." Presence of pain for data analysis purposes was defined as feeling pain "sometimes" or "always" with reference to a previous study [13].

*2.5. Other Covariates.* Grip strength was assessed as the representative indicator of muscle strength using a Jamar hydraulic dynamometer (Sammons Preston, USA) set at the second handle position. Grip strength of each participant was measured by trained physical therapist. The participants sat with the wrist in a neutral position and the elbow flexed at 90° [22]. Two trials were completed for each hand and the strongest value was used for the analysis [23]. In our previous study, grip strength was an independent associated factor of slow gait in older women aged 75 years and above [6]. Executive function was assessed using the Trail

Making Test (TMT) [24]. TMT is a visual task to connect circles by drawing a line from one point to the next as quickly as possible, in numerical order (TMT-A), and in alternating between both numerical and Japanese-character order (TMT-B). The time to finish TMT-B minus that to finish TMT-A (ΔTMT) was calculated. The ΔTMT score is used for controlling the effect of motor speed on TMT performance and is considered a more accurate measure of executive functions than TMT-B alone [25]. The ΔTMT has also been reported to be correlated with walking performance in Japanese older people [26]. Depression was assessed using the 5-item Geriatric Depression Scale (GDS-5) which is a questionnaire that assesses depression symptoms using five items, and a score of ≥2 points is defined as depression [27]. Depression assessed using GDS-5 was also associated with slow gait in older women [6].

*2.6. Statistical Analyses.* Characteristics of the participants with and without a decline in mobility function were compared by the Mann–Whitney U test or chi-square test. Then logistic regression analysis was performed to examine the relationship between the study outcome and MVPA or LPA. In this analysis, variables that showed a $P$-value of < 0.1 in the univariate analysis were used as independent variables.

In baseline data, missing values were observed in several variables. The logistic regression analysis was first performed only for participants without missing data. Then, to avoid bias associated with excluding missing data, the logistic regression analysis was performed for all participants as a sensitivity analysis. Missing values were imputed using the median for continuous variables and the most frequent category for categorical variables from the available data.

Finally, if MVPA was independently associated with a decline in mobility function, receiver operating characteristic (ROC) curve analysis was conducted to identify the possible cut-off value of MVPA. The ROC curve was constructed by plotting sensitivity against 1-specificity, and cut-off value was selected by optimizing the sensitivity-specificity relationship.

All statistical analyses were performed using the STATA version 14 software package (SPSS Inc., Chicago, IL, USA), and a $P$-value < 0.05 was considered statistically significant.

## 3. Results

Of all the 345 older women who could walk without a walking device at baseline, 330 participants who were successfully monitored were enrolled in the analysis (Figure 1). During the two years after the baseline survey, 37 participants (11.2%) newly required walking device or assistance in their daily living. Detailed information about study outcome was shown in Table 1.

Participant characteristics and comparisons of the measured variables between those with and without the study outcome are shown in Table 2. Of the 330 participants analyzed in this study, 300 participants provided PA measurement for five or more valid days (seven days, n = 161; six days, n = 130; five days, n = 9). Participants who required walking device or assistance after two years were older ($P < 0.001$) and used more prescribed medications ($P = 0.005$), had weaker grip strength ($P < 0.001$), and had longer ΔTMT ($P = 0.002$) compared to those who did not experience the study outcome. Participants who experienced the study outcome also showed shorter duration of daily MVPA ($P < 0.001$) and LPA ($P = 0.002$) and tended to have a higher prevalence of depression at baseline survey compared to those without study outcome ($P = 0.078$).

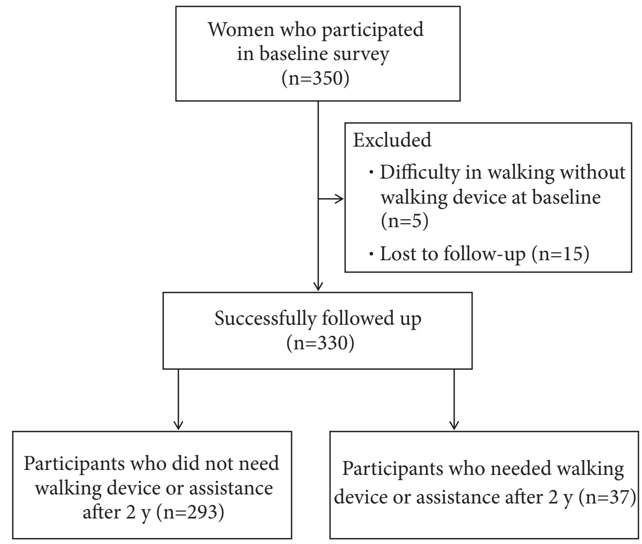


Figure 1: Flow diagram of the study participants.

Results of logistic regression analysis using complete data are shown in Table 3. MVPA and LPA were inversely and significantly associated with the need of walking device or assistance after controlling for potential confounding factors (MVPA: adjusted odds ratio (OR) = 0.92 per 1 min/d, 95% confidence interval (CI) = 0.87-0.97; $P = 0.004$, LPA: adjusted OR = 0.97 per 1 min/d, 95% CI = 0.95-0.99; $P = 0.023$). The significant relationship between MVPA and study outcome remained after further adjusting for LPA (adjusted OR = 0.93 per 1 min/d, 95% CI = 0.88-0.99; $P = 0.017$), but LPA was not after adjusting for MVPA (adjusted OR = 0.99 per 1 min/d, 95% CI = 0.96-1.01; $P = 0.245$). The sensitivity analysis, including all participants, also showed the inverse and independent relationship between increased MVPA and study outcome (Table 4).

The ROC curve analysis, using a change in mobility function as an outcome, identified a 7.9 min/d of MVPA as the optimal predictive value, with a sensitivity of 72.4% and a specificity of 74.3%; the AUC was 0.773 (95% CI = 0.666-0.881; $P < 0.001$) (Figure 2).

## 4. Discussion

The main finding of this study was that duration of daily MVPA predicted the change in mobility function, defined as the future need of walking device or assistance, in community-dwelling women aged 75 years and above, even after controlling for potential confounders. Our results suggest that MVPA plays a key role in maintaining mobility function in this population.

Table 1: Detail information about study outcome.

| | Number of participants who newly required walking device or assistance after 2 years | |
|---|---|---|
| | In a house | Outside |
| Need of walking device | 16 | 28 |
| Need of assistance for walking | 10 | 20 |

Table 2: Characteristics of the study participants and comparison of characteristics of those with and without the study outcome.

| Variables | Overall (N = 330) | n | Participants who did not need walking device and assistance (n = 293) | n | Participants who newly required walking device or assistance (n = 37) | n | $P$ |
|---|---|---|---|---|---|---|---|
| Age, years | 79 [77-82] | 330 | 79 [77-82] | 293 | 83 [78-85] | 37 | <0.001 |
| BMI, kg/m$^2$ | 21.6 [19.6-23.9] | 330 | 21.6 [19.7-24.0] | 293 | 21.6 [18.3-23.2] | 37 | 0.243 |
| Hypertension, n (%) | 168 (50.9) | 330 | 149 (45.2) | 293 | 19 (51.4) | 37 | 0.938 |
| Diabetes, n (%) | 47 (14.2) | 330 | 41 (14.0) | 293 | 6 (16.2) | 37 | 0.685 |
| Dyslipidemia, n (%) | 147 (44.5) | 330 | 135 (46.1) | 293 | 12 (32.4) | 37 | 0.118 |
| Stroke, n (%) | 14 (4.2) | 330 | 12 (4.1) | 293 | 2 (5.4) | 37 | 0.669 |
| Heart disease, n (%) | 28 (8.5) | 330 | 23 (7.8) | 293 | 5 (13.5) | 37 | 0.235 |
| Prescribed medication, number | 1 [1-4] | 330 | 1 [1-4] | 293 | 4 [1-6] | 37 | 0.005 |
| Pain, n (%) | 83 (25.2) | 330 | 70 (24.0) | 293 | 13 (35.1) | 37 | 0.141 |
| Grip strength, kg | 20 [18-22] | 327 | 20 [18-23] | 291 | 18 [16-20] | 36 | <0.001 |
| ΔTMT, sec | 78.0 [57.0-125.7] | 327 | 75.8 [54.2-117.1] | 291 | 126.3 [74.5-188.2] | 36 | 0.002 |
| Depression, n (%) | 55 (16.7) | 328 | 45 (15.3) | 291 | 10 (27.0) | 37 | 0.078 |
| MVPA | 13.8 [6.3-24.0] | 300 | 14.6 [7.7-24.7] | 269 | 2.1 [0.5-10.7] | 31 | <0.001 |
| LPA | 50.5 [39.1-63.4] | 300 | 51.2 [40.3-63.9] | 269 | 39.3 [22.6-51.7] | 31 | 0.002 |

Continuous variables are shown by median [interquartile range]. BMI, body mass index; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; and LPA, light-intensity physical activity.

In this study, 37 of the 330 participants (11.2%) required the walking device or assistance during the subsequent two years and this study outcome was inversely associated with objectively measured MVPA at baseline. A previous study in older Japanese men and women aged 65 years and above reported that 3.9% of the study participants had incident disability, defined as the care-needs certification in the national long-term care insurance system of Japan, during the two-year period [28]. Although the definitions of study outcome are different, inclusion of older women aged 75 years and above in the present study may result in a relatively high ratio of incident of change in mobility function.

The association between PA in old age and onset of disability has been well documented by observational study [29]. The effects of the intervention based on promoting moderate-intensity PA on reduced risk of mobility limitation have also been shown by a large-scale randomized controlled trial [5]. However, there is little evidence to build robust recommendations for promoting MVPA in older people aged 75 years and above. To this end, we performed a prospective cohort study to examine the relationship of MVPA with a change in mobility function in this population. In our study, daily MVPA was inversely associated with the future need of walking device or assistance after controlling for potential confounding factors. In contrast, LPA was not associated with study outcome, implying the importance of daily MVPA for preserving mobility function.

The ROC curve analysis identified a 7.9 min/d of daily MVPA as a cut-off value for predicting decline in mobility function. This amount is less than 150 min/wk recommended by the World Health Organization [30]; however, the minimum amount of MVPA may differ from population to population. A previous longitudinal study implied that ≥ 15 min/d of MVPA was associated with lower probability of losing muscle mass over 5 years in older people aged 65 years and above [8]. Another cross-sectional study in women aged 60 years and above demonstrated that 107.4 min/d was a cut-off value for predicting mobility limitation [31]. From our results, approximately 60 min/wk may be a target amount of MVPA at which health gains in individuals aged 75

Table 3: Results of the logistic regression analysis in participants with complete data (n=300).

| | Model 1 | | | Model 2 | | | Model 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* | OR | 95% CI | *P* | OR | 95% CI | *P* |
| Age, per 1 year | 1.16 | [1.03-1.31] | 0.016 | 1.15 | [1.03-1.30] | 0.014 | 1.14 | [1.01-1.29] | 0.032 |
| Prescribed medications, per 1 medication | 1.09 | [0.95-1.26] | 0.213 | 1.12 | [0.98-1.28] | 0.089 | 1.09 | [0.95-1.25] | 0.197 |
| Grip strength, per 1 kg | 0.93 | [0.82-1.06] | 0.279 | 0.91 | [0.80-1.03] | 0.141 | 0.91 | [0.81-1.05] | 0.213 |
| ΔTMT, per 1 sec | 1.00 | [0.99-1.01] | 0.107 | 1.00 | [0.99-1.01] | 0.189 | 1.00 | [0.99-1.01] | 0.153 |
| Depression, yes | 1.55 | [0.56-4.25] | 0.397 | 1.75 | [0.65-4.73] | 0.271 | 1.56 | [0.56-4.31] | 0.390 |
| MVPA, per 1 min/d | 0.92 | [0.87-0.97] | 0.004 | | - | | 0.93 | [0.88-0.99] | 0.017 |
| LPA, per 1 min/d | | - | | 0.97 | [0.95-0.99] | 0.023 | 0.99 | [0.96-1.01] | 0.245 |

Dependent variable: need of walking device or assistance; OR, odds ratio; CI, confidence interval; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; and LPA, light-intensity physical activity.

Table 4: Results of the logistic regression analysis including all participants (n = 330).

| | Model 1 | | | Model 2 | | | Model 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* | OR | 95% CI | *P* | OR | 95% CI | *P* |
| Age, per 1 year | 1.13 | [1.02-1.27] | 0.018 | 1.14 | [1.02-1.26] | 0.016 | 1.13 | [1.01-1.25] | 0.032 |
| Prescribed medications, per 1 medication | 1.09 | [0.97-1.23] | 0.136 | 1.12 | [0.99-1.26] | 0.053 | 1.10 | [0.97-1.24] | 0.126 |
| Grip strength, per 1 kg | 0.91 | [0.81-1.01] | 0.081 | 0.89 | [0.79-0.99] | 0.041 | 0.89 | [0.80-1.00] | 0.059 |
| ΔTMT, per 1 sec | 1.01 | [1.00-1.01] | 0.011 | 1.00 | [1.00-1.01] | 0.026 | 1.01 | [1.00-1.01] | 0.017 |
| Depression, yes | 1.33 | [0.54-3.26] | 0.534 | 1.43 | [0.59-3.47] | 0.431 | 1.33 | [0.54-3.26] | 0.535 |
| MVPA, per 1 min/d | 0.93 | [0.89-0.98] | 0.004 | | - | | 0.94 | [0.90-0.99] | 0.017 |
| LPA, per 1 min/d | | - | | 0.97 | [0.95-0.99] | 0.030 | 0.99 | [0.96-1.01] | 0.255 |

Dependent variable: need of walking device or assistance; OR, odds ratio; CI, confidence interval; TMT, Trail Making Test; MVPA, moderate to vigorous physical activity; and LPA, light-intensity physical activity.

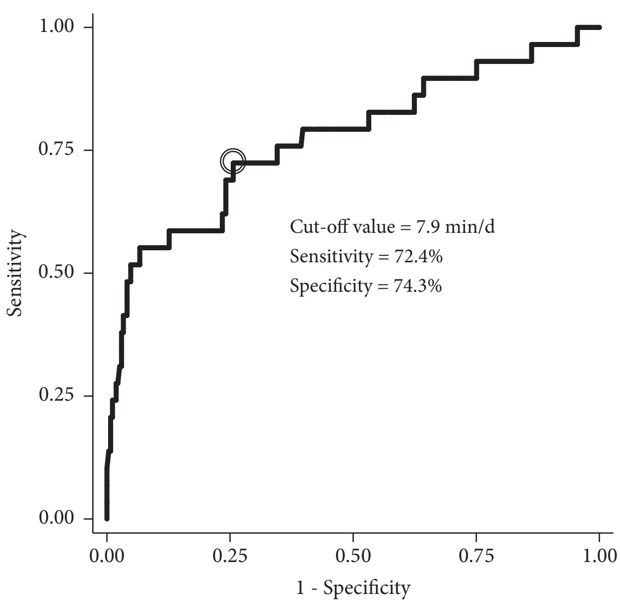


Figure 2: Receiver operating characteristic curve to predict the need of walking device or assistance using moderate to vigorous physical activity. Area under the curve was 0.773 (95% CI: 0.666-0.881).

years and above. Further studies are needed to examine the generalizability of our results because of the inclusion of healthier participants in this study.

Increased MVPA resulted in a reduced risk of the need of walking device or assistance due to several possible mechanisms. First, daily MVPA may maintain mobility function through preserving muscle mass and strength that declines with aging and becomes a determinant of mobility function [32]. A previous cohort study reported that objectively measured MVPA had a negative correlation with loss of lean body mass in older people [8]. A more recent cohort study showed that a higher amount of self-reported MVPA was related to reduce risk of sarcopenia [9]. The effect of PA on peripheral nerve function is another possible mechanism. It has been reported that long-term moderate- to high-intensity brisk walking improves peripheral nerve function in diabetic patients [33]. Considering the relationship between peripheral nerve function and walking ability [34], daily MVPA is likely to affect mobility function via peripheral nerve function.

Furthermore, a lack of social participation due to physical inactivity has a possibility of playing a role in declined mobility function. A previous longitudinal study reported that social participation outside the home was inversely related to onset and progression of disability [35]. Because moderate-intensity activity but not light intensity is related to life-space mobility that refers to the area a person moves through in daily life in older individuals [36], decreased MVPA could lead to a negative cycle of reduced life-space mobility and social participation and in turn to decline in mobility function.

The study has several limitations that should be discussed. First, the study participants voluntarily participated in the main cohort study. Added to this, they were recruited at senior citizen's clubs, potentially causing selection bias. This may limit the generalization of our findings to frailer or physically disabled participants. As noted before, generalizability should be examined by further study. Second, although the participants were blind to their PA during the measurement period and were instructed to continue their normal activity, wearing accelerometer might have stimulated their PA. Hence, the amount of walking activity might be overestimated, possibly affecting the cut-off value of MVPA identified by the ROC analysis. Third, there may be other unknown confounding factors such as level of education or living circumstance. Finally, the causal relationship should be confirmed by an interventional study. Nevertheless, the present study has clinical significance in terms of implying a preventive effect of MVPA on change in mobility function in women aged 75 years and above.

## 5. Conclusions

In this prospective study, we examined the association between daily MVPA and change in mobility function among community-dwelling older women aged 75 years and above. The results showed that objectively measured MVPA predicted the future need of walking device or assistance, independent of LPA and other potential confounders. In contrast, LPA was not related to the study outcome when controlling for MVPA and other confounding factors. Our results indicate that 60 min/wk can be appropriate amount of MVPA for the target population due to the small sample size.

## Data Availability

All relevant data are within the paper.

## Conflicts of Interest

No potential conflicts of interest were disclosed.

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