EFFECT OF A COMLEX EXERCISE PROGRAMME ON POSTURAL BALANCE, ENDURANCE AND FALLS IN WOMEN WITH ESTABLISHED OSTEOPOROSIS

PhD Thesis

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I . **Mikó I**, Szerb I. Komplex mozgásprogram hatásának kontrollált vizsgálata törésen átesett postmenopauzás, osteoporotikus nők állóképességére, esési gyakoriságára. Osteológiai Közlemények 2013; 21: 78-83.

II. **Mikó I**, Szerb I, Szerb A, Poór Gy. Effectiveness of balance training programme in reducing the frequency of falling in established osteoporotic women: A randomized controlled trial. Clin Rehabil 2017; 31: 217-224. **IF: 2,823**

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LIST OF ABBREVIATIONS

BBS	Berg Balance Scale
BMD	bone mineral density
BMI	body mass index
B220+	CD45 isoform
CD3+	cluster of differentiation 3+
CD56+	cluster of differentiation 56+
CI	confidence interval
CONSORT	CONsolidated Standards of Reporting Trials
CP	centre of pressure
DXA	dual-energy X-ray absorptiometry
EBM	evidence-based medicine
ECG	electrocardiograph
FEV1	forced expiratory volume in 1 second
FET	forced expiratory time
FRAX	fracture risk assessment tool
FVC	forced vital capacity
IFN-γ	interferon gamma
IGF-1	insulin-like growth factor 1
IgM	immunglobulin M
IL-1	interleukin-1
IL-6	interleukin-6
IL-7	interleukin-7
IL-17	interleukin-17
IV	intravenous

LRP5	low-density lipoprotein receptor related protein 5
M-CSF	macrophage colony-stimulating factor
MET	metabolic equivalent
MMF	mean maximal flow
NF- κB	nuclear factor kappa-light-chain-enhancer of activated B cells
OCP	osteoclast precursor
ODM	osteodensitometry
OPG	osteoprotegerin
p53	phosphoprotein p53
PGE	prostaglandin E
PRT	progressive resistance training
PTH	parathyroid hormone
RANK	receptor activator of nuclear factor-κB
RANKL	receptor activator of nuclear factor-κB ligand
RCT	randomized controlled trial
ROS	reactive oxygen species
TNF-α	tumor necrosis factor alpha
TGF- β	transforming growth factor beta
TUG	Timed „Up &Go" Test
SC	subcutaneous
SD	standard deviation
SOST	sclerostin
VC	vital capacity
VO2	oxygen consumption
W	watt

WHO	World Health Organization

CLINICAL OVERVIEW OF OSTEOPOROSIS

Definition

Osteoporosis has been defined as a skeletal disorder of reduced bone strength that leads to an increased risk of fracture, typically with a relatively low level of trauma such as a fall from standing height (1). Osteoporosis can be divided into primary types attached to evolutionary processes, and secondary types developing in consequence of other illnesses. Within involutionary osteoporosis we can distinguish between postmenopausal cases and senile forms starting from the ages of 65 to 70. In its pathomechanism, remodelling – i.e. an upset in the balance of osteoblast-mediated bone formation and osteoclast-mediated bone resorption – plays the main role. The RANKL/OPG cytokine system – both in primary and secondary manifestations – plays a determining role in the defective coupling of osteoblasts and osteoclasts.

The development of critical bone mass for bone fracture is affected by the peak bone mass in youth and the speed of bone loss. Fifty to eighty per cent of the peak bone mass, which develops between the ages of 20 and 30 years is genetically determined. Studies found several genetic variants, which are related to bone mass, including LRP5, OPG, SOST, oestrogen receptor 1, and the RANK pathway genes (2). In addition to these, certain epigenetic factors (e.g. low weight at birth, inactive lifestyle, late puberty, lower than required calcium intake) may contribute to the individual not reaching his or her genetically encoded highest bone mass. Research relating to the metabolism of the bone shows that, due to a fall in the speed of bone building, the slow phase of bone loss may begin as early as in the third decade. At this point, bone resorption does not yet increase. This process is independent of sex hormones, it is likely to be a consequence of oxidative stress affecting bone cells (3, 4).

Significant changes start at around the time of the onset of the menopause. According to current information, postmenopausal osteoporosis is a compelling example of the close dialogue that exists between the bone, the immune system and the endocrine system. The lack of oestrogen developing in menopause results in a significant change in both the bone and the immune system. The immune system responds to reduced oestrogen levels with an increased production of cytokines and mediators (IFN- γ, M-CSF, TNF-α, IL-1, IL-6 and IL-7, PGE, ROS); at the same time, these inflammatory factors are molecules which also play a key role

in the development of osteoporosis. Their multiplication, with an increased osteoclast activity, results in bone resorption (a 90% fall in the level of oestrogen leads to rapid bone loss which lasts for approximately 5 years and may result in as much as a 3% annual bone loss), and additionally in oestrogen deficiency TGF-β, IGF-1 cytokines, OPG and type I collagen expression decrease. Based on the latest osteoimmunological observations, in postmenopausal osteoporosis lymphocyte subsets CD3+ and CD56+ T – which were demonstrated in large quantities in postmenopausal woman's peripheral blood – and B220+ IgM-B lymphocyte precursors – which develop into osteoclast precursors in response to certain stimuli and produce proinflammatory cytokines – may be responsible for significant TNF-α production levels. Today primarily enhanced TNF-α production by activated T lymphocytes is seen as the main driver for the development of oestrogen-deficient postmenopausal osteoporosis (5).

Osteoporosis in old age is characterised by a slow, life-long process of bone loss (0.5 to 1% annually). A shared profile can be observed regarding both immunosenescence and osteoporosis. The multiplication of inflammatory cytokines observed with ageing is due to the chronic activation of both macrophages and memory/effector T cells, while a reduced Treg function also plays a part in this process. One particular finding apparent in immunnosenescence is the multiplication of senescent memory cells, which release both RANKL and secrete osteo-clastogenic cytokines; these tend to be TNF-α, IL-1, IL-6 and IL-17. These cytokines can facilitate OCP expansion, which, in turn, increases systemic inflammation as a result of an increased production of additional proinflammatory factors, which are capable of recruiting other inflammatory cells, and thus maintain the vicious circle. The increase in the transcriptional activity of NF-kB as a result of genotoxic, inflammatory and oxidative stresses occurring in ageing, combined with chronic activation generated by the age-related progressive depletion of telomere length, leads to diminished OB proliferation and the development of osteoporosis (5). Bone loss can be equally observed in the trabecular and cortical bones. With the progress of age cortical bone loss becomes more prevalent (6).

Epidemiology

As regards the *epidemiology* of the illness, based on representative densitometric screening tests, in the United States (USA) 30% of postmenopausal women's BMD values fall within the range of osteoporosis (7). In relation to the entire population, osteoporosis is

prevalent in 9 to 15% of civilised societies, which means some 75 million patients in the United States, Europe and Japan in total at present. Over the next decade, there will be a 26.8% increase in the prevalent cases of osteoporosis in nine countries (USA, France, Germany, Italy, Spain, United Kingdom, Japan, India, China). In 2012, there were 164 million prevalent cases of osteoporosis in the nine countries, with more than 100 million cases in India and China. GlobalData epidemiologists forecast that there will be 208 million prevalent cases in the nine countries by 2022, with 142 million cases in India and China (8). In Hungary epidemiological analyses regarding populations over the age of fifty estimate over 900,000 prevalent cases of osteoporosis; some two thirds of them occur in women. The domestic population's bone density values are among the lowest European averages found in the European Vertebral Osteoporosis Study (3**).** The number of vertebral fractures and lower arm fractures occurring in Hungary in consequence of osteoporosis is not known precisely; annual occurrences are estimated to be around 40,000. The number of hip femoral fractures which fundamentally affect the illness's mortality rate stands at around 14,000 to 15,000 in Hungary, with 80% of these occurring in populations over the age of 50, primarily in osteoporotic individuals (9). Its frequency in individuals over the age seventy increases steeply, and it is more prevalent among women, which is also due to their longer lifespan. There are similar fracture frequency data in Europe, with a north to south downward trend.

Today 8.9 million osteoporotic fractures occur every year all over the world (10). As for hip fractures, the mortality rate in the year following the fracture is over 20%, which is in line with that of thyroid or breast cancer. Loss of function and autonomy among the survivors is a further concern as well as the continuous 24-hour care required in several cases (11).

Clinical presentation

Osteoporosis itself is not a painful process, and it is therefore difficult to recognise at an early stage based on clinical symptoms. In an advanced state the illness's complications, micro- or macrofractures cause *pain* and deformities. Symptoms manifest themselves in increased back and lower back pain when changing position. Due to rib cage deformities developing in consequence of rib cage fractures and vertebral compression fractures and the segmental radiation of pain, these symptoms are often combined with chest complaints and root pain in the legs and arms. In consequence of vertebral compression fractures and

weakened core muscles, back kyphosis increases, the stomach falls forward and the height of patients gradually decreases. The illness often progresses without particular complaints, and only spontaneous fractures or fractures occurring in response to minor trauma draw attention to its prevalence.

Diagnosis

DXA is the reference method for measuring bone mineral density at the lumbar spine and hip. Bone strength correlates strongly with BMD. In postmenopausal women, BMD results are reported as T-scores. The T-score is the number of SDs of the measured BMD value above or below the same-site mean BMD in young women. The WHO defines osteoporosis as a T-score ≤-2.5 at the femoral neck or/and lumbar spine (12). A diagnosis of osteoporosis can only be established once other forms of calcipenic osteopathy have been ruled out, if the results of laboratory tests concerning calcium metabolism are negative. In clinical practice, for the purpose of diagnosing osteoporosis, a -2.5 T score value based on a bone mineral density test – which is mostly rigidly applied – on its own is not enough to assess the probability of the most serious consequence of osteoporosis: fragility fractures. Many patients who have osteoporosis by bone density testing will not fracture and many fractures due to osteoporosis occur in patients whose bone density is better than the osteoporosis cut point. Therefore beyond recognising the condition, it is important to identify those in need of treatment, and to select the group most at risk of bone fracture in which the highest number of fracture risks are present (Table 1). The FRAX tool serves to estimate the risk of fracture in a given individual: based on the input parameters, it estimates a ten-year absolute risk of osteoporotic fractures occurring in response to minor trauma, in particular, the risk of major fractures. It calculates on the basis of the answers given to questions concerning eleven fracture risk factors in a questionnaire available to patients on the Internet, with or without an ODM test result, with regard to the Hungarian age-specific mortality rate, by using its large fracture database. FRAX is suitable for orientation and as a screening test (but not for setting up a diagnosis or monitoring), and its result usually precisely identifies those who need therapeutic intervention (3). The applicability of FRAX should be considered in type 2 diabetes mellitus where, paradoxically, a higher BMD value compared with the average population is associated with an increased fracture risk. Taking into consideration clinical risk

factors, which demonstrate a verified dose-effect relationship, such as smoking, alcohol consumption and use of glucocorticoids, requires further clarification in the interest of an even more realistic assessment of fracture risks.

Table 1. The most common risk factors for fractures

- age*
- falls*
- Caucasian ethnicity
- menopause before 40 years of age
- family history of bone fragility fractures*
- history of fractures*
- low body mass index*
- visual impairment*
- neuromuscular disorders*
- smoking*
- immobility*
- glucocorticoid therapy*
- vitamin D deficiency

*increases the risk of osteoporotic fractures independently of bone mineral density

Treatment

The fundamental purpose of treating osteoporosis is to reduce the risk of bone fracture.

Pharmacological treatment

By treating osteoporosis pharmacologically, not only is it possible to prevent ongoing bone loss, but it equally helps to increase the mineral contents of bones and to improve bone quality. Based on approved therapeutic guidelines, both in international and domestic practice, it is possible to start the treatment of osteoporosis in postmenopausal women and in men aged 55 and older based on any one of three elements: traditional BMD-based T-score of ≤ -2.5 at the hip (total hip or femoral neck) or lumbar spine, a qualifying low trauma fracture, or a FRAX score meeting or exceeding the recommended treatment intervention cut points. The FRAX cut points chosen as diagnostic indicators of osteoporosis reflect the two being used as treatment intervention thresholds in the current international and national guidelines,

namely ≥3% 10-year absolute risk for hip fracture or ≥20% for major osteoporotic fracture in older adults (13).

In addition to increasing bone density, substances, which are proven to be effective on the basis of the principles of evidence-based medicine also provably reduce fracture risks for patients (Table 2)(14). In monotherapy it is advantageous to administer antiporotic medicines in combination with calcium and vitamin D. In each patient the effectiveness of medicines must be ascertained on the basis of monitoring, using the same equipment every 12 to 16 months (not more frequently) with repeated ODM examinations. If it is possible to monitor the treatment with the use of biochemical markers, the effectiveness of the medicine administered can be determined on the basis of the changes in bone turnover parameters within just 3 to 6 months.

Table 2. Medications for treatment of postmenopausal osteoporosis

Drug	**Route, frequency**	**Evidence for fracture reduction**	**Duration**
Initial treatment for most patients			
Alendronate	oral, weekly	spine, hip, nonvertebral	Consider a "drug holiday" after 5 years
Risedronate	oral, weekly or monthly	spine, hip, nonvertebral	Consider a "drug holiday" after 5 years
Zoledronic acid	iv, yearly	spine, hip, nonvertebral	Consider a "drug holiday" after 3 years
Denosumab	sc, twice yearly	spine, hip, nonvertebral	No limit
Raloxifene	oral, daily	spine only	No limit
Ibandronate	oral, monthly, iv, fourth yearly	spine only	Consider a "drug holiday" after 5years
Anabolic agent, usually reserved for most severely affected patients or those failing to respond to other drugs			
Teriparatide	sc, daily	spine, nonvertebral	Two-year limit; should be followed by agent from the list above

Non-pharmacological treatment

The non-pharmacological treatment of osteoporosis involves complex physiotherapy; however, corrective gymnastic therapy is key from among the available physiotherapeutic options.

The rationale for utilizing physiotherapy programmes is pain reduction, and complex exercise programmes are used for *fall prevention* through improving *balance* and *endurance***.**

Background of falls

The definition of a fall is when one experiences an unexpected loss of balance resulting in coming to rest on the floor, ground, or an object below knee level (15).

The vast majority of antiosteoporotic medications introduced in the last two decades primarily aim to improve bone mineral density. Even if some of these medications reduce the risk of fracture as well as increase bone mineral density, *falls* in most cases result in osteoporotic fractures, despite optimised pharmacological therapy and increased mineral density.

According to data recorded in the relevant literature, in one half of patients having sustained a femoral neck fracture, density does not increase in response to antiporotic therapy (16). Falls are responsible for 90% of the growing increase in hip fractures (17**).** One third of the population over 65 years of age is reported to fall at least once a year, 10-15% of these falls cause fractures and nearly 60% of those who experienced a fall in the previous year fall again (18). Although one in five falls may require medical attention, less than one in 10 results in a fracture (19).

Falls are events attributable to multiple factors. Causes can be divided into personal or internal factors and environmental or external factors. Most frequent internal factors: deterioration of balance control and postural adaptation, neurological illnesses, sensory processing disorder, illnesses of the musculoskeletal system, muscle weakness (e.g. weakening of the m. quadriceps femoris increases the number of falls 7.5-fold, while weakening of the m. tibialis anterior increases the number of falls 4.5-fold), and effects of medicines taken on a regular basis (20, 21). From among external factors mention should be

made of the lack of accessibility for the disabled, poor footwear, or the lack of hip protectors, which reduce the force of the impact. At present the method for assessing the risk of fall is clinical assessment as there is no standard, validated method available for the purpose.

Balance

Loss of *balance* can be one of the greatest risk factors for falling in established osteoporotic patients (22). *Postural control* is the inherent ability to maintain the centre of mass on a supporting base, between stability limits. These limits are the operational areas up to which the centre of mass can be displaced without the need to change the supporting base. Thus, balance depends on the individual's ability to maintain postural control under a great variety of conditions, as well as the ability to perceive the stability limits. In order to avoid falling, the centre of body mass must be kept within the supporting base or, even better, within the stability limits. Control of an upright posture is a complex function achieved through multisensory integration, central motor control, and context-specific response. During normal aging, physiological changes occur in one’s visual, vestibular, somatosensory inputs, as well as in central processing and muscular effectors. Moreover, interjoint coordination is also affected. Among the likely causes of postural instability among the elderly, changes in the relationship between sensory information and motor action are of importance. The elderly have greater difficulty in interpreting sensory information and prioritizing it according to its relevance, and in selecting the proper response in order to maintain their balance in specific positions. Postural control among individuals with osteoporosis is different from postural control among the general elderly population. Individuals with osteoporosis are more likely to present higher sway velocities and greater maximum shift of the centre of pressure or centre of mass because of spinal extensor muscle weakness that is associated with hyperkyphosis, and consequential flexed posture. It may limit activities, including bending, reaching, reduced gait speed, greater difficulty climbing stairs, and poorer balance. Hyperkyphosis changes the joint position sense because of poor alignment of the joints. All these factors could influence control over the centre of mass position or centre of pressure and the ability to recover from balance perturbation (23, 24). In most cases, the lack of balance cannot be attributed to a specific cause, but to a compromise of the balance system as a whole (including afferent and efferent neural pathways and musculoskeletal components of postural response).

Endurance

Apart from strengthening postural control and balance, improving endurance among the elderly also has a key role to play in reducing the risk of falling given that it is also an indicator of physical performance. Endurance is understood as the ability of a muscle or muscle group to perform repeated contractions against a load for an extended period of time (25). With aging, the musculoskeletal system capacity is reduced, with loss of muscle mass and strength, in addition to the effects of changes in the nervous and cardiopulmonary system (26**,** 27). Therefore, in elderly osteoporotic patients, endurance is often impaired.

Given that biochemical processes are more efficient when they take place under aerobic conditions and therefore the body is capable of more endurance, increasing aerobic capacity is one of the most important goals of fitness programmes for both athletes and healthy people. Aerobic capacity is the product of the capacity of the cardiorespiratory system to supply oxygen (i.e. cardiac output) and the capacity of the skeleton muscle to utilize oxygen (i.e. arterial-venous oxygen difference) (28). Aerobic capacity is therefore an indicator of physical activity and performance, and has been reported as a significant predictor of physical disability and dependence in the elderly (29, 30). A decrease in aerobic capacity and in endurance can reduce patients' ability to sustain balance, which increases patients' susceptibility to falls and causes impairment in the functional capacity of the elderly (31).

One of the most relevant tools for assessing aerobic capacity is peak VO_2, which is most often measured by placing individuals under conditions of high intensity exercise, such as running on a treadmill or cycling in order to measure the maximum amount of oxygen that can be carried and consumed by the body during incremental exercise.

Therefore exercises that aim to improve aerobic capacity and endurance, along with exercises that strengthen postural control and balance, should complement pharmacological treatment for elderly osteoporotic patients in order to significantly reduce the risk of falling and avoid fractures.

Evidence supporting effectiveness of exercise programmes for balance and endurance

The first controlled, randomised study, which examined the effects of physical activity in women with decreased bone mineral density, was published in 1996. The study results suggest that after 12 months, exercising can produce a significant increase above initial levels in the functional fitness, well-being, and self-perceived health of osteopenic women. Intensity of back pain can also be lowered by exercise (32). A large range of literature has since become available for review. Randomised controlled trials are particularly valuable.

In a 20-week randomised controlled trial conducted in 2002, *Carter* and his team examined the effectiveness of exercise programmes prescribed in general for osteoporotic patients, and found that relative to controls, participants in the exercise programme experienced improvements in dynamic balance (by a timed figure-eight run) and knee extension strength (by dynamometry), both important determinants of risk for falls (33).

In 2006 *Korpelainen* and colleagues, while in 2008 Hourigan and her team looked into the effects of balance training and weight-bearing exercise programmes on balance, muscle strength, gait and bone mineral density in osteopenic women (34**,** 35). In both trials there was a significant improvement in balance control and muscle strength, and walking distance and patient density also improved. Some RCTs use body balance and its changes to assess the results of exercise programmes in osteoporotic patients. The effect of Thai Chi was examined in relation to osteoporotic and osteopenic men, and it was found to be effective for balance control (36).

In 2007 *Madureira* examined the effects of a 12-month balance training programme for balance, mobility and falling frequency in osteoporotic women. These were evaluated by performance tests (BBS, Clinical Test Sensory Interaction Balance, TUG). This longitudinal study demonstrated that balance training is effective in improving functional and static balance, mobility and falling frequency in elderly women with osteoporosis (37).

The RCT conducted by *Swanenburg* and his team was a three-month programme consisting of exercise/protein, including training of muscular strength, co-ordination, balance and endurance. Calcium/ vitamin D was supplemented in all participants for a 12-month

period. Significant reductions of risk of falling, an increase in muscular strength and an increase in activity level were found in the experimental group as compared to the control group. Furthermore, there was an 89% reduction of falls reported in the experimental group (38).

A systematic review published by *Howe* and his team in 2011 examined exercise for improving balance in older people. Eight classes of exercise programme were set up. In some instances, more than one type of exercise was tested. It is a factor of critical importance that the evidence for each conclusion was, in most cases, collected from only a few of the trials for each class of exercise. These conclusions appear to indicate an effect of exercise on bone density which is relatively small from a statistical point of view, but which may yet be important. Potentially, exercise can be developed as a safe and beneficial method to prevent bone loss in postmenopausal women. Typically effective exercise programmes were organised three times weekly for a period of three months and are included standing dynamic exercises. The conclusion of the review was that there was weak evidence to suggest that some types of exercise are of moderate use in improving balance skills in older people immediately following intervention. Nevertheless, as a result of missing data and the compromised methods employed in many of the trials, further high-quality research is indispensable (39).

In 2012 *Gillespie* and colleagues published a systematic review on interventions for preventing falls in older people living in the community. Current evidence shows that this type of intervention reduces the number of falls in older people living in the community but not the number of people falling during follow-up. These are complex interventions, and their effectiveness may be dependent on factors yet to be determined (19). This summary is an update of a study by Cochrane published in 2009 (40) which includes an overview of the effectiveness of fall prevention programmes for older people living in the community as well as in care facilities and hospitals, but it does not separate the osteoporotic patient population.

In 2014 *Gianoudis* and team published a 12-month community-based randomized controlled trial. The aim of the study was to evaluate the effectiveness and feasibility of a multimodal exercise programme incorporating high-velocity (HV)-PRT, combined with an osteoporosis education and behavioural change programme, on bone mineral density, body

composition, muscle strength and functional muscle performance in older adults. Fall incidence was evaluated as a secondary outcome. This programme led to modest but significant net gains in femoral neck and lumbar spine, muscle strength, functional muscle power and dynamic balance relative to controls. There was no effect on total body lean mass or mobility (TUG), and no difference in fall rates (41).

Sherrington and colleagues reviewed studies evaluating effective fall-prevention exercises among elderly people. This systematic review with meta-analysis provides strong evidence that exercise as a single intervention prevents falls in older people living in the community. The meta-regression suggests programmes that involve a high challenge to balance and include more than 3 hours/week of exercise have greater fall prevention effects. The pooling of results from 62 trials across a range of countries suggests the results can be broadly generalised to community-dwelling older people. Fewer studies have been undertaken in residential care settings and in people with particular clinical conditions, so there is less certainty about the impact of exercise as a single intervention in these groups (42).

In 1998, as part of a one-year prospective study, *Grahn Kronhed* evaluated the effects of regular, weight-bearing exercises on bone mass, muscle strength and flexibility, balance skill and aerobic capacity. Following the training period, significant increases in BMD at the greater trochanter, balance skill, and oxygen uptake capacity were observed in the exercise group. A significant increase in BMD ($p<0.05$) was observed at the lumbar spine in the control group. These results, however, should be considered with caution due to the fact that several of the participants involved in the study were over the age of 60, at which age degenerative changes in the lumbar spine may increase to a greater or lesser extent. It does appear that regular weight-bearing exercises have an effect on BMD measured at the greater trochanter in an exercise group comprised of both men and women. Theirs study, however, was based on a small population, and further training studies are required to enable an assessment of weight-bearing exercises on bone mass in varying sex- and age-specific groups (43).

Lima and colleagues demonstrated in a three-year study that balance skills and aerobic capacity deteriorating with age can also be improved with an active lifestyle, which may in turn also reduce the risk of falls (44).

In a study, *Ordu Gokkaya* highlighted that patients in an advanced state of osteoporosis suffer from significantly diminished pulmonary function and aerobic capacity, in addition to serious deconditioning due to a number of causes. Accordingly, a cardiopulmonary test assessment should be incorporated into the management of osteoporotic patients. It is possible that in this patient group, ventilatory muscle training and aerobic exercise could provide a useful supplement to current osteoporotic therapies (45).

Tests to measure balance and endurance

In the relevant international literature, body balance and changes therein are used in a number of studies for evaluating the test results of osteoporotic patients (46). However, these results are highly diverse, and therefore balance tests were classified into two groups: performance tests and posturography tests. Performance tests such as the TUG, standing on one leg and the BBS assess balance from a functional point of view. By contrast, posturography tests examine body sway, which can be regarded as a physiological test. Posturography is a general term that covers all the techniques used to quantify postural control in upright stance in either static or dynamic conditions.

Balance tests

In the relevant literature performance (functional) tests and computerised balance measurements (posturography) are used for determining an individual's balance skills.

Performance-based balance tests (Timed up and Go, Berg Balance Scale)

Timed Up and Go is a simple test to evaluate a patient's mobility. We assess the time individuals need to rise from a chair, walk 3 metres, turn, walk back to the chair and sit down. Less than 10 seconds is considered as normal mobility, times between 10 and 20 seconds are acceptable in the older population or those with movement disability (47).

The *Berg Balance Scale* is used for a computerised performance-based assessment of balance. It takes 15-20 minutes and the patient is required to accomplish 14 simple balance-related tasks; for example, to stand up from a sitting position. The tasks are scored from 0 to 4, where 0 means the patient is unable to perform it and 4 points are given when he/she fulfils it completely and independently. The final score of the Berg Balance Scale is the sum of the

points awarded for each task, and in this study we used a score between 41 and 56 points to determine that a patient could walk independently (48).

Computerised balance measurement (Bretz stabilometer)

The computerised stabilometer measures the individual's balance skills in dynamic and static situations. The Bretz stabilometer, a similar device to other new balance assessment tools (49**,** 50), has been proven to be a reliable device for the quantitative assessment of changes in postural sway, which is necessary to regain balance. This allows static as well as dynamic posturometric examinations (51).

Measurements with the Bretz stabilometer

Balance in *static posture* is assessed with the Romberg test, carried out in two positions. Movement of the patient's CP is analysed standing erect, with eyes open ('Romberg' 1 position) and eyes closed ('Romberg' 2 position) for 20 seconds. A practice measurement is conducted in all participants. Motion of the patient's CP is displayed on a monitor during the assessment and is subsequently stored on a computer for further evaluation. During the test, without seeing the screen, participants are asked to minimise the movement of their CP, which measures postural sway. The software of the stabilometer is used to evaluate the movement of CP, enabling the examiner to determine lateral movement, movement backwards and forwards, the total length of movement (millimetres) and the radius of the circle that captures 95% of the motion path (Fig. 1).

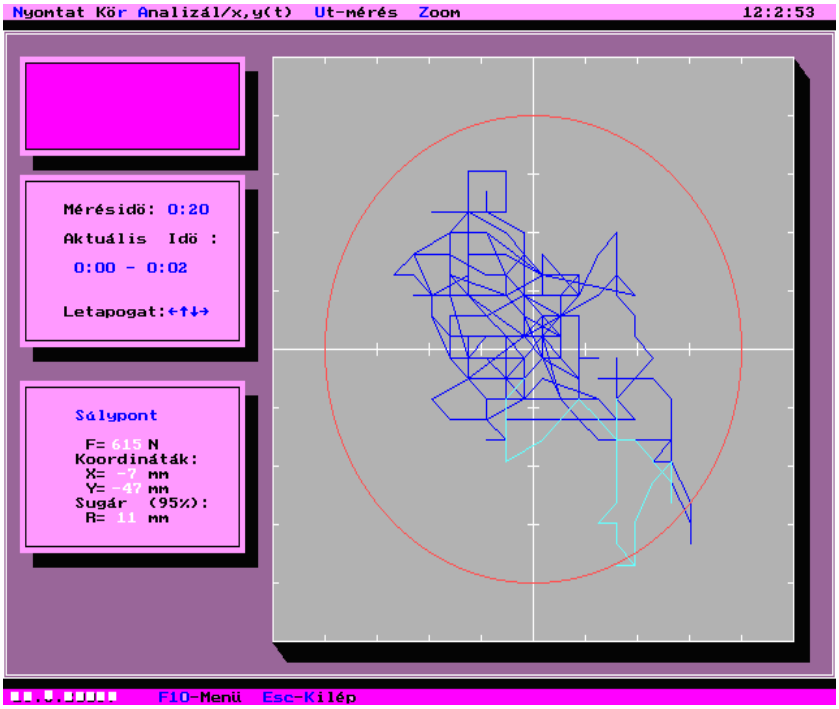

Fig. 1. Movement of CP as displayed on the stabilometer screen

To evaluate *dynamic postural balance*, participants have to complete three tasks (Coordination tests 1, 2 and 3), where they have to move their centre of pressure individually according to the specific task. The monitor is placed in front of the participants at a distance of 1.5 metres, 1.1 metres above the floor, and different figures are displayed to them that form the basis of the exercise. All participants can practise the exercise once before measurements are taken. The programme evaluates the results automatically and data are stored on computer for further analysis.

Coordination test 1: A triangle (schematic pine tree) is displayed on the monitor (Fig. 2), and the corners and midpoints of the sides are marked as the target points (candy form). Participants are required to move their centre of pressure in a way as to reach these target points as quickly as possible. When their CP has covered all the target points, the figure disappears from the screen, indicating the successful completion of the task. Participants have 20 seconds to accomplish this task. Test performance is based on the percentage of points removed from the monitor display within 20 seconds. If all points are reached, the time required to perform this task is calculated.

Fig. 2. Dynamic balance test: Coordination test 1 on monitor of stabilometer

Coordination test 2: Participants are required to direct the cursor signalling the position of the CP into an asymmetrically located point on the monitor (Fig. 3). The programme calculates the performance time in seconds.

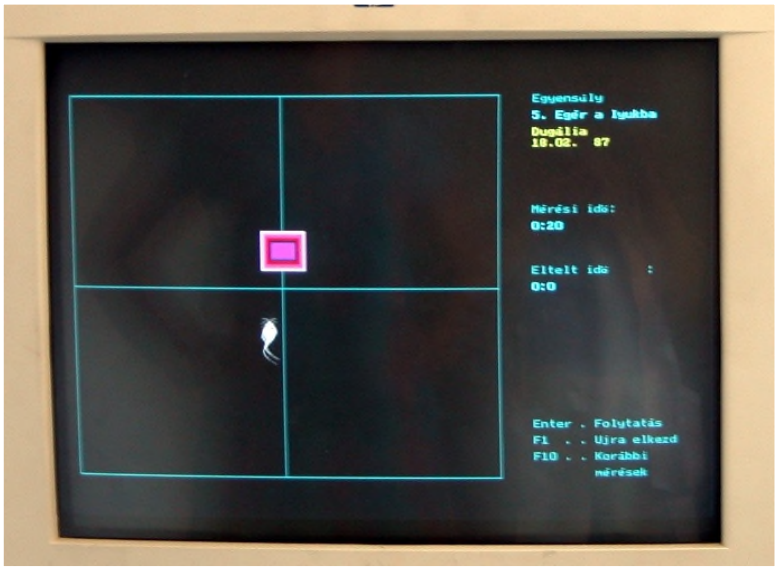

Fig. 3. Dynamic balance test: Coordination test 2 on monitor of stabilometer

Coordination test 3: A 2x2 cm square is displayed in the middle of the screen (Fig. 4). Participants are required to move their CP so that they colour in as much of the square as possible in 20 seconds, and to minimise time spent outside the box. Participants can see the motion of the CP and the coloured-in area on the monitor. Dynamic posture balance is assessed and described by the size of the area the participant manages to colour in within the time limit by moving their CP (as a % of the total area). In addition, the time their CP remains within the square is also measured and recorded (as a % of the total time).

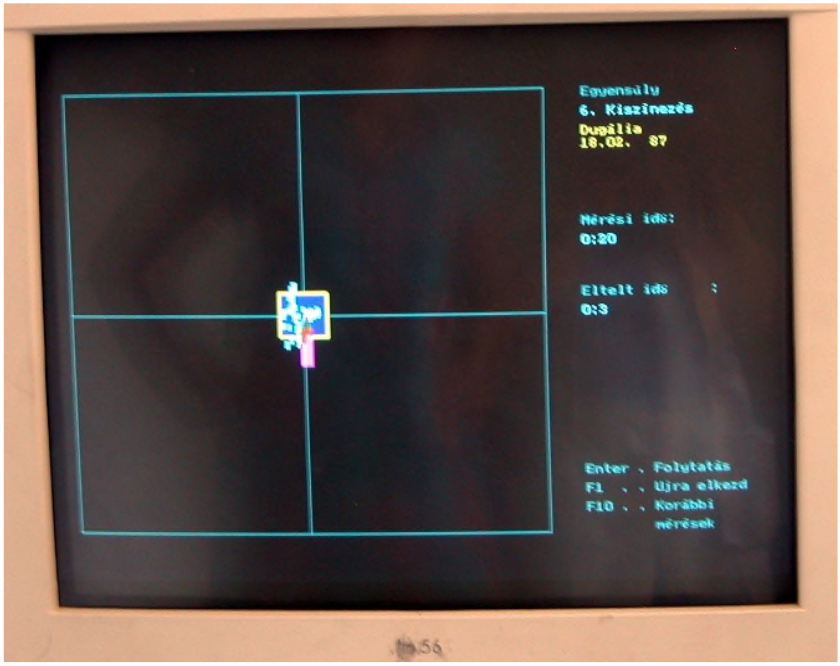

Fig. 4. Dynamic balance test: Coordination test 3 on monitor of stabilometer

Endurance tests

Bicycle ergometry

A maximal exercise test with direct measurement of oxygen uptake is considered the most accurate method of assessing aerobic power. Exercise stress testing is most commonly carried out using a treadmill or bicycle ergometer. The treadmill has a greater diagnostic sensitivity than the bicycle ergometer, however, exercise on a treadmill may not be appropriate for many older individuals with balance deficit or conditions, such as arthritis, in which weight-bearing exercise may cause excessive joint pain.

The Bruce protocol (52, 53) is followed during bicycle ergometry measurements. After a one-minute warm-up at 10 W, the exercise starts from 0 W, with an increment of 25W/ 3 minutes. Speed and resistance are increased periodically (cardiac work and oxygen demand increase parallel with physical workload); at the end of the test there is a five-minute cool-down at 10 W. Maximum heart rate is calculated by subtracting the participant's age from 220. Ergometry is carried out in cc. 30 minutes. The test finishes when participants reach the target heart rate, experience angina during the exercise, have a significant blood pressure elevation, or any abnormal ECG patterns appear (Fig. 5).

If some participants in an older age group cannot reach the target heart rate due to fatigue, the maximum rate of oxygen consumption (VO2max) cannot be calculated; therefore MET is used to characterise their aerobic capacity (1 MET= 3.5 ml/min/kg at rest). Intensity of the workload is thus expressed as a number, which reflects the extent to which the exercise completed by the patient increased VO2max. The fitter the patient, the lower the value of MET, i.e. the lower the oxygen consumption when completing a given task.

Fig. 5. Bicycle ergometry

Spirometry

Spirometry is the foundation of pulmonary function testing and provides timed measurements of expired lung volumes. With automated equipment it is possible to interpret more than 15 different measurements from spirometry alone. VC, FVC, FEV_1, FEV_1/FVC ratio (Tiffeneau-index), and flow between 25% and 75% of the FVC (MMF) are the most clinically helpful indices obtained from spirometry. Changes in endurance can be best demonstrated on the basis of changes in forced vital capacity. Before measurement, the instrument must be in an authenticated state, with the latest temperature, pressure and humidity data, and must be freshly calibrated. After the patient's verbal consent, the planned manoeuvre must be explained, and if necessary demonstrated, to the patient, and the patient must also be informed about what depends on the outcome of the test. During the test it is necessary to ascertain that the patient is willing to cooperate. It is desirable to place the patient in a safe and comfortable sitting position. The use of a nose clip is recommended (experiences show that this may reduce the patient's cooperation). It is desirable to discreetly request the patient to remove any unstable dentures.

FVC manoeuvre

After breathing calmly, the patient performs an unforced, maximum inhalation through the mouth, then places the mouthpiece into the mouth, and immediately and forcefully exhales into the mouthpiece until there is no more air left. In theory the manoeuvre is completed if the volume-time curve ends in a horizontal level. According to the relevant recommendation, 6 seconds of FET is sufficient for adults. In practice the FVC manoeuvre is either stopped by the patient if he or she is unable or unwilling to exhale further, or must be stopped by the person conducting the test if an undesired event (dizziness, cyanosis) is detected. Out of three successful manoeuvres, the difference of the two highest FVCs cannot be greater than 0.150 litre. A maximum of four manoeuvres can be performed. The highest FVC will be entered in the measurement records.

Measurements of spirometry were calculated as a percentage of the normal range adjusted for age, sex, and height using equations for the normal values of the European Respiratory Society (ERS) standards (54).

AIMS OF THESIS

In advanced cases of osteoporosis, even against the background of an adequate pharmacological therapy fractures or repeated fractures may occur in the event of falls, and therefore preventing falls and fractures associated with falls is even more important in these patients than in healthy individuals. It is proven that in older, osteoporotic women both balance skills and muscle strength are diminished compared with non-osteoporotic women of the same age (41). In consequence, from the viewpoint of fractures or multiple fractures sustained earlier, impaired balance skills and diminished muscle strength may be regarded as increased risk factors for these patients. Strengthening the balance and posture of elderly osteoporotic patients can reduce the risk of falling, thus preventing fatal events or hospitalisation with enormous healthcare costs. Therefore, exercise programmes that aim to improve the balance of patients need to address this reduced proprioception and strengthen sensomotor function as well (17). Furthermore, given that aerobic capacity and endurance are often impaired in this patient group, which can cause further challenges to maintaining balance, exercise programmes that form part of the non-pharmacological therapy of this patient group should have a measurable positive impact on patients' aerobic capacity.

THESIS I

The aim of our study was to investigate the effectiveness of a 12-month sensomotor balance training programme combined with aerobic elements. As a primary endpoint, we aimed to monitor changes in postural control in women with established osteoporosis using both performance tests and a computerised stabilometer. The secondary endpoint was to record the frequency of falling.

THESIS II

In our study we sought to find an answer to the question as to whether in response to a 12-month sensomotor balance training programme combined with aerobic elements any meaningful change occurs in the aerobic endurance of women with advanced and established osteoporosis as indicated by ergometer and spirometry results.

STUDY METHODS

Participants

Individuals who underwent osteodensitometry in the Osteoporosis Centre of the National Institute of Rheumatology and Physiotherapy in the year prior to the study were selected to be enrolled in the trial according to the following criteria.

Inclusion criteria: aged over 65 years, community-dwelling (living on their own, with or without a partner), established postmenopausal osteoporosis based on the WHO criteria (T-score below -2.5 SD in lumbar spine, femur neck or total femur region) (12**)** and at least one osteoporotic fracture in their personal medical history.

Exclusion criteria: significant degenerative spine disorders, congenital or acquired deformity of the spine, thorax or feet, traumatic fracture, severe visual or auditory impairment, neuromuscular diseases, organic psychosyndromes, advanced cardiorespiratory or cerebrovascular diseases, predisposition to orthostasis or hypoglycaemia, use of assistive walking devices, inability to walk 10 metres independently, participation in clinician-guided exercise programme (as osteoporotic therapy) in the previous six months.

Ethics approval was obtained from the Semmelweis University Regional and Institutional Committee of Science and, Research Ethics and the trial was registered under registration number 152/2010. All participants were informed about the trial, had the opportunity to ask questions and provided written consent prior to the study.

The study was carried out between 1st January 2011 and 31st March 2012 at the Osteoporosis Centre of the National Institute of Rheumatology and Physiotherapy.

Trial design and outcomes

100 participants were randomly assigned to the intervention or the control group; randomisation was performed based on the assigned number in the patient diary (using a numbered series of pre-filled envelopes specifying the group). Individuals in both groups continued to receive their standard antiosteoporotic medication (such as calcium and vitamin D); the intervention group (n=50) attended a complex balance exercise programme, while the

control group (n=50) did not participate in any clinician-guided physical exercise programme (Fig. 6).

A blind physiotherapist assessed balance in static and dynamic positions and a blind internist assessed aerobic capacity in both groups at the start and at the end of the study. Patients kept a falls diary, in which they recorded the number of times they fell every month and mailed it back to the blind physiotherapist.

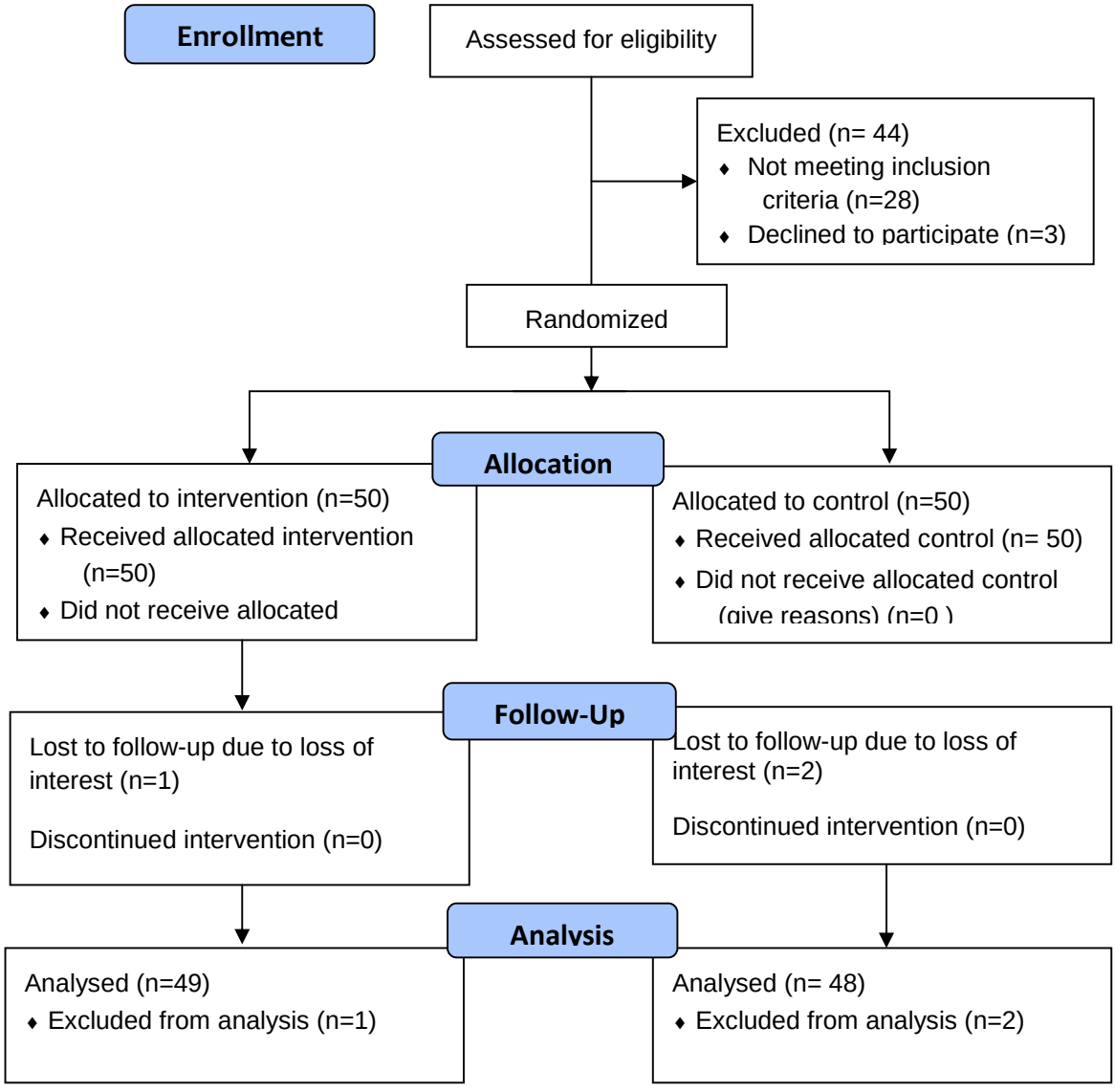

Figure 6. CONSORT map

Measurements with Bretz stabilometer

The static and dynamic postural balance of all participants was measured at the start and at the end of the trial with a computer-controlled device, the Bretz stabilometer (51).

Performance-based balance tests

We used performance-based TUG and BBS tests according to their respective protocols (47, 48) at the beginning and end of the study.

The methodologies of the stabilometry and performance-based tests are described in the chapter “Tests to measure balance”.

Determination of aerobic endurance

To determine the endurance of patients we measured their aerobic capacity with a bicycle ergometer (53), expressed in MET, at the beginning and end of the test. We used an Ergoselect 100 bicycle ergometer combined with a blood pressure monitor and oxygen saturation measurement. Regardless of speed, the load capacity of the bicycle which features an LCD display and can be controlled both manually and automatically, ranges between 20-990 Watts, while its speed range is between 30-130 pedal revolutions per minute.

For the further assessment of the endurance of patients we used a MicroPlus Spirometer made by Micro Medical (Fig. 7) where we measured one of the most important parameters, vital capacity, in litres, in standardised circumstances (54) at the beginning and end of the programme. This spirometer is a small and light instrument, with an accuracy of ±3%, which reaches and even exceeds the accuracy of any known spirometer. Its flow range can fluctuate between 0.2 and 15 l per second, while its volume range changes between 0.1 and 9.99 l. At the end of the test the instrument immediately displays the result measured. By entering the age, sex and height in the lung function calculator before spirometric measurements, we can obtain the predicted values of the parameters to be measured. The results obtained during measurements can then be compared with these values. They can be used both as absolute values and expressed in percentage of the predicted values.

The methodologies of bicycle ergometry and spirometry are laid down in the chapter describing the measurement of endurance.

Fig. 7. Spirometer MicroPlus

Frequency of falls

Participants were provided with a falls diary consisting of monthly fall sheets, in which they could record whether they have fallen (with a cross) or not (with a tick) each day. Participants were asked to record the fall as soon as it happened or at the end of the day and return fall sheets in pre-addressed envelopes every month. Fall sheets were collated by the blind physiotherapist leading the assessments who also followed up on any missing fall diaries with patients monthly.

Interventions

The complex balance exercise programme compiled by our physiotherapists combined postural balance improving exercises and aerobic elements that were completed in the outpatient setting as well as at home. Patients attended the programme three times a week for a 30-minute physiotherapist-guided session, and they also received printed materials of exercises they could practise at home on days they did not attend an exercise session at the hospital. The exercises patients completed at home were less complex postural control exercises and included elements from the Otago exercise programme, which is a controlled

fall prevention programme, designed to improve muscle strength and balance, and which has been shown to reduce the number of falls by approximately 30% (56).

Our sensomotor balance exercise programme is a combination of functional stabilisation training and exercises focusing on improving balance. It therefore includes conventional back, torso and lower extremity muscle strengthening exercises as well as proprioceptive dynamic posture training (57), modified in its sensomotory elements in order to improve balance control and reduce falling in the study population. This training follows a learning principle with a focus on strengthening the transversus abdominis and multifidus muscles, thus enhancing stability through improving the function of the deep and postural muscles. We adapted this training programme for older participants who have an elevated risk of falls by combining elements from the Otago programme with exercises that aim to strengthen the torso and to improve balance.

There are three levels of progressivity in our exercise programme, which are completed in a step-wise manner (one phase needs to be completed to allow progression to the next level). The first, static phase focuses on stabilisation and participants practise maintaining static posture first in a sitting position, then progressively moving on to standing on both feet, leading to unilateral support of standing on one foot. The exercises were made progressively more difficult by changing the size or the quality of the supporting surface (e.g. using unstable surfaces such as a stability trainer or Dynair cushion, thereby making the body's centre of gravity position more difficult to maintain). In the second, dynamic phase, additional arm and leg exercises are performed once the exercises in the static phase can be performed confidently. The therapeutic effect is increased by varying the speed of the movement and by adding elastic resistance using elastic straps. In the final, functional phase, the goal is to achieve automatic stabilisation of the torso when performing different exercises and the activities of daily life. The functional phase also assists participants with developing stabilisation skills when changing position and posture during sports and work activities.

Participants in the intervention group were also asked to complement their exercise programme with regular walking, for which they received a structured schedule put together by our physiotherapists. The walking programme consisted of 25-35mins walks that included

2-3 minute fast-paced intervals and the walks became progressively more difficult with the inclusion of more frequent fast-paced intervals.

The aim of the walking programme was to complement the balance exercise programme with aerobic elements and thus to increase participants' aerobic capacity. Participants discussed their progress in the walking programme with the physiotherapists at their regular exercise appointments.

Statistical methods

Sample size justification was not performed at the beginning of the study because all eligible patients in our database had been considered for the study. A statistical analysis was carried out using SPSS version 19.0 for Windows software. The baseline characteristics of the participants were analysed using descriptive statistics. Independent-sample t-tests and Mann-Whitney U tests for continuous data and χ^2 test for categorical data were used to compare baseline values of the intervention and control groups, and to determine whether there was a statistically significant difference between the outcomes of the intervention and control groups after the intervention, i.e. group difference in change scores (statistically significant difference was considered at $p<0.05$). Relative risk (RR) was also calculated for falling.

RESULTS

Anamnestic and demographic (baseline) data were collected before randomisation using a questionnaire, and these were summarised (Table 3). The participants' average age was 69.33 and 69.10 years in the intervention and control groups, respectively (SD= 4.56 in the intervention group and 5.30 in the control group). According to the inclusion and exclusion criteria, 100 osteoporotic women out of the 144 screened could enrol in the trial. Those that were excluded following screening either did not meet the inclusion criteria (most often did not have an osteoporotic fracture in the past) or had to be excluded due to the exclusion criteria ('Other exclusions', Fig. 6).

Table 3. Baseline characteristics of participants (n=100)

Group	Intervention group (n=50) Mean	Control group (n=50) Mean
Age (SD)	69.33 (4.56)	69.10 (5.30)
BMI	24.17	24.38
Medical history		
Hip osteoarthritis, number (%)	1 (2)	0 (0)
Knee osteoarthritis, number (%)	2 (4)	3 (6)
Diabetes mellitus, number (%)	6 (12)	4 (8)
Hypertension, number(%)	29 (58)	31(62)
Pulmonary disease, number (%)	2 (4)	1 (2)

Categorical data are presented as frequency and percentage, continuous data are presented as mean and standard deviation (for normally distributed data).

Results supporting Thesis I.

In terms of postural balance assessments, *performance-based* TUG and BBS test scores showed a statistically significant difference between the intervention and the control groups after a one-year follow-up (TUG $p<0.005$, BBS $p<0.001$, Table 4).

Both static postural balance tests assessed by *stabilometer* showed significant improvement at the end of the trial, including the ‘Romberg I’ and ‘Romberg 2’ positions ($p<0.001$, Table 4).

During *Coordination test 1* (Dynamic 1 in Table 4), to evaluate dynamic postural balance we calculated the average time required to complete the task; *Coordination test 2* (Dynamic 2 in Table 4) also measures the average performance time. We found a statistically significant improvement in the intervention group after one year regarding both tests

(Dynamic 1 p<0.001, Dynamic 2 p<0.003, Table 4). *Coordination test 3* (Dynamic 3 in Table 4) determines the period of time the CP is located within the designated area (as a % of the total area). We found a significant improvement in the intervention group regarding this measurement as well (p< 0.001, Table 4).

Table 4. Static and dynamic postural test results at baseline and 1-year assessment

Tests	Intervention group, n=49 (95% CI)	Control group, n=48 (95% CI)	p-value
TUG (mean time, in seconds)			
Baseline	8.89 (6.77, 11.01)	9.95 (6.46, 13.44)	
1 year	6.74 (5.84, 7.64)	10.64 (6.62, 14.66)	
Absolute change	-2.15 (-2.56, -1.72)	0.69 (-0.23, 1.62)	0.005*
BBS (mean time, in seconds)			
Baseline	49.23 (46.63, 51.83)	48.52 (38.72, 58.32)	
1 year	42.27 (40.47, 44.07)	50.15 (44.95, 55.35)	
Absolute change	-6.96 (-7.47, -6,44)	1.63 (-0.27, 3.54)	0.001*
Romberg 1 (open eye; average radius in mm)			
Baseline	14.25 (11.65, 16.85)	13.73 (10.49, 16.97)	
1 year	10.47 (8.77, 12.17)	14.50 (12.12, 16.88)	
Absolute change	-3.78 (-4.24, -3.31)	0.77 (0.11, 1.42)	0.001*
Romberg 2 (closed eye; average radius in mm)			
Baseline	20.87 (18.17, 23.57)	19.76 (16.16, 23.36)	
1 year	16.07 (13.87, 18.27)	19.75 (17.15, 22.35)	
Absolute change	-4.80 (-5.48, -4.11)	-0.01 (-0.82, 0.79)	0.001*
Dynamic 1 (mean time, in seconds)			
Baseline	13.15 (8.62, 17.68)	13.25 (7.75, 18.75)	
1 year	11.05 (6.94, 16.06)	14.00 (9.06, 18.94)	
Absolute change	-2.10 (-3.38, -0.83)	0.75 (-0.65, 2.15)	0.001*
Dynamic 2 (mean time, in seconds)			
Baseline	5.74 (0.44, 10.77)	5.80 (1.20, 10.40)	
1 year	4.22 (0.42, 8.02)	5.57 (0.87, 10.27)	
Absolute change	-1.52 (-2.72, -0.31)	-0.23 (-1.70, 1.25)	0.003*
Dynamic 3 (% of assigned time spent within boundaries)			
Baseline	88.07 (79.20, 97.57)	88.87 (80.13, 97.61)	
1 year	93.72 (87.12, 100.32)	88.76 (80.86, 96.66)	
Absolute change	5.65 (3.74, 7.53)	-0.11 (-2.04, 1.82)	0.001*

*Significant result

As for the *frequency of falls*, 6 patients fell in the intervention group and 11 patients fell in the control group, and there were 7 and 16 falls in the intervention and control groups, respectively. Therefore, we calculated the experimental event rate for the number of patients who fell to be 0.122 and the control event rate to be 0.229; thus the relative risk of falls is 0.534 ($p=0.17$). While the result is not significant, it is important to note that in the intervention group the percentage of falls was one half of that observed in the control group.

Results supporting Thesis II

Regarding the assessment of aerobic capacity by *bicycle ergometry*, during our one-year programme the registered initial MET values of the intervention group were between 2.40 and 7.80, with an average of 4.91. In the control group, initially the MET values averaged at 4.83 (2.94-8.10). The difference between the two initial average values was not significant. A year later the average value in the intervention group decreased to 3.82 (1.84-7.34) and to 4.95 (2.57-8.93) in the control group with a significant difference between the two in terms of the change scores ($p<0.0017$); Table 5).

During *spirometry*, at the beginning of the test, the average vital capacity measured in the intervention group was 2.44 litres; the lowest measured value was 1.38 litres, while the highest VC value was 3.45 litres. In the control group the initial VC average value was 2.37 litres; the lowest value was 1.43 litres, while the highest value was 3.51 litres. There was no significant difference between the results of the intervention and control groups at the beginning of the test. In measurements taken after a year, the average vital capacity value in the intervention group was 2.77 litres (1.53-3.64); the corresponding value in the control group was 2.21 litres (1.16-3.25). The difference in absolute values between the two groups was significant ($p<0.01$; Table 5).

Table 5. MET and vitalcapacity results at baseline and 1-year follow-up

Tests	Intervention group, n=49 (95% CI)	Control group, n=48 (95% CI)	p-value
MET (metabolic equivalent)			
Baseline	4.91 (2.4, 7.8)	4.8 3 (2.94, 8.1)	
1 year	3.82 (1.84, 7.34)	4.95 (2.57, 8.93)	
Absolute change	-1.09 (-1.79, - 0.38)	0.12 (-0.59, 0.83)	0.0017*
Vitalcapacity (in liter)			
Baseline	2.44 (1.38, 3.45)	2.37 (1.43, 3.51)	
1 year	2.77 (1.53, 3.64)	2.21 (1.16, 3.25)	
Absolute change	0.33 (0.07, 0.58)	-0.16 (-0.41, 0.11)	0.01*

*Significant result

There were no reported adverse events and those participants who completed the exercise programme had high adherence (over 80%). Participants who were lost during the study were not included in the analysis because they were lost at the beginning of the study.

DISCUSSION

A large number of studies have been conducted to investigate the effect of different exercise programmes on balance ability in osteoporotic patients (32, 33, 34, 35, 37, 38, 42, 58, 59, 60, 61, 62). Most of them used performance-based tests, mainly TUG and BBS to assess the efficacy of these programmes. Studies analysing the movement of the centre of mass (i.e. the change in balance position) via a computer-based technique (50, 63) represent a quantitative assessment, in addition to performance-based tests. A decrease in physical activity levels and aerobic capacity can result in changes in balance, increased susceptibility to falls, and impairment in functional capacity in older age (20, 21, 64). Therefore, in addition to strengthening postural control and balance, improving aerobic endurance has a key role to play in reducing the risk of falls among patients with established osteoporosis.

At this point in time there is no systematic review or meta-analysis assessing fall-prevention physiotherapy programmes for patients suffering from *advanced osteoporosis resulting in fractures*. Likewise, in the relevant literature there are hardly any studies, which

assess the effectiveness of complex exercise programmes with an impact on *aerobic endurance* and balance skills in osteoporotic patients or even in the elderly population.

Our study is the first to our knowledge that used both types of balance examinations to assess the effectiveness of a 12-month sensomotor balance exercise programme combined with aerobic elements on postural control, endurance and the incidence of falling in women with established osteoporosis.

The stabilometric measurements that were carried out in our study – an example of a postural balance examination – provided us with a more objective and reliable measurement of improved balance than the use of only performance-based tests. Both static and dynamic balance parameters measured by a stabilometer showed a significant improvement in the intervention group at the one-year follow-up. The results of performance-based tests (TUG and BBS), too, improved significantly in the intervention group at the end of the one-year test. Results indicating endurance which were measured with bicycle ergometer and spirometer tests also showed a significant improvement in the intervention group at the end of the one-year combined exercise programme.

The balance examinations of this study prove that our new, complex balance training programme, which is a programme combining conventional muscle strengthening exercises and proprioceptive dynamic posture training, modified in its senso-motory and aerobic elements, can improve the balance and endurance parameters of postmenopausal women who have already suffered at least one previous osteoporotic fracture. According to the results of this study, the one-year exercise programme also decreased the observed rate of falling in the intervention group compared with the control group.

The study has some *limitations*. The method of randomisation may have introduced bias; however, this is unlikely because the assignment sheets were locked away by the examiner in a secure office to which the person who generated the sequence for allocation had no access. Complete blinding was not possible as physiotherapists leading exercise sessions were knowledgeable about the participants in the intervention group. Sample size justification was also not conducted at the beginning of the study, which might have reduced the study power and the ability to generalise based on the results; however, all potentially available patients were screened for the study. Furthermore, while participants were exercising and

walking at home, they were not supervised by a physician, which could have had a negative impact on the quality of the exercises performed. During bicycle ergometry, the MET was used to measure aerobic capacity and not VO2 max due to easy exhaustion of older participants during this assessment. Fall diaries were only checked monthly by physiotherapists and participants may not have accurately recorded their falls as this was not supervised. Our results are only able to offer generalisation as far as postmenopausal, community-dwelling women with established osteoporosis are concerned.

CONCLUSIONS AND NEW RESULTS

I. Based on our randomised, controlled study conducted among women with established osteoporosis, it appears that the intervention group which completed a sensomotoric balance training programme performed significantly better in keeping balance (a crucial factor in prevention of falls), which was confirmed by performance-based tests such as TUG and BBS tests as well as by static and dynamic posturometric tests assessed using a Bretz stabilometer. There was no significant difference in the number of falls at the end of the one-year balance training programme; it is remarkable, however, that at the end of the programme there were half as many falls among participants of the intervention group as in the control group.

II. The results of our investigation suggest that a sensomotor balance training programme combined with aerobic elements significantly improves aerobic capacity, assessed by bicycle ergometry and spirometry, as one of the most important indicators of aerobic endurance.

The primary significance of this study is that both performance-based and computer-based methods were used to evaluate the effect of a complex exercise programme on postural balance and staying power in women with advanced osteoporosis. This study is also novel in that traditional strengthening exercises of the back, trunk and lower extremities were combined with elements of proprioceptive posture training (49). These exercises need to be carried out with caution in osteoporotic patients, given their high complexity and thus increased difficulty compared to conventional strengthening exercises. Participants in this

study exercised with respect to antigravitation load, both in sitting and in standing positions, which supported them in practising common everyday life situations and activities encountered in their daily lives.

Another novelty and strength of our study is that by means of bicycle ergometry and spirometry, we assessed aerobic capacity as one of the most important indicators of stamina. Results of ergometry and spirometry provided evidence that a balance exercise programme combined with aerobic elements influenced simultaneously the muscular, respiratory and cardiovascular systems and resulted in improved aerobic capacity. This resulted in a more precise performance of the exercises and reduced completion time, and improved participants' mobility by the end of the programme by ameliorating the sensomotor system, thereby rendering clinical significance for this study.

SUMMARY

Osteoporosis is the most common cause of fragility fractures because of reduced density and quality of bone. These fractures - most frequently occurring at the hip, vertebra, proximal humerus and distal radius - are associated with an increased morbidity and mortality, and have a large medical and economic impact on healthcare systems (65**).** Fragility fractures in women and men older than 50 years are among the most frequent musculoskeletal manifestations for which patients consult healthcare providers specialising in multiple areas of medicine (66). The lifetime risk of osteoporotic fracture from age 60 in men has been estimated to be between 10-25%, in women 40-48%, depending on the population studied (67**,** 63).

The most important goal of osteoporosis therapy is the prevention of fragility fractures and thus the improvement of patients' mobility, quality of life and the preservation of their self-sufficiency. The currently available therapies in advanced osteoporosis significantly increase bone mineral density and therefore limit the risk of fracture; however, it is also known that when osteoporotic patients fall, they tend to suffer a fracture despite antiosteoporotic medication (68). Prevention of falls in older osteoporotic patients is further complicated by several fall risks such as impaired sight and hearing, muscle strength and proprioception. It is therefore necessary to use an exercise programme that is proven to reduce the frequency of falls in this population to optimise treatment.

Our results confirm our hypothesis that exercise programmes, which aim to address reduced proprioception and to strengthen sensomotor function, in addition to strengthening muscles and endurance, are effective in reducing the number of falls owing to balance instability for established osteoporotic women.

In conclusion, regular exercise is indispensable, in addition to medical therapy, for patients with established osteoporosis. Combining elements of traditional exercises, sensomotor training and aerobic exercises has proven effective in improving postural balance, increasing aerobic capacity and preventing falls. Therefore, this type of exercise programme, adapted to osteoporotic patients with a high risk of falling, is recommended for inclusion in the physiotherapeutic protocol for this population.

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Appendix