Clinical experience and epidemiological data demonstrate that mobility is a key determinant of successful aging and quality of life in old age. Loss of mobility is one of the most prominent threats in old age. Gait disorders and falling are manifestations of mobility impairment and increase with advancing age. Gait and balance disorders, falling, and fall-related fractures are interrelated in a pathogenetic cascade. Multiple falling is a sign of locomotor failure and physical frailty.

Falling in old age has disastrous consequences. About five per cent of falls lead to fractures, a fifth of them are hip fractures. Another 5% to 10% of falls result in serious injuries which require medical care. Falls break bones, self-esteem and activity. Fear of falling leads to self-restriction of physical activity and social contacts and initiates a vicious cycle of deconditioning.

Fractures are also the relevant outcome of osteoporosis. Sixteen per cent of all postmenopausal women will sustain a hip fracture, and up to 40% some type of osteoporotic fracture during their lifetime. In the year 2000 in Germany 114,000 hip fractures, 63,000 humeral, 23,000 pelvic and 110,000 forearm fractures, which led to in patient treatment, have been registered. In relation to falling vertebral and extravertebral fractures have a different pathogenesis. The common term "osteoporotic fracture" is focused on bone strength and does not reflect the fact that 90% of all extravertebral fractures, i.e., hip, humerus, wrist and pelvic fractures, are the result of a fall.

In the Rotterdam study only 20.7% of men and 44.1% of women with non-vertebral fractures had osteoporosis defined by the WHO criteria (T-score<2.5).

It is the combination of reduced bone strength and increased fall risk which causes these types of age-, fall- and osteoporosis-related fractures. Therefore, preventing falls means preventing fractures. However, most vertebral fractures occur without trauma because of material failure.

The strong correlation between falls and extravertebral fractures requires inclusion of a fall risk assessment and a fall prevention program in the management of osteoporosis — in contrast to the traditional approach, which is mainly concentrating on bone strength alone. The steep increase in the incidence of hip fractures with advancing age arises from the interaction between bone strength, propensity to fall and fall mechanisms. Bone strength is one but not the only determinant of hip fractures.

Falls in the aged are frequent occurrences. About one third of all elderly (65+) experience one or more fall a year. Eighty per cent of these falls happen without loss or change of consciousness, and without overwhelming external force, during normal daily activities. We speak of non-syncopeal or locomotor falls.

Falling from a standing height generates enough energy to break even a non-osteoporotic elderly femur. The use of simple physics illustrates this point. We calculate the force resulting from a fall of 50 kg from a height of 80 cm, decelerated by a soft tissue of 4 cm thickness. The potential energy (which equals the kinetic energy in the moment of impact) is 400 J (500 N, height 0.8 m). Because energy respectively work is the product of force times distance, we have to divide the energy by the decelerating distance to get the resulting force. 400 J divided by 0.04 m tissue thickness results in a force of 10 000 N, which the femur is loaded with. That can hardly be called a "minimal" trauma.

Most falls in the elderly are not caused by external hazards in contrast to younger age groups. External hazards are not found strongly correlated to falling. In the environment of elderly fallers, we find the same amount of hazards as in non-fallers, and fallers have lived for decades in the same environment with the same hazards without having fallen. What has changed, when some elderly start to sustain frequent falls? The answer is deceptively obvious. Their ability...
to control body posture during locomotion has declined.

Falls are not randomly distributed among the elderly population. People who fall show a certain pattern of characteristics. It is a consistent finding of prospective studies, that the faller accumulates an individual profile of fall risk factors. It is not a single disease or a single factor which causes a fall. For 100 falls we can find 300-400 causes. Each fall is caused by a combination of multiple risk factors. \(^3,23-25\)

We need an understanding of the risk factors for identifying persons at high risk in order to aim our preventive measures, and we need the knowledge of the individual risk profile to guide an individualized therapy in case of fall propensity.

Hundreds of parameters have been found to be significantly correlated with falling in bi-variate analysis, but most of them are highly interrelated. Their bi-variate correlation has not proved them to be independent risk factors in multivariate analyses. Only a small number of factors have been found to be independently correlated with falling. Unfortunately each research team has investigated its own selection of factors. Many studies have not investigated the variables that have been already proved to be risk factors in other studies. Therefore, the precise relationships between different risk factors remain unresolved.

Not surprisingly, all methodologically convincing studies have found some parameters of neuromuscular function to be highly fall-related. Unfortunately neuromuscular function has been operationalized in very different ways. The following list comprises these factors that have been found most consistently to be independent risk factors in multivariate analysis. \(^3,10,11,25-33\)

1. Muscle power or muscle strength of lower extremities,
2. postural competence/lateral balance,
3. impairments of vision,
4. taking multiple (>4) medications or taking certain groups of fall-related drugs,
5. cognitive impairment.

Two test procedures of lower extremity function have been found to be good independent predictors of falling: chair rising — representing muscle power, and tandem maneuvers — representing lateral postural capacity. Quantifying these performances by timed tests enables us to evaluate therapy effects. \(^3,10,19,26,30,34-35\)

Test procedure - chair rising:
To stand up from a chair of usual height 5 times as quickly as possible without using the arms.

Test procedure - tandem standing/ tandem walking:
To stand in a position with both feet directly in line: the heel of the leading foot is directly in front of the toes of the other.

In combination with freely chosen gait velocity these two motor performances are predictive for increased mortality, impending impairment of mobility, increasing probability of functional dependence, additional nursing home placement, and additional hospitalization. \(^1\)

As a preliminary conclusion: we have some clinical tests which give us valuable information about risks of falling, but operationalization of neuromuscular function related to falling remains variable and unsatisfying. There are too many motor performance tests, which are highly interrelat-
the vertical movements of the COG and power during physiological unrestricted movements. In the mechanogram eccentric and concentric phases of movements can be differentiated and the storage of energy in the elastic elements of the body can be examined. Without release of previously stored energy the motor system cannot produce quickly enough the necessary energy to jump. The force we need for a movement against gravity is a summation of quickly released energy which has been previously stored in elastic elements during eccentric countermovements, and currently generated muscle force by the actin-myosin-system. During the eccentric phases the elastic elements are stretched by which energy is stored. The Leonardo system enables us to analyse these eccentric phases, which cannot be adequately clinically tested. They have been proven to be most sensitive to motor disorder and are early and pathognomonic signs of motor disorder. In contrast to this kind of measurement the commonly used muscle testing methods have certain shortcomings. Isometric motor tests are by definition without movement and can therefore not reveal these developments. Physiological movements are not isokinetic, isokinetic ones have another speed compared with physiological movements.

A standard motor task of mechanography is a vertical jump of maximal exertion with both feet, measured after instruction and practice. The first phase of jumping is squatting as a countermovement to store energy in the elastic elements. The velocity curve shows during the squating a negative velocity, because we are moving downwards. The deepest point of the velocity curve represents the slowing of downward movement, braking the downward movement and simultaneously storing the kinetic energy of downward movement in elastic elements of the muscle-tendon unit. This is a classic eccentric muscle task. The curve reaches the zero point again, when the deepest point of squating is reached. Kinetic energy is now zero and has been transformed to potential energy, stored spring-like in the elastic elements. The mechanogram demonstrates that the maximal force has already been generated before the upward movement of jumping. The momentary production of force by the actin-myosin-system would not be quick enough to accelerate the body to jump, but the elastically stored energy can be released quickly enough. The subsequent development of the force after peak point demonstrates declining force during increasing velocity. This corresponds to Hill’s equation!

The energy for jumping (like any other movement) is the summation of released elastically stored energy and continual production of force by the actin-myosin-system. So the mechanography gives deep insight into the kinetics and timing, respectively, coordination of movements, representing an ideal tool for studying influence of any treatment on muscle function. The comparison of mechanography with usual locomotor tests demonstrates a high reliability. The muscle power, measured by mechanography, shows a strong correlation to the aging process.

Because the fall-related (extravertebral "osteoporotic") fractures are both associated with reduced bone strength and propensity to fall, a comprehensive treatment should have two targets: enhancing bone strength and reducing fall risk. The traditional approach of treating osteoporosis focuses on bone without regarding either the whole muscle-bone system with its feedback loop or the role of falls, but nature has interconnected muscle and bone with each other (Wolff’s law, Utah paradigm). Form follows function, growth of bone is ruled by the stress, which is generated by muscle forces. These interrelationships could be used to supplement and optimize osteoporosis treatment. We have to understand the vital role
of muscle function on bone and falls.

Aiming at the muscle means therefore improving bone and reducing falls simultaneously. A systematic review and meta-analysis of 40 randomized clinical trials has been performed. A multifactorial fall risk assessment and management programme to prevent falls in older adults was the most effective component on risk of falling (adjusted RR = 0.82; 95% CI, 0.72 - 0.94). Exercise interventions also had a beneficial effect (adjusted RR = 0.86; 95% CI, 0.75 - 0.99).

There is a continuous positive relationship between physical activity and bone mass in normal white men, and a site-specific influence of muscle force on bone mass (further references). Strengthening exercises can maintain or enhance bone mass. Unfortunately, the evidence for the negative impact of reduced muscle force or immobilisation on bone strength is far more overwhelming than the positive effect of muscle training on bone development. There are not yet convincing data proving the reduction of fracture rate by physical exercise. A number of animal studies have proven that bone strength can be effectively improved by muscle activities which lead to an increase of bone loading. In rats five jumps of 40 cm height a day are sufficient to improve the maximal breaking force of femur and tibia from a bending moment of 354 (+ - 30) to 409 (+ - 30) Nmm and 216 (+ - 15) to 266 (+ - 21) Nmm, respectively.

Corresponding to the multifactorial pathogenesis of falling, a multifactorial treatment is the most promising approach to counteract gait disorders and the risk of falling.

Firstly we have to avoid bad advice. We find patient advice leaflets which advise patients to always use their arms for support when standing up from a chair. This habit would deprive the patient of one of the best conditioning stimulus of lower extremity force in daily life.

For a person at high risk of falling, hip protectors should be advocated. The safe hip protector, developed by Lauritzen and colleagues, has been found to be effective in preventing hip fractures.

The deterioration of locomotor and balance functions associated with advancing age can be counteracted by gait and balance training. Tai Chi and balance programs have been proven effective in reducing fall frequency. A multifactorial program, including strength training and revision of medication has also reduced fall frequency.

We should minimize using fall-related drugs like neuroleptics, benzodiazepines, tricyclic antidepressants, SSRI-antidepressants and cortisone.

Besides adequate exercising we have to look for drugs with positive effects on muscle function and postural capacity. The D-hormones (alfacalcidol, calcitriol) are promising candidates for enhancing muscle function. D-hormone receptors (VDRs) have been found in skeletal muscles and nerves through which muscle contraction and relaxation will be controlled by influx and efflux of calcium and in addition the muscle protein synthesis. It has been recently confirmed in VDR gene-deleted mice that the absence of VDRs cause a reduction of skeletal muscle fiber size based on an increased expression of myogenic regulation factors (Myf5, Myogenin, E2A) through which the strict regulated differentiation and maturation of muscle cells will be disturbed. The muscular abnormalities are independent from secondary, metabolic changes,
e.g., hypocalcemia or hyperparathyroidism. This confirms the direct efficacy of VDRs. The fact that a treatment with D-hormone of VDR-positive myoblasts in vitro downregulates the mentioned myoregulating transcription factors, point out in addition the important role of D-hormone and VDRs in muscle development. Older age is significantly associated with decreased VDR expression in human skeletal muscle tissue. A positive correlation was found between femoral muscle strength and function and D-hormone serum levels in the elderly. These results suggest that the age-related decline in muscle strength and function and the increase of falls could be in part explained by a decrease of VDRs and a decrease of D-hormone in serum and/or at receptor level.

There is emerging clinical evidence that alfacalcidol, a prodrug of D-hormone, improves muscle function. Histochemical classification based on muscle biopsies of the fibre composition revealed that a treatment of osteoporotic patients with 1μg alfacalcidol for 3-6 months induced an increase in the relative number of fast-twitch fibers. The time taken to dress was significantly less after treatment. The serum concentrations of 25(OH)D were constant during the study.

Alfacalcidol, 0.5μg daily, improved muscle strength (isometric knee extension strength) and functional ability (walking distance over 2 minutes) significantly after 6 months of treatment in elderly D-hormone deficient women.

In patients with rheumatoid arthritis and osteopenia, muscle strength increased significantly by 60% receiving 1μg alfacalcidol daily compared to 18% in patients receiving 1000 IU vitamin D daily.

Gallagher et al. described a significant decrease in the number of falls and the incidence rate of falls and fall-related fractures after 3-years treatment with 0.5μg D-hormone daily in osteopenic elderly women without vitamin D deficiency (Figure 2). In a randomized, double-blind, placebo controlled study Dukas et al. have shown that 1μg alfacalcidol daily reduce significantly the number of falls (-54%) and fallers (-55%) in community dwelling elderly women and men with a total calcium intake of more than 500 mg daily and normal vitamin D serum levels (Figure 3).

A reduced creatinine clearance (CrCl) of <65 ml/min is significantly associated with low D-hormone serum levels and with a significant four-fold increased risk of falls. Thirty six weeks of treatment with alfacalcidol (1μg daily) significantly and safely reduces in community dwelling elderly women and men with a CrCl of <65 ml/min the low CrCl associated increased number of fallers (-74%) and the high risk of falls (-71%).

Alfacalcidol was able to reduce the hip fracture rate significantly and very quickly after 6-months treatment with 1μg daily in stroke patients and after 18 months in elderly patients with Parkinson’s disease.

The positive effects of alfacalcidol and calcitriol on the muscle fibers, daily living activities, muscle strength in patients with rheumatoid arthritis and especially on the reduction of falls was not due to correction of age-related vitamin D deficiency like in some other studies since most of the patients had normal vitamin D serum levels at baseline.
The D-hormone preparations acted as pharmacological treatments by increased levels or action of D-hormone in the target organs muscle and/or nerves.

Based on further confirmation of these findings alfacalcidol opens a new therapeutic strategy for treating osteoporosis by simultaneously increasing bone strength and decreasing falls by improving muscle function. D-hormones could have a double impact on fracture risk by both enhancing bone strength and muscle function.

Regarding the interrelationships between muscle, falls and bones, the traditional bone-oriented approach on extravertebral, osteoporosis-related fractures should be supplemented by fall risk assessment, fall management and treatment of muscle function66.

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