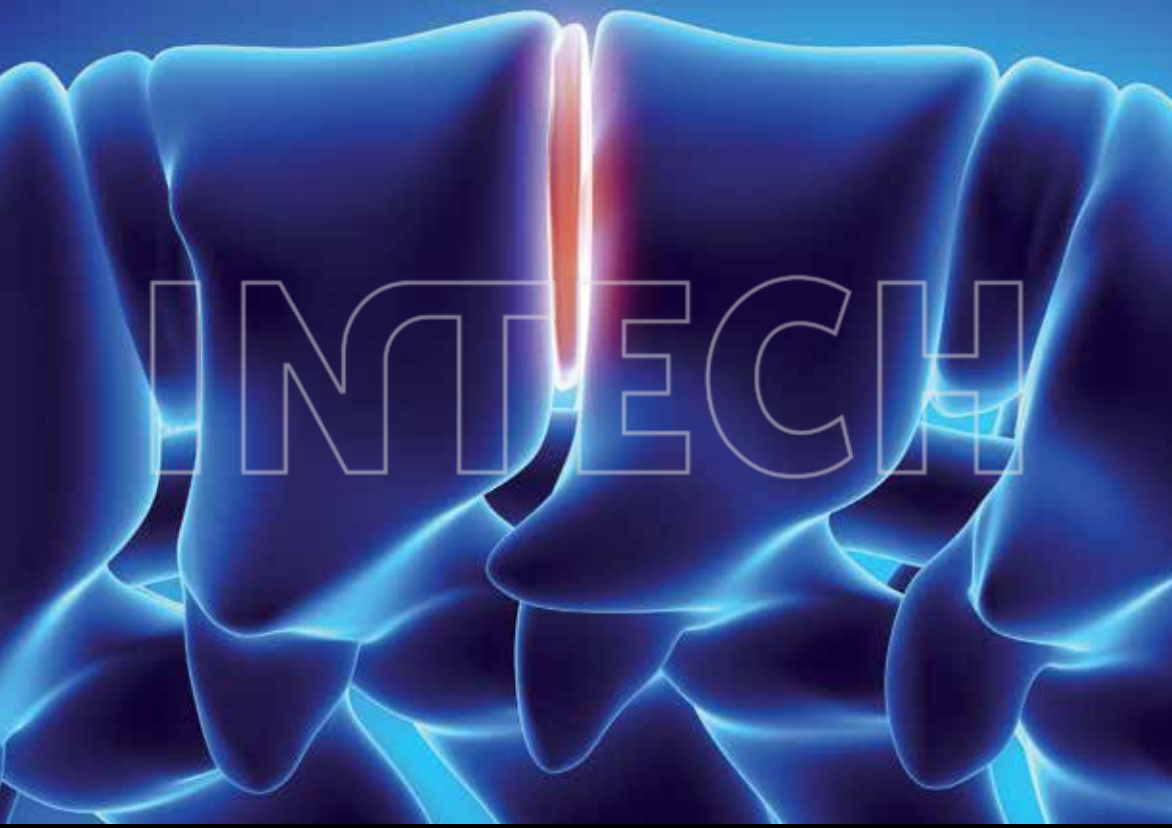
CAUSES AND TREATMENT OF BONE AND MUSCLE CONDITIONS

RESEARCH COLLECTION

by **Yannis Dionyssiotis**



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Preface

Health conditions in which muscle function is impaired and bones are damaged can be highly debilitating. This makes study of their causes and potential therapeutic protocols highly important, and this book offers state of the art knowledge regarding aspects of such conditions. Osteoporosis, the degeneration of bone mass, is considered in several contributions to this book, with chapters on rehabilitation techniques, neurological osteoporosis and paraplegia-related osteoporosis. Body composition is another special concern, with two chapters on body composition's role in disabilities of the central nervous system and paraplegia. Finally, there is a chapter on the effects of malnutrition in paraplegia. Given the range of these studies, this book has much to offer health practitioners and patients alike.

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Body Composition in Disabilities of Central Nervous System

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1. Introduction

Disability leads to immobilisation associated with profound changes in body composition. The potential risks involved with these changes i.e. loss of lean tissue mass (LM) and bone mineral density (BMD) vs. gain in fat mass (FM) in body composition have implications for the health of the disabled individuals (Jones et al., 1998). Body fat has been identified as a significant predictor of mortality in humans making body composition measurement to quantify nutritional and health status an important issue for human health. (Seidell et al., 1996; Bender et al., 1998; Van Der Ploeg et al., 2003). Moreover, some disorders such as carbohydrate intolerance, insulin resistance, lipid abnormalities, and heart disease occur prematurely and at a higher prevalence in disabled populations may be related to adverse changes in body composition that result from immobilization and skeletal muscle denervation (Spungen et al., 2003).

In traumatic and pathological lesions of the central nervous system (CNS) there are differences according to the evolution or not of the lesion (i.e. progressive multiple sclerosis vs. complete paraplegia), the type of injury (i.e. lesion with a level of injury vs. upper motor neuron pyramidal lesion), life expectancy, the residual mobility and functionality, the ability to walk and stand (i.e. incomplete paraplegia vs. quadriplegia vs. high-low paraplegia) and drug treatment (i.e. frequent corticosteroid therapy in multiple sclerosis vs. long-term therapy with anticoagulants in paraplegia). In addition there are differences in the degree of spasticity which is likely to play a regulatory role in maintaining bone density (Dionyssiotis et al., 2011a). We need to take into account the element of fatigue and muscle weakness in disabilities, especially in diseases like multiple sclerosis, which significantly reduces the mobility of these patients (Krupp et al., 2010).

The relative difference in energy expenditure between individuals with multiple sclerosis (MS) and able-bodied subjects is probably lower than the relative difference in physical activity, because individuals with MS have a higher energy expenditure of physical activity (Olgiati et al., 1988). Reduced physical activity (and probably reduced energy expenditure) in MS need to be accompanied by a reduction in energy intake otherwise body fat will increase (Lambert et al., 2002). Subjects with those motor disorders often face problems of depression and limit mobility (Dionyssiotis, 2011b). Moreover, in children with cerebral palsy (CP) studies suggest that increased stretch reflexes and muscle tone, weakness of

involved musculature, and severe limitation of movement reduce the capacity to perform normal movements creating ambulation barriers limiting physical activity. The dependency on mobility devices, common in all disabilities, and the frequent periods of immobilization after multiple operative procedures contribute to the hypoactivity status of such children. It could be assumed that, under these conditions, body composition may be significantly compromised (Chad et al., 2000).

Studies found that lean mass of the contralateral limb was lower compared to the ipsilateral limb in upper motor neuron injury, as occurs in stroke (Ryan et al., 2000; 2002). Similar findings of reduced muscle mass and increased intramuscular fat have been also published in individuals with incomplete spinal cord injury (SCI) (Gorgey et al., 2007) suggesting that reduced muscle mass is fundamentally related to poor fitness and physical performance capacity after stroke (Hafer-Macko et al., 2008).

On the other side the clinical equivalence of diseases with different physiopathology, location, evolution, etc. could be similar; i.e. a severe form of MS can result in a wheelchair bound patient a clinical figure equivalent to paraplegia or a MS patient may have a more appropriate walking gait pattern vs. a patient with incomplete paraplegia but may also be unable to walk at all, is bedridden and vice versa (Dionyssiotis, 2011b; 2011c; 2011d). In addition to these differences and according to osteoporosis the role of factors which do not change, such as race or gender of patients has not been yet clarified, although there are few studies in women debating that bone mass in women with disabilities is more affected than men (Smeltzer et al., 2005; Coupaud et al., 2009).

Therefore, the purpose of this chapter was to present the bone-mineral density, bone-mineral content, and bone-mineral-free lean and fat tissue mass alterations of ambulatory and non-ambulatory subjects with disabilities of the central nervous system.

2. Body composition measurements

2.1 Anthropometric and various techniques of body composition measurements

In a study which investigated a chronic spinal cord injury (SCI) population with paraplegia (Dionyssiotis, 2008a, Dionyssiotis et al., 2008b) values of body mass index (BMI, kg/m^2) did not present statistical significance in relation to the controls, which is a finding in line with the literature (Maggioni et al., 2003; Mamoun et al., 2004).. Nevertheless, there are studies which demonstrate the usefulness of BMI as an indicator of obesity, in body composition in people with spinal cord injury (Gupta et al., 2006). These studies, however, included both tetraplegics and middle-aged people unlike the Greek one which included relatively young individuals (Dionyssiotis et al., 2008a). Whether the criteria of BMI may assess obesity in people with spinal cord injury the latest studies show the opposite (McDonald et al., 2007).

BMI of a male paraplegic group was slightly greater compared to a tetraplegic one and distribution of BMI by level of injury was similar with 37.5% and 40.5% of the male tetraplegic and male paraplegic groups, respectively, falling into the recommended BMI range. Approximately 50% in each male group were overweight by BMI, and 12.5% and 10.8%, respectively, were classified as obese. Overall, when compared with the general population-observed distribution by BMI, a greater proportion of men with SCI fell into the desirable BMI range and fewer fell into the obese category (Groah et al., 2009).

No differences were found in BMI between paraplegics in the acute phase of injury and controls, which is a finding in accordance with other studies in which, despite the same BMI, the body composition and the distribution of fat and fat free mass were altered in patients with spinal cord injury, with the fat free mass being statistically significantly lower in paraplegic patients in total body composition and in the lower, but not the upper limbs. As far as the fat mass is concerned, it was statistically significantly higher (kilograms and %) in the total body composition in the upper and lower limbs (Maimoun et al., 2006).

These findings show that using the BMI does not contribute substantially in determining the body composition of paraplegics and lowers the percentage of fat in this population, finding that agrees with other studies and shows that the anthropometric measurement with BMI in paraplegics, underestimates fat in body composition when measurements are compared with healthy subjects (Jones et al., 1998).

Body mass index is a very simple measurement of fat; however it does not distinguish the individual components of weight. The applicability of conventional BMI cut off values is into question (Buchholz, 2005; McDonald et al., 2007). BMI is an insensitive marker of obesity in subjects with SCI and measuring fat with BMI in chronic paraplegic patients is not enough to determine subject's percentage of fat in the body (Olle et al., 1993).

To standardize or index physiological variables, such as resting metabolic rate and power fat free mass (FFM) is usually used (Van Der Ploeg et al., 2003). Skeletal muscle represents 50% of the non fat component in the total body (Clarys et al., 1984; Modlesky et al., 2004) and exact quantification of the amount of skeletal muscle is important to assess nutritional status, disease risk, danger of illnesses, physical function, atrophic effects of aging, and muscle-wasting diseases (Forbes, 1987; Mojtahedi et al., 2008).

Because muscle wasting is a common sign of cerebral palsy (CP), even in well nourished children, the validity of using muscle wasting as evidence or measurement of malnutrition in CP is in doubt. Studies found that the triceps, midthigh, and calf skinfold thicknesses of the affected side were greater than those of the no affected side among children with hemiplegic CP (Stevenson et al., 1995). Useful information regarding fat provide triceps, subscapular skinfolds and arm-fat area (Patrick & Gisel, 1990). Other studies support the concept that the validity of skinfold thickness as an assessment of limb fat storage is dependent on the preservation of limb muscles (Ingemann-Hansen T et al., 1977) and suggested good sensitivity and specificity of triceps skinfold thickness for predicting mid-upper arm fat area probably were attributable to good preservation of mid-upper arm muscles among children with CP (Samson-Fang et al., 2000).

In disabled children techniques for measuring skinfolds are well established and standardised (Lohman et al., 1988) and equations are available for calculation of body fat from skin fold thickness (Slaughter et al., 1988) although unvalidated in this population, as are normative values for skinfold thickness (Frisancho, 1981; Kuperminc & Stevenson, 2008). Consequently, use of skinfold thickness as a measurement, especially for the affected limb, should be used with discretion in the assessment of children with CP, who tend to have muscle wasting.

In cerebral palsy neither bioelectrical impedance analysis nor predictive equations for skinfold thickness generated from normal, able-bodied adults accurately determined

percentage body fat (Hildreth et al., 1997). Body mass index (BMI), triceps skinfold thickness, subscapular skinfold thickness, suprailiac skinfold thickness, and circumferences of the biceps, waist, forearm, and knee were all significantly correlated with percentage body fat (Bandini et al., 1991).

BMI in patients with MS was statistically less compared to age comparable controls (Formica et al., 1997). In a recent study both total body fat and mass percent showed consistent significant dependence from BMI, as among normal subjects. Multiple linear regression analysis of bone mineral percent at all studied sites showed consistent dependence from BMI (increased with higher BMI) for both patient and control groups (Sioka et al., 2011).

Changes in body composition in spinal cord injured subjects can be assessed with various techniques including isotope-labelled water (Jones et al., 1998) total body potassium counting (Lussier et al., 1983; Spungen et al., 1992) anthropometric measures (Bulbulian et al., 1987) hydrodensitometry (Lussier et al., 1983; Sedlock, 1990) dual photon absorptiometry (DPA) (Spungen et al., 1992; Changlai, 1996) and dual energy X-ray absorptiometry (DXA) (Jones et al., 1998). However, some of these methods are not particularly suitable for use in the SCI population.

The hydrodensitometric model was regarded as the "gold standard" for body composition assessment. This model partitions the body into two compartments of constant densities [fat mass: 0.9007 g/cm^3 and FFM: 1.100 g/cm^3] and assumes that the relative amounts of the FFM components [water, protein, protein, bone mineral (BM), and non-BM] are fixed (Brozek et al., 1963; Van Der Ploeg et al., 2003). Hydrodensitometry is clearly inappropriate for individuals who deviate from these fixed and/or assumed values (e.g., children, elderly, blacks, obese), and its application is, therefore, somewhat limited (Womersley et al., 1976; Schutte, 1984; Lohman, 1986; Fuller et al., 1996).

Bioelectrical impedance analysis (BIA) has been used to measure cerebral palsy subjects. However, the inclusion of weight in the BIA predictive equation may reduce its accuracy in determining change in lean body mass (Forbes et al., 1992). The inability of BIA to accurately predict percentage body fat in the sample may be related to several factors. In the BIA method where the impedance of a geometrical system (i.e., the human body) is dependent on the length of the conductor (height) and its configuration, it is almost impossible to measure accurately height in subjects with CP because of their muscle contractures. An over- or underestimation of height by 2.5 cm can result in a l.0-L error in the estimation of TBW, producing a small error in the estimation of percentage body fat (< 5%). The second major problem is body asymmetry which renders the assumption of a symmetrical configuration of the human body invalid in this case. (National Institutes of Health Technology Assessment Conference Statement, 1994; Hildreth et al., 1997).

Isotope dilution measures the water compartment of the whole body rather than a single area assumed to mimic the composition of the whole body. Thus, the use of a stable isotope to measure body composition is ideal for people with CP because it is non-invasive, does not require the subject to remain still for the measurement, and is independent of height and body symmetry. However, the prohibitive cost of the isotopes and the need for a mass spectrometry facility and highly trained technicians make this method impractical for routine clinical use (Hildreth et al., 1997).

To determine whether bioelectrical impedance analysis and anthropometry can be used to determine body composition for clinical and research purposes in children with cerebral palsy 8 individuals (two female, mean age=10 years, mean gross motor function classification=4.6 [severe motor impairment]) recruited from an outpatient tertiary care setting underwent measurement of fat mass, fat-free mass, and percentage body fat using BIA, anthropometry (two and four skinfold equations), and dual-energy x-ray absorptiometry. Correlation were excellent for determination of fat-free mass for all methods (i.e., all were above 0.9) and moderate for determination of fat mass and percent body fat (range=0.4 to 0.8). Moreover, skinfolds were better predictors of percent body fat, while bioelectrical impedance was a better predictor for fat mass (Liu et al., 2005). On the contrary another study investigated the pattern of body composition in 136 subjects with spastic quadriplegic cerebral palsy, 2 to 12 years of age, by anthropometric measures, or by anthropometric and total body water (TBW) measures (n = 28), compared with 39 control subjects. Body composition and nutritional status indicators were significantly reduced. Calculation of body fat from two skinfolds correlated best with measures of fat mass from TBW (Stallings et al., 1995; Kuperminc & Stevenson, 2008).

Magnetic resonance imaging (MRI) provides remarkably accurate estimates of skeletal muscle in vivo (Modlesky et al., 2004). MRI and also quantitative computed tomography (QCT) have been validated in studies of humancadavers in the assessment of regional skeletal muscle (Mitsiopoulos et al., 1998). Although, these devices have disadvantages of high radiation exposure and are expensive.

2.2 Dual-energy X-ray absorptiometry (DXA)

Recently, dual-energy X-ray absorptiometry (DXA) has gained acceptance as a reference method for body composition analysis (Mahon et al., 2007; LaForgia et al., 2009). Originally designed to determine bone density, DXA technology has subsequently been adopted for the assessment of whole body composition and offers estimation rapidly, non-invasively and with minimal radiation exposure (Van Der Ploeg et al., 2003; Dionyssiotis et al., 2008a). Moreover, is well tolerated in subjects who would be unable to tolerate other body composition techniques, such as underwater weighing (hydro-densitometry) (Laskey, 1996). DXA software determines the bone mineral and soft tissue composition in different regions of the body being a three-compartment model that quantifies: (i) bone mineral density and content (BMD, BMC), (ii) fat mass (FM); and (iii) lean mass (LM), half of which is closely correlated with muscle mass and also yields regional as well as total body values (Rittweger et al., 2000) for example in the arms, legs, and trunk (figure 1).

DXA analyzes differently the dense pixels in body composition. Soft tissue pixels are analyzed for two materials: fat and fat-free tissue mass. Variations in the fat mass/fat free tissue mass composition of the soft tissue produce differences in the respective attenuation coefficients at both energy levels. The ratio at the two main energy peaks is automatically calculated of the X-ray attenuation providing separation of the soft tissue compartment into fat mass and fat-free tissue mass (lean mass) (Peppler & Mazess, 1981; Pietrobelli et al., 1996). A bone-containing pixel is analyzed for "bone mass" (bone mineral content, BMC) and soft tissue as the two materials. Thus, the fat mass/fat free tissue mass of the soft tissue component of the bone pixels cannot be measured, but only estimated (Ferretti et al., 2001).

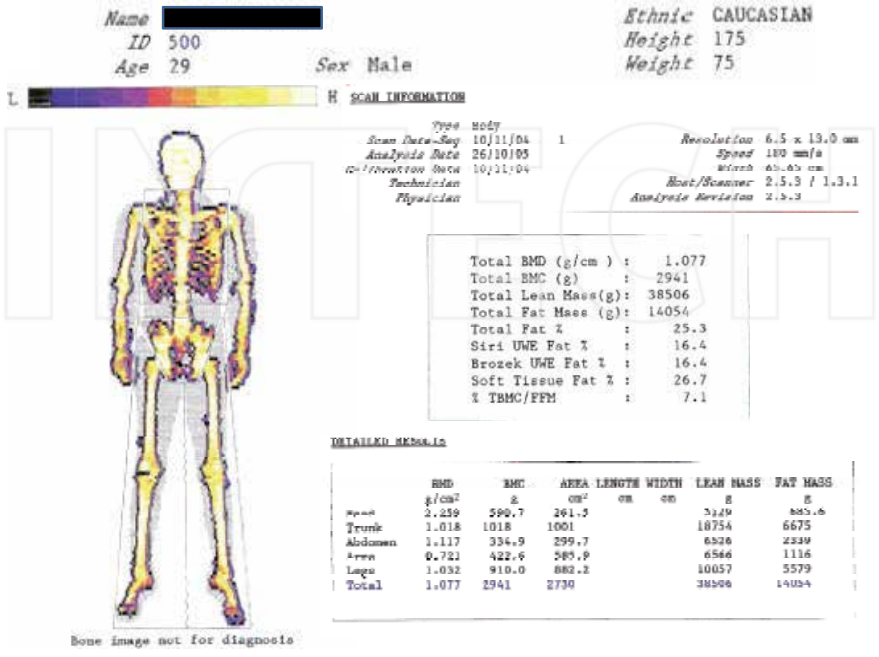
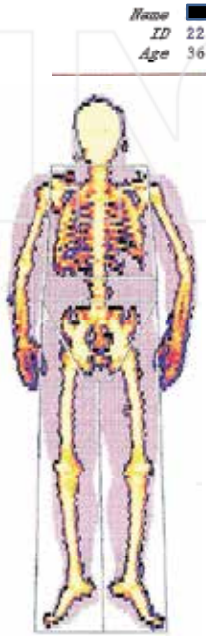


Fig. 1. Whole body and regional distribution of fat mass, lean mass, bone mineral content (BMC) and bone mineral density (BMD) from paraplegic subject thoracic 6 using whole body DXA (Norland X-36, Fort Atkinson, Wisconsin, USA) and values of measured parameters. Modified and translated with permission from Dionyssiotis, 2008a.

The important issue on this is the investigation of distribution of bone mineral, fat and mass throughout the body. These changes induce the risk for diseases such as diabetes, coronary heart disease, dyslipidaimias and osteoporosis (Bauman et al., 1992; Bauman & Spungen, 1994; Kocina, 1997; Garland et al., 1992). There is a need to quantify the alterations in body composition to prevent these diseases and their complications. Studies also reported that bone density measurements at one site cannot usefully predict the bone density elsewhere (Heymsfield et al., 1989) because different skeletal regions, even with similar quantities of trabecular or cortical bone, may respond variably in different physiopathological conditions (Laskey, 1996).

In disabled conditions the accuracy of skeletal muscle measured by DXA may be compromised when muscle atrophy is present. A lower ratio of muscle to adipose-tissue-free mass indicates a lower proportion of muscle in the fat-free soft tissue mass. Cross-sectional area of skeletal muscle in the thighs after SCI is extensively reduced (Castro et al., 1999). If this is the case muscle mass would be overestimated by prediction models that assume that muscle represents all or a certain proportion of the fat-free soft tissue mass, i.e.

in spinal cord injured subjects (Modlesky et al., 2004). DXA technique has been used in assessment of SCI and appears to be tolerated well by this population (Szollar et al., 1997; Uebelhart et al., 1995; Chow et al., 1996).



Name [redacted] Ethnic cauc
ID 2210 Height 180
Age 36 Sex Male Weight 125

Total BMD (g/cm) :	1.256
Total BMC (g) :	3527
Total Lean Mass(g):	79838
Total Fat Mass (g):	40884
Total Fat % :	32.9
Siri UWE Fat % :	29.6
Brozek UWE Fat % :	28.6
Soft Tissue Fat % :	33.9
% TBMC/FFM :	4.2

DETAILED RESULTS

	BMD g/cm2	BMC g	AREA cm2	LENGTH cm	WIDTH cm	LEAN MASS g	FAT MASS g
Head	2.218	586.9	264.6			4142	1035
Trunk	1.254	1181	942.0			48757	25158
Abdomen	1.542	564.3	365.8			17188	12251
Arms	0.781	456.0	583.7			8784	4205
Legs	1.280	1302	1017			26661	11536
Total	1.256	3527	2807			79838	40884

Fig. 2. Whole body and regional distribution of fat mass, lean mass, bone mineral content (BMC) and bone mineral density (BMD) from control male subject using whole body DEXA Norland X-36 and values of measured parameters. Modified and translated with permission from Dionyssiotis, 2008a.

3. Physiopathological context

3.1 Spinal cord injury

Spinal cord injury (SCI) always results in substantial and rapid bone loss predominately in areas below the neurological level of injury. The predominant finding of SCI on bone is a large loss of bone during the first year of injury (Spungen et al., 2003) and an ongoing demineralisation 3 years after trauma in tibia (Biering-Sörensen et al., 1988) with a progressive bone loss over 12 to 16 months prior to stabilizing (Lazo et al., 2001) was demonstrated.

Cancellous bone is more affected than cortical bone after SCI. In a prospective study, six acute tetraplegics were followed up for 12 months, and the trabecular and cortical BMD's of the tibia were found to be decreased by 15 and 7% (Frey-Rindova et al., 2000), while in

paraplegics trabecular metaphysical-epiphyseal areas of the distal femur and the proximal tibia are the most affected sites (Jiang et al., 2006). A cross-sectional study (Dauty et al., 2000) in SCI subjects demonstrated a significant demineralization at the distal femur (-52%) and the proximal tibia (-70%), respectively.

There is no demineralization of the upper limbs in paraplegics. Studies reported a minor increase of BMD while at the lumbar spine trabecular bone demineralization remains relatively low compared to long bones cortical bone demineralization of (Dauty et al., 2000). Normal (Chantraine et al., 1986; Biering-Sorensen et al., 1988; Kunkel et al., 1993) or even higher than normal values were found (Ogilvie et al., 1993), a phenomenon known as "dissociated hip and spine demineralization" (Leslie, 1993) One reason for preservation of bone mass in the vertebral column is because of its continued weight-bearing function in paraplegics but also lumbar spine arthrosis, bone callus, vertebral fracture, aortic calcification, osteosynthesis material, etc. Degenerative changes in the spine may be the most possible reason to give falsely higher values of BMD (Dauty et al., 2000).

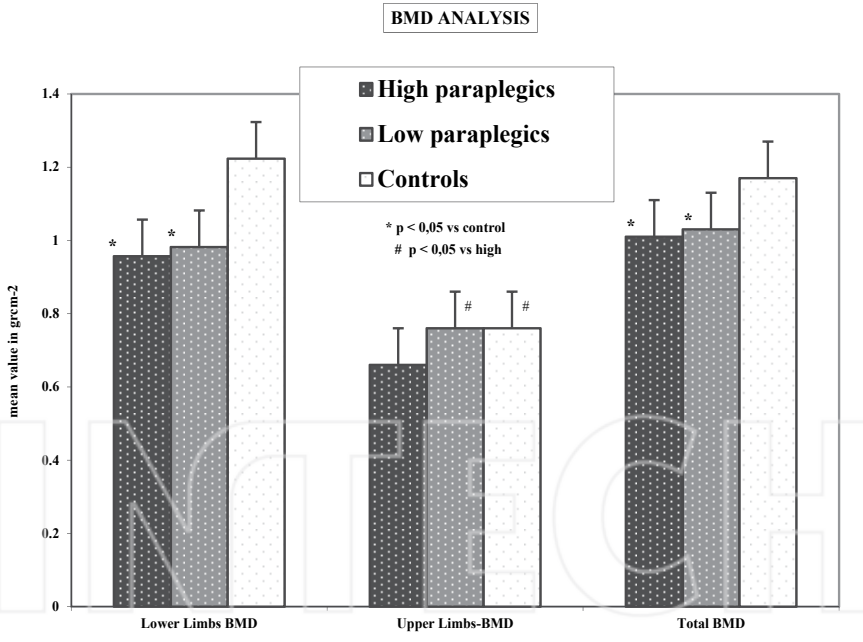


Fig. 3. The picture depicts the analysis of bone mineral density (BMD) in high and low level paraplegics and controls. A statistically significant reduction in total BMD ($p<0.001$) and lower limbs BMD in body composition compared to able-bodied males was observed. On the contrary, upper limbs BMD was higher in low paraplegics and controls, an unexpected finding explained in the paper of Dionyssiotis et al., 2008b. Diagram modified and translated from Dionyssiotis, 2008a.

The neurological level of the lesion i.e. the extent of impairment of motor and sensory function is important, because tetraplegics are more likely to lose more bone mass throughout the skeleton than paraplegics (Tsuzuku et al., 1999). In paraplegics legs' BMC was reduced vs. controls, independently of the neurological level of injury and negatively correlated with the duration of paralysis in total paraplegic group, but after investigation according to the neurological level of injury this correlation was due to the strong correlation of high paraplegics' legs BMC with the duration of paralysis, meaning that the neurological level of injury determines the extent of bone loss (Dionyssiotis et al., 2009). The similar severity of demineralization in the sublesional area was shown between paraplegics and tetraplegics, and the extent of the bone loss may be variable (Demirel et al., 1998; Tsuzuku et al., 1999; Dauty et al., 2000).

The duration of paralysis has an inverse relationship with leg percentage-matched BMD and trunk percentage-matched BMD (Clasey et al., 2004). In addition in complete paraplegics, with high (thoracic 4-7) and low (thoracic 8-12) neurological level of injury, upper limbs FM and lower limbs BMD were correlated with the duration of paralysis in total paraplegic group but after investigation according the neurological level of injury this correlation was due to the strong correlation of high paraplegics' lower limbs BMD with the duration of paralysis. The explanation of this strong correlation could possibly lie on higher incidence of standing in the group of low paraplegics and direct effect of loading lower limbs while standing and walking with orthotic equipment. Moreover, the association of the duration of paralysis with parameters below and above the neurological level of injury (upper limbs FM) raises the question of the existence of a hormonal mechanism as an influential regulator in paraplegics' body composition (Dionyssiotis, 2008a; Dionyssiotis et al., 2008b; 2009).

Actually, little is known regarding the nature and time frame of the influence of complete SCI on human skeletal muscle because published data are coming from cross-sectional studies, where different groups with few subjects have been examined at different times, usually in the chronic phase of paralysis. Disuse was thought to be the mechanism responsible for the skeletal muscle atrophy in paraplegics, but muscle fibres following SCI begin to change their functional properties early post injury. Muscle fiber cross-sectional area (CSA) has been suggested to decline from 1 to 17 months after injury and thereafter to reach its nadir. Conversion to type II fibers has been suggested to occur between 4 months and 2 years after injury, resulting in even slow-twitch muscle becoming predominantly fast twitch thereafter (Castro et al., 1999). Metabolic enzymes levels in skeletal muscle might be expected to be reduced after SCI because of inactivation. In support of this contention, succinic dehydrogenase (SDH) activity, a marker of aerobic-oxidative capacity, has been reported to be 47–68% below control values in fibers of tibialis anterior muscle years after injury in support of this contention (Scelsi, 2001).

The muscle atrophy in SCI is of central type and depends on the disuse and loss of upper connections of the lower motor neuron, sometimes associated to the loss of anterior horn cells and transinaptic degeneration. The last alteration may be responsible for the denervation changes seen in early stages post SCI. In the later stages (10-17 months post SCI) diffuse muscle atrophy with reduction of the muscle fascicle dimension is associated to fat infiltration and endomysial fibrosis. In all stages post SCI, almost all patients showed myopathic changes, as internal nuclei, fibre degeneration and cytoplasmic vacuolation due to lipid accumulation (Scelsi, 2001)

It is evident that other co-factors as spasticity and microvascular damage, contribute to the induction of the marked morphological and enzyme histochemical changes seen in the paralyzed skeletal muscle (Scelsi, 2001). Small fibers, predominantly fast-twitch muscle, and low mitochondrial content have been reported years after injury in cross-sectional studies. These data have been interpreted to suggest that human skeletal muscle shows plasticity (Castro et al., 1999).

On the contrary, force loss during repetitive contractions evoked by surface electrical stimulation (ES) of skeletal muscle in humans does not appear to be altered within a few months of injury (Shields, 1995) but it is greater a year or more after SCI (Hillegass & Dudley, unpublished observations). The greater fatigue, when evident, was partially attributed to lower metabolic enzyme levels (Scelsi, 2001).

Muscular loading of the bones has been thought to play a role in the maintenance of bone density (de Bruin et al., 1999; Dionyssiotis et al., 2011d). However, the ability to stand or ambulate itself does not improve BMD or prevent osteoporosis after SCI.

Controversial results have also been reported regarding the effect of spasticity on BMD in SCI paraplegics. A cross-sectional study of 41 SCI paraplegics reported less reduction of BMD in the spastic paraplegics SCI patients compared to the flaccid paraplegic SCI patients (Demirel et al., 1998). Others reported that spasticity may be protective against bone loss in SCI patients, however, without any preserving effect in the tibia (Dionyssiotis et al., 2011a; Eser et al., 2005). A possible explanation for that could lie in the fact paraplegics to be above thoracic (T)12 level with various degrees of spasticity according to the Ashworth scale. In addition, muscle spasms affecting the lower leg would mainly be extension spasms resulting in plantar flexion thus creating little resistance to the contracting muscles. Furthermore, the measuring sites of the tibia did not include any muscle insertions of either the knee or the ankle extensor muscles (Dionyssiotis et al., 2011a, 2011d). Other investigators also have not been able to establish a correlation between BMD and muscle spasticity (Lofvenmark et al., 2009).

The hormone leptin is secreted by fat cells and helps regulate body weight and energy consumption (Fruhbeck et al., 1998). The percentage of fat in people is positively correlated with the amount of leptin in the circulation (Maffei et al., 1995). In SCI, when compared with healthy subjects, higher levels of leptin have been found, possibly due to greater fat tissue storage (Bauman et al., 1996). Leptin activates the sympathetic nervous system (SNS) through a central administration. The disruption of the sympathetic nervous system i.e. in tetraplegia and high level paraplegia may modify the secretion and activity of the leptin, because the sympathetic preganglionic neurons become atrophic in these subgroups (Elias et al., 1998; Correia et al., 2001) leading to disturbed irritation from leptin below the neurological level of injury. In addition, extensive obesity is known to reduce lipolytic sensitivity (Haque et al., 1999; Horowitz et al., 1999, 2000).

In high level spinal cord injuries there is a disorder of the autonomic nervous system and combined to the fact that the hormone leptin activates the sympathetic nervous system through central control it could be suggested that "the closure of paths" of the central nervous system disrupts the effect of leptin and possibly increases the risk of obesity in SCI subjects with high-level injury (Krassioukov et al., 1999; Jeon et al., 2003). However, after separation of SCI subjects into those with an injury above or below Thoracic (T) 6, leptin levels were significantly higher in the former group. T6 appears to be the lowest level of

injury in most patients with SCI to develop autonomic dysreflexia. With SCIs above the level of T6, there is reduced SNS outflow and supraspinal control to the splanchnic outflow and the lower-extremity blood vessels while serum leptin levels in men with SCI correlated not only with BMI but also with the neurologic deficit. This finding supports the notion that decentralization of sympathetic nervous activity relieves its inhibitory tone on leptin secretion, because subjects with tetraplegia have a more severe deficit of sympathetic nervous activity (Wang et al., 2005).

3.2 Multiple sclerosis

No significant difference between ambulatory multiple sclerosis (MS) patients and non MS controls in body composition was found despite lower physical activity in ambulatory MS patients (Lambert et al., 2002). In MS subjects there was no significant relation between any of the body composition measures and the level of disability as measured by the Expanded Disability Status Scale (EDSS). Others found no difference in body fat percent between ambulatory MS patients (Formica et al., 1997) and lower physical activity in ambulatory MS patients vs. controls (Ng & Kent-Braun, 1997). A possible explanation for the similar body composition may be lower energy intake in MS individuals who are ambulatory and greater energy cost of physical activity (walking) in MS than it is with non MS controls (Lambert et al., 2002).

A significant inverse relation between free fat mass (FFM) and EDSS score when ambulatory and non ambulatory MS subjects were combined was found (Formica et al., 1997). On the contrary others without including non ambulatory subjects did not find a significant inverse relation between FFM percent and EDSS score (Lambert et al., 2002). It would seem apparent that ambulatory patients with MS and controls would strengthen the inverse relation between FFM and EDSS score.

The finding of no relation between EDSS score and body fat percent (Lambert et al., 2002) fits well with studies which found no significant relation between the level of physical activity, and the level of disability in individuals with MS (Ng & Kent-Braun, 1997) because MS would likely have a much greater effect on physical activity than on energy intake. According to these findings it appears that the level of disability of ambulatory individuals with MS does not predict body composition. This suggests that a significant level of disability does not force these individuals to be physically inactive and does not result in a greater body fat content. There are many detrimental manifestations of excess body fat, such as hyperlipidemia, insulin resistance, and type II diabetes (Lambert et al., 2002). The largest component of FFM is muscle mass (Lohman, 1986). If muscle mass is lower in individuals with MS than in controls, it may also contribute to the impaired ability to ambulate and perform other activities of daily living. Muscle fiber size from biopsy specimens of the tibialis anterior were 26% smaller than specimens from control subjects (Kent-Braun et al., 1997). Thus, at least for this small muscle, muscle mass was lower in MS. This relationship may not hold for other muscle groups or for whole-body muscle mass (Lambert et al., 2002).

Another reason for skeletal muscle alterations is glucocorticoid usage. The prolonged duration of glucocorticoid causes catabolism of skeletal muscle. Decreased amino acid transport into muscle and increased glutamine synthesis activity with resultant muscle atrophy are some of the concomitant effects of glucocorticoid use on skeletal muscle.

Endogenous glucocorticoid excess also produces generalized osteoporosis, most prevalent in trabecular-rich skeletal regions (Formica et al., 1997).

Beside corticosteroids, immunomodulatory, antiepileptic and antidepressant drugs usually used in individuals with MS, high incidence of vitamin D deficiency, molecular mechanisms and disuse-loss of mechanical stimuli in bone have an effect on bone integrity (most believe that immobilization of these patients is a minor factor in the etiology of osteoporosis) (Dionyssiotis, 2011).

3.3 Stroke

Longitudinal studies of body composition in the elderly have shown that body cell mass decreases with age and is lower in women than in men (Steen et al., 1985). A decline in body fat in both the dependent and independent groups nine weeks after admission was found, indicating consumption of energy stores. In contrast, the change of body cell mass between admission and after 9 weeks was significantly greater in the dependent patients compared with the independent (Unosson et al., 1994). Immobilized individuals lose muscle mass irrespective of nutritional intake because of reduced synthesis of proteins, while the rate of breakdown of proteins is unchanged (Schonheyder et al., 1954). During the recovery period the stroke patients seemed to break down body fat to compensate for energy needs, independent of their functional condition. However, change of body cell mass appeared to relate to the patients' functional condition after stroke (Unosson et al., 1994).

A study in 35 stroke patients compared the body composition, including lean tissue mass, fat tissue mass, and bone mineral content, of the paretic leg with that of the non affected leg in patients with stroke and evaluated the effects of time since stroke, spasticity, and motor recovery on the body composition specifically within the first year after stroke found lean tissue mass and bone mineral content of the paretic side to be significantly lower than those of the non affected side; a significant correlation was found between the lean tissue mass and bone mineral content of both the paretic and non affected legs after adjusting for age and weight. On the contrary bone mineral content and lean tissue mass of both the paretic and non affected sides were negatively correlated with time since stroke in patients with stroke for less than 1 year and a higher lean tissue mass and bone mineral content were found in patients with moderate to high spasticity in comparison with patients with low or no spasticity (Celik et al., 2008).

3.4 Cerebral palsy

Bone mineralization in children with CP has been found lower (bone-mineral values for the total body and total proximal femur) than sex- and age-matched able bodied children. This is illustrated by the BMC Z – scores determined at each skeletal site. The factors that contribute to low bone mineralization include genetic, hormonal, and nutritional problems (especially calcium and vitamin D) and weight-bearing physical activity, oral-motor dysfunction and anticonvulsant medication (Henderson et al., 1995).

Free fat mass (FFM) in cerebral palsy subjects was found significantly lower than that in a normal adolescent population. In 60% of the studied population body fat exceeded the 90th

percentile for age, even if most of the CP children had a low height and weight for age. In female subjects anthropometric measurements were highly correlated with measures of body fatness. Measuring fat by ^{18}O dilution a hydration factor of 0.73 was assumed for FFM. A possible increase in the hydration factor would diminish measured FFM meaning that body fat appears increased. Moreover muscle spasms and spasticity in CP subjects deplete body glycogen. If glycogen is reduced the intracellular water would be reduced and the ratio extracellular water/total body water would increase. The same could result with a loss of body cell mass or an increase in the hydration factor (Bandini et al., 1991).

4. Conclusions

Other important issues according alterations of body composition are the completeness of lesions (an absence of sensory or motor function below the neurological level, including the lowest sacral segment), because body composition seems to be worst than subjects with incomplete lesions (partial preservation of motor and/or sensory function below the neurological level, including the lowest sacral segment) (Sabo et al., 1991; Demirel et al., 1998; Garland et al., 1992) and aging which contributes to major alterations of body composition.

In disabled subjects the most important issue according to body composition is how to promote optimal body weight to reduce risk of diseases such as coronary heart disease, non-insulin dependent diabetes mellitus, lipid abnormalities and fractures because of bone loss. Dietary changes, individualized physical activity programs and medication should be taken in mind in therapy when we deal with this subgroup of subjects. However, self-management of dietary changes to improve weight control and disease should be the case, which means they need to follow diets with lower energy intake and at the same time to eat regularly foods rich in nutrients (Groah et al., 2009).

We need to take in mind that healthy BMI values often underestimate body fat and may mask the adiposity and spasticity did not defend skeletal muscle mass and bone, supporting the concept that in neurologic disabilities the myopathic muscle could not recognize correctly the stimulation because of the neurogenic injury. Moreover, disabled subjects mostly transfer much of the weight-bearing demands of daily activities to their upper extremities reducing the weight-bearing of the affected paralyzed muscles triggering a cycle of added muscle atrophy which interacts with the continuous catabolic action caused by the neurogenic factor. Finally, an irreversible (once established) decline in bone mineral density, bone mineral content as well as geometric characteristics of bone is expected and the duration of lesion-injury is positively correlated with the degree of bone loss.

Further research about body composition is needed in all physical disabilities and more longitudinal studies to quantitate and monitor body composition changes and to modify our therapeutic interventions. However, prevention rather than treatment may have the greatest potential to alleviate these major complications. Therapies should focus on how to perform weight bearing, standing or therapeutically walking activities early in the rehabilitation program to gain benefits according to muscles and bones.

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Rehabilitation in Osteoporosis

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1. Introduction

Osteoporosis is a metabolic bone disease usually occurring with increasing age and is defined as a skeletal disorder characterized by reduced bone mineral density and strength. Osteoporosis is characterized as the "silent disease" because is painless until the first occurrence of a fracture and thus remain unnoticed. The first symptom of osteoporosis is the bone fracture with a preference of distal radius or proximal humerus fracture, vertebral collapse and femoral neck fractures beyond the 50th, 60th and 70-75th year respectively (Pfeifer et al., 2005). This phase of the disease is characterized by acute pain. Moreover, vertebral fractures cause acute musculoskeletal pain in the back in the acute phase of the fracture and chronic pain resulting from the associated skeletal deformity, joint incongruity, and tension on muscles and tendons, leading to disability. In generally osteoporosis represents one of the main causes of back pain in postmenopausal women because of common clinical or subclinical vertebral fractures causing back pain. On the other hand, in the same population, no osteoporotic vertebral deformities are seen as often as osteoporotic ones, and back pain was found to be mostly due to degenerative disorders of the spine in women above 60 years (Dionyssiotis, 2010b).

Osteoporosis is a disease that predominantly affects postmenopausal women and older people although in individual cases could concern people in younger age i.e. in the juvenile form, mainly men with idiopathic osteoporosis, pregnancy-associated osteoporosis, the form of secondary osteoporosis in young steroid-treated patients with chronic inflammatory diseases etc. The goals of rehabilitation are changing depending on the stage of disease. In the acute phase of a vertebral body collapse the therapy is to the relief pain by a limited period of bed rest, local and systemic analgesia, bracing, physical therapy, education with proper exercises and instructions according to daily living activities in order to mobilise the patient with safety. Rehabilitation after surgical stabilization of a hip fracture is crucial in order to optimize post-injury mobility and the functional recovery of the patient, restore pre-fracture function and avoid long-term institutionalization. Most evidence-based guidelines suggesting possible treatments and rehabilitation pathways for hip fracture patients, agree that it would be best if they underwent multidisciplinary rehabilitation (Dionyssiotis et al., 2008a).

In prevention and management of osteoporosis modern rehabilitation medicine should not only focus on bone ignoring muscular strength and balance. These elements are directly related to the disease offering protection against predisposing a person to an increased risk of falls and fall-related fracture. An extensive research in the area of pharmacological

treatment is ongoing. Pharmacologic treatment increases bone strength, but has no effect in muscle strengthening or balance. Moreover beyond drugs there are other interventions often overlooked: supplementation with calcium, exercise programs, orthoses, vitamin D, and fall prevention.

2. Calcium, vitamin D and vitamin D analogues

All of the studies on the effectiveness of anti-osteoporotic drugs required the taking of calcium and vitamin D and recent findings reveal a decreased effectiveness of therapy in individuals with low levels of vitamin D during the therapy (Nieves et al., 1998; Koster et al., 1996; Adami et al., 2009). Trials reporting bone-mineral density, calcium and calcium in combination with vitamin D were associated with a reduced bone loss at the hip and in the spine. A positive treatment effect on bone-mineral density was evident in most studies (Tang et al., 2007). In opposition to findings on the use of calcium and vitamin D together, studies which researched the relative role calcium or vitamin D separately, produced conflicting results. Moreover, calcium and vitamin D or vitamin D by itself increase muscular strength and decrease the number of falls Bischoff-Ferrari, et al., 2006; Bischoff et al., 2003).

Pooled data comparing vitamin D alone with placebo or no treatment showed no statistically significant effect on vertebral fracture or deformity. Vitamin D (including 25-hydroxy vitamin D) with calcium was no more effective than calcium alone on vertebral fracture. Evidence has shown that vitamin D alone was less effective than calcium for the prevention of vertebral fracture or deformity. There was no evidence of a statistically significant preventive effect on clinical vertebral fractures from the administration of vitamin D and calcium and vitamin D plus calcium versus placebo or no treatment. In participants with osteoporosis no statistically significant effect of alfacalcidol (1-alpha-hydroxy vitamin D3) compared with vitamin D and calcium on people with new vertebral deformities was found. Calcitriol (1,25 dihydroxy vitamin D3) and additional supplementation with calcitriol in people with osteoporosis already taking calcium had no statistically significant effect on new vertebral deformity. No statistically significant effect on the number of people developing new vertebral deformities receiving calcitriol plus vitamin D and calcium versus vitamin D and calcium was found. Overall, there was no statistically significant effect on the incidence of vertebral deformities with calcitriol versus calcium. When calcitriol was compared with vitamin D in people with pre-existing osteoporosis no statistically significant effect was seen for vertebral deformities (Avenell et al., 2009).

3. Exercise in osteoporosis

3.1 Biomechanics and mechanobiology of bone

One useful introduction to understanding the response of bone in physical activity is to understand bone's morphology and mechanical properties (Dionyssiotis, 2008b). Bone is a unique material, within the functional structure of the skeleton, which is strong enough to withstand the demands of intense physical activity and external forces exerted, adjusted to changes in those requirements, and light in weight to allow efficient movement and energy saving. The mechanical capacity of bone is a function of internal properties of material (mass, density, stiffness, strength) and geometrical characteristics (size, shape, thickness of cortical cross-sectional area and architecture of trabeculae). The peripheral bone adapts to mechanical loading through endosteal resorption and periosteal apposition of bone tissue

(Figure 1) (van der Meulen, 1993). This increases the diameter of the bone and therefore provides greater resistance to the loads. This adaptive process allows the bone to resist in compression, tension and shear forces, but also to be light enough for efficient and economical movement (Wolff,1870).

Fig. 1. An increase in bone dimensions during development and the gradual age-related endosteal resorption, periosteal apposition and cortical thinning. The increase in bone strength because of the increase in diameter replaces the loss of density (adapted, modified and translated with permission from Dionyssiotis, 2008b).

According to Wolff's law bone will optimize its structure, to withstand the functional burden and to ensure the metabolic efficiency of movement (Wolff, 1892). The loading of the skeleton is described as a strain that produces the modified response of bone to loading. It has been suggested that the osteocyte reacts-perceives the strain and transmits signals to osteoblasts to build bone. The magnitude of strain can be defined as the amount of relative change in length of the bone under mechanical loading (Beck et al., 2001). Mechanical stimulation generated by exercising has at least two opposite effects on bone. The bone as a material is weakened by repeated strains, causing minor damages on bone structure; on the other side, stress strain which exceeds a certain threshold leads to generation and thereby adjusts the strength of the bone load usually applied (Wolff, 1870). This is a feedback cycle, which is usually called as the mechanostat (Frost, 1987a).
The mechanostat theory describes a system in which a minimum effective strain (MES) is essential for maintaining bone (Frost, 1987b). In the overload zone of the system (2000–3000 micro strain) bone is stimulated and new bone is added in response to mechanical requirement. This leads to increased bone strength. Finally, in the pathological overload zone (>4000 micro strain), a minor damage of bone is present and bone mineral is added as part of the repair process. A sufficient number of studies suggest the ability of estrogen to alter the set point of bone strain in responses to mechanical loading as the result of indirect effect of oestrogen' receptors number (Lanyon & Skerry, 2001; Lee & Lanyon, 2004). The decrease in sensitivity of oestrogen receptors as a result of oestrogen deficiency may reduce the response of bone to mechanical loading (Cheng et al., 2002; Jessop et al., 1995). Strain of about 1.000 micro strain increases bone formation, in the presence but not in the absence of oestrogen. Loading forces in the skeleton are caused by gravity (weight bearing), muscles and other external factors.

3.2 Targeted exercise for osteoporosis

Physical activity targeting muscles and balance is the cornerstone of each rehabilitation program for osteoporosis and fracture prevention. Although, in postmenopausal individuals, results of physical activity studies on the positive association of physical activity with bone status are conflicting (Burger et al., 1998; Nguyen et al., 1998). However, it is clear that physical activity is vital in adults (Kelley, 1998; Beitz & Doren, 2004) because it reduces the rate of bone loss during the peri-menopausal period, and decelerates bone loss associated with aging (Asikainen et al., 2004).

In the design of an exercise program to increase bone mass we need to take in mind the following five principles (Drinkwater, 1994) 1. Specificity: The program must be designed to load specific bones or body regions, 2. Overload: To induce stimulation for increasing bone density according to mechanostat theory exercise must overload the bone, 3. Reversibility: In adults, any gains in bone density during an exercise program will be lost if the program stops. However, in children and adolescents the benefits achieved by increased mechanical loading during exercise program remain even if the exercise program stops, 4. Initial Values: The response of bone to increased loading is greater when bone mass is below average. Patients with bone mass below normal will experience greater gains in bone density with exercise programmes, compared with people who have a good bone density, 5. Diminishing Returns: The greatest gains in bone density will be seen early in an exercise program. After the initial increase, the benefits continue but at a slower pace. We added the 6th principle of Variety which is a component of success in all exercise programs. We need to enrich the programs with various exercises and not perform the same exercises, at the same duration and interval. By changing the way of bone and muscle stimulation we challenge them in new way shifting the loading stress causing new results (Dionyssiotis, 2008b).

To summarize the principles: Not all types of physical activities that provide bone loading to the skeleton produce bone mass benefits. Some activities (i.e. a progressive jogging program) charge and stimulate adaptation of the cardiovascular system, but do not stimulate an adaptive bone response that would increase bone density (Khan et al., 2001). The bone has a lazy zone! Each exercise that stimulates the metabolism in the body (i.e. exercise for the cardiovascular system etc.), is not able to stimulate the adaptation of bone to increase bone density. The load on a bone during the exercise should be substantially greater than the load experiencing of the bone during activities of daily living. There is definitely a threshold load which must be reached to generate gains in bone mass. Moreover, loading of the bone should be done in such a way that mimics the physical loads (Skerry, 1997).

There are also activities that provide bone loading at one site of the body, but not at other sites. The osteogenic effects of exercise should be specific to the anatomical sites where the mechanical strain occurs (Lohman et al., 1995). The most common types of physical activities (e.g., gardening, swimming) use many muscles but do not involve targeted bone loading, and therefore do not produce loads heavy enough to exceed the load threshold on bones achieved by usual daily activities (Beck & Snow, 2003; Madalozzo & Snow, 2000). The duration of the physical activity is also important; up to 2 hours per week is considered to positively affect bone mass maintenance (Snow-Harter & Marcus, 1991). Muscle strengthening, weight bearing combined with flexibility, posture control, balance, coordination and training in daily living activities to improve functional capabilities of the subjects should be part of a rehabilitation program in osteoporosis. The following subchapters explain basic exercises of each category (except balance and coordination exercises which will be analyzed in the subchapter of falls prevention) in detail.

3.2.1 Muscle strengthening exercises

In osteoporosis we do not recommend muscle strengthening in generally. Programs are focused on specific regions of the skeleton where fractures are most commonly expected, namely the spine, the hip and the wrist. For this reason in all ages, but particularly in postmenopausal women, exercise programs focusing on muscles in these regions (Table 1) including exercises for the back muscles, the hip and the hand (with weights or pulleys) but also for the thighs because research has shown that the quadriceps is an important muscle for balance and falls prevention.

Type Muscle strengthening	Target	Intensity Frequency Duration	Time to target	Contradictions
Using body weight, free weights, elastic bands, sophisticated equipment in the gym etc.	Increasing strength, stimulate bone to increase bone density (targets are mostly hip muscles, back muscles, biceps, triceps)	8-10 repetitions 2 sets 2-3 times weekly 20-30 minutes	6 months for bone mineral density changes	Subjects with kyphosis should avoid bending and turning the spine and perform the exercises seated

Table 1. Muscle strengthening exercises in osteoporosis; the table summarises the following characteristics of this type of exercise: how we can do them, which are the targets, the intensity, frequency and duration of the program, when to expect the results and the contradictions (Dionyssiotis Y. , 2010 c).

Fig. 2. *(1 to 6) Back muscles:* This group of muscles is usually underestimated in exercise programs, but it requires special attention. The subject should begin warm up in the prone position with the hands flat on the ground and the elbows facing outwards and hold for one minute (photo 1), then raise the head keeping this position for five seconds (photo 2), then return to the starting position. The exercise needs to be repeated five times. The simplest style is photo 3: from the prone position to raise only the hands, with the elbows bent at 90 degrees, whereas it becomes more difficult when the arms are placed at the side of the body and the head is gently raised (photos 4, 5). The exercise needs 15 repetitions 6 times per day (3 in the morning – 3 in the evening). As strength increases it is possible to do more difficult exercises; from a kneeling position, extend one arm and raise the opposite leg. This exercise should be repeated ten times every day. (Dionyssiotis Y., 2010 c).

Fig. 3. *Resistance against a wall (such as push-ups)*: The subject stands opposite a wall and place the hands against the wall with the palms flat on the wall. The feet are spread 15 cm apart. In the next step the subject presses against the wall with the elbows bent and then returns to the initial position. This exercise needs 20 repetitions 3 times per day (Dionyssiotis Y., 2010 c).

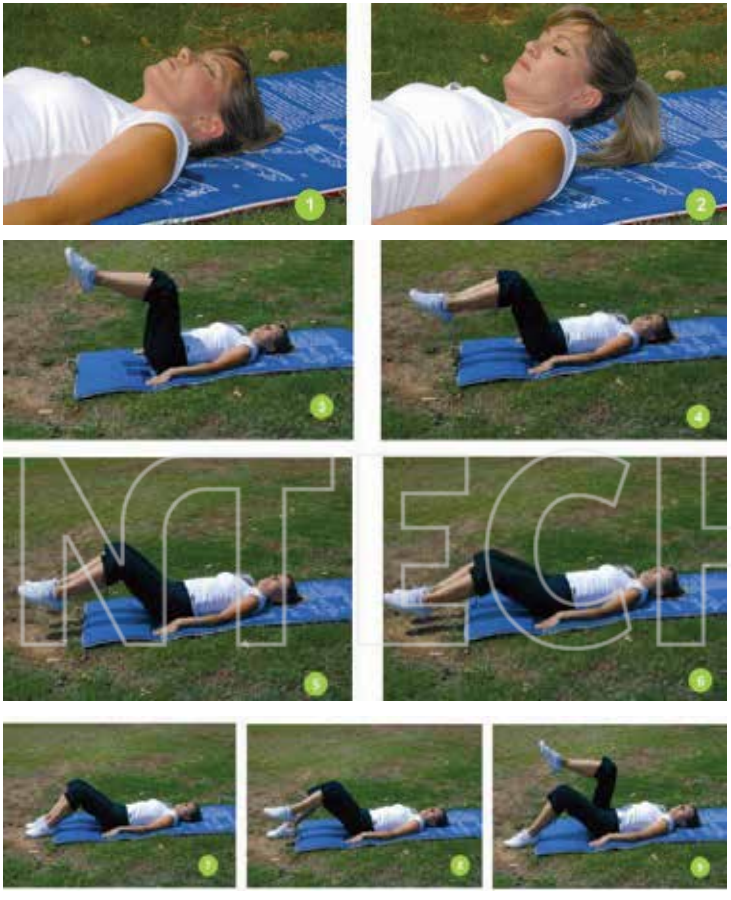

Fig. 4. *Abdominal muscles strengthening*: The subject should begin warm up in the supine position, bringing the chin to the chest for five to ten repetitions (photos 1, 2). The safest exercise for abdominal muscle strengthening includes performing from the supine position with the back flat on the ground, the legs raised and the knees bent at ninety degrees (photo 3). The knees are then extended while lowering the legs with movement coming from the hip joint (photos 4, 5, 6). The spine must be flat on the ground while this exercise is performed. If it is not possible to perform the total movement of this exercise, it should be performed in the half of range as shown in photograph 4. If this exercise causes pain, the subject should alter it as follows: with the legs bent and the sole of the foot on the ground, bend one leg to the abdominals then lower the leg to the ground and the same movement with the other leg (photos 7, 8, 9). Another option is to raise the head with the arms extended to touch the knees (photo 10), (Dionyssiotis Y., 2010 c).

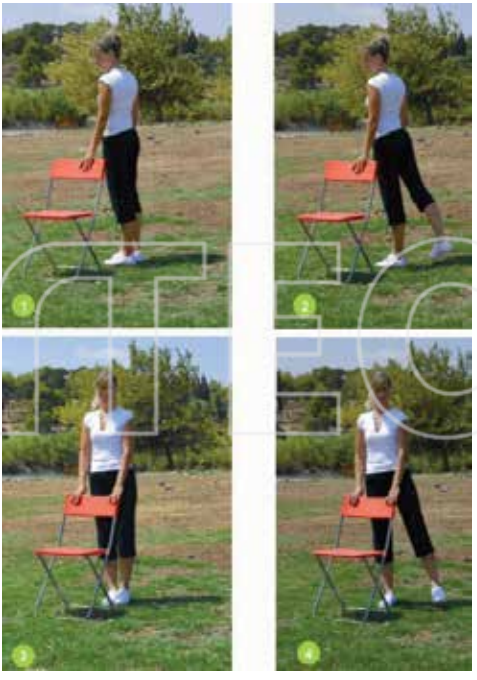

Fig. 5. *Extensor and abductor muscles of the hips:* The subject places the hand on a fixed spot for safety (i.e: chair photo 1) and lift one leg backwards in order to exercise the gluteus maximus muscle extensor muscle (photo 2). Then the movement is repeated with the other leg. From the same position lifts one leg to the side, in order to strengthen the gluteus medius muscle abductor muscle (photo 3); then the other leg follows. For each leg three sets of 15 repetitions are needed. Both exercises can be done with pulleys (at home or at the gym), lying sideways on the ground and also with specific equipment at the gym under the guidance of a qualified instructor (see photos 5-9). Keeping good technique during this exercise is very important and four sets of fifteen repetitions are necessary (Dionyssiotis Y., 2010 c).

Fig. 6. *Quadriceps:* The subject sits upright in a chair with the back as straight as possible, the knees bent and the feet flat on the ground (a chair with armrest is recommended), grips the chair firmly and extends one knee at a time keeping it extended for 4 seconds. This exercise is particularly indicated for elderly people and after hip surgery. The exercise can be done with pulleys and with special equipment in the gym. Each leg needs fifteen repetitions (Dionyssiotis Y., 2010 c).

Fig. 7. *Exercises with dumbbells for the arms:* Exercises for strengthening the biceps and triceps can be done from a standing or seated position. From a standing position the subject flexes the knees slightly, and using medium weights performs three sets of 10 repetitions with each arm (photos 1, 2, 3). Weights can be replaced with pulleys for lower resistance (Dionyssiotis Y., 2010 c).

Subjects need to perform the exercise as above with the same number of repetitions remembering to maintain the correct posture while exercising. For additional safety, exercises should be performed in a seated position by patients with severe osteoporosis.

3.2.2 Weight bearing exercises

Weight bearing exercises are exercises during which the weight of the body passes through the bones. Examples of these types of exercises are walking, jogging, dancing, gardening, tennis, football, basketball and trampoline etc. There is a variety of this type of exercise to suit every age group. The impact to the bone during this exercise should be higher than that during normal everyday activities. Many women believe that housework and the level of

activity it involves constitutes a good level of exercise. However, this is not correct as in order for exercises to be effective they need to be performed with specific technique and systematically.

Type Weight bearing	Target	Intensity requency Duration	Time to target	Contradictions
Walking, jogging, dancing, gardening, tennis, basketball etc.	Maintenance of bone mass Improvement in physical function	40-70% max. Power 3-5 times/ week 20-30 min	9-12 months to improve BMD	Bending and turning in patients with osteopenia

Table 2. Weight bearing exercises; the table summarises the following characteristics of this type of exercise: how we can do them, which are the targets, the intensity, frequency and duration of the program, when to expect the results and the contradictions (Dionyssiotis Y., 2010 c)

Fig. 8. *Walking:* Dynamic walking is the best option for prevention of osteoporosis. Simple walking is not enough; it should be in an open environment without obstacles, not around the house or workplace. Dynamic walking differs from regular walking and to achieve maximum benefit to the skeleton a special technique is required. Brisk walking (dynamic walking) does not require any special equipment except for a good pair of training shoes. Moreover it has the advantage of low risk of injury. Walking should begin at a normal pace, progressively increasing after five minutes to a medium and then to a fast pace for twenty minutes. The pace must be sufficient to allow normal speech but not so fast that the person is out of breath. The level of intensity however should be sufficient for the person to sweat. In order to move the feet faster it is necessary to move the hands faster. Arms should move in the opposite direction to the feet. During the movement of the hands, the subject need to flex the elbows and keep the arms close to the body. Attention should be paid to change of pace, using bigger steps and the feet should be kept in a forward facing direction and not sideway. This kind of walking should be done as often as possible (Dionyssiotis Y., 2010 c).

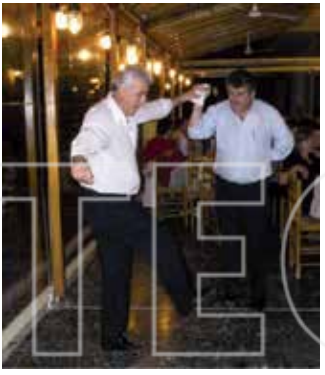

Fig. 9. *Dancing* as exercise is safe and social which in turn makes this an attractive activity. Jumps and aerobic weight bearing exercises during dancing or gymnastics are related to increasing and maintaining bone density. Traditional Greek dances include movement like jumps, sideways steps and squatting which have a weight bearing effect on the hip and spine (Dionyssiotis Y., 2010 c).

3.2.3 Postural exercises

The aim of these exercises is to: Eliminate the bent-over position (hunchback), which increases the pressure on the front part of the vertebrae and to improve stability. Exercises can be done in the sitting or standing position with eyes open or closed. The optimal is to be performed in front of a mirror and next to a wall. The reason why the exercises are performed in front of a mirror is that the trainees can see their reflection and can correct the possible mistakes in their posture, with the guidance of the experts (visual biofeedback). The wall assists the safe performance of the exercises.

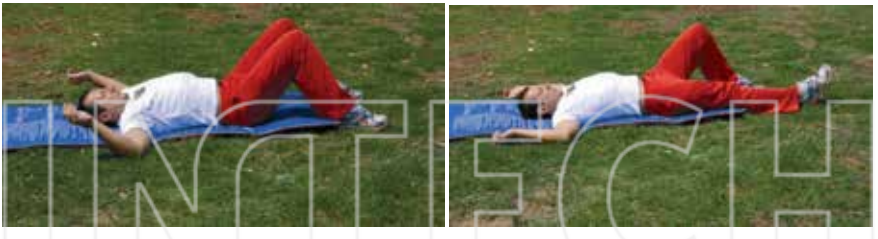

Fig. 10. *Exercises in patients with osteoporosis for correction of posture: Decompression of the spine*: the exercise starts lying on the ground with the knees bent, the feet flat on the ground, the elbow bent and the palms facing upwards and this position is kept for five minutes. This exercise decompresses the spine and relieves back pain. *Shoulder press:* beginning from the same position, the shoulders are pressed to the ground holding for three seconds, and then the subject relaxes himself and repeats three times. This exercise strengthens the muscles of the upper back. *Leg press:* beginning with the position of exercise 1) above, the subjects extends one leg with foot pointing upwards, presses the full length of the leg into the ground, concentrates for 2-3 seconds and relaxes himself. The same steps are performed with the other leg (4 repetitions with each leg). This exercise helps with posture and strengthens the extensor muscles of the thigh (Dionyssiotis Y., 2010 c).

3.2.4 Flexibility exercises

During aging the body becomes more rigid which results in movement difficulties leading to falls and increasing risk of fracture. For this reason it is necessary to perform exercises to maintain flexibility. The exercises in this category help to maintain the elasticity and the length of the muscle, the range of movement of the joints, improve posture and reduce pain (mostly back pain etc).

Fig. 11. *Stretching the pectoralis major (stretching of the chest):* From the standing or sitting position (for greater safety), with the arms bent at the elbows and to the side of the torso, the subject moves the elbows backwards (photo 1). The arms can also be raised in front of the chest with the elbows bent up to the height of the shoulders (photo 2) and then spreads open the arms stretching them out (photo 3). The exercise should be performed daily with 10 repetitions, 3 times (Dionyssiotis Y., 2010 c).

Fig. 12. *Stretching the upper torso:* In this exercise the subject stands or sits on a comfortable chair, the fingers are placed behind ears, palms facing forwards and elbows pointing outwards (photo 1). Stretching the chest by pushing the elbows backwards (without pressing the head) is followed holding this position for 4 seconds and then bringing the elbows together, in front of the face, in order to stretch the muscles of the upper back (photo 2). Exercise is repeated 5-10 times (Dionyssiotis Y., 2010 c).

Fig. 13. *Stretching muscles of the lumbar spine:* The subject is kneeling on the floor with knees slightly apart (photo 1), raises the arms high towards the ceiling and carefully bends forwards, until the palms touch the floor (photo 2, 3), keeping this position for several seconds and repeats 5 times (Dionyssiotis Y., 2010c).

3.2.5 Exercises to improve functional ability – Osteoporosis and daily living activities

The program of exercises becomes more efficient if combined with the use of proper body mechanics and posture in everyday activities.

Fig. 14. *Lifting, carrying and placing weights; the correct and wrong way to lift and place objects:* The correct way for the osteoporotic patient to lift an object is to bend the knees, the hips and the ankles so that the object is at waist level. Bringing the object towards him with both hands and returning to the upright position using the strength of both feet. The spine should be straight during this movement, keeping the head and chest upright and the abdominal muscles tight. An osteoporotic patient is not allowed to lift more than 5-10 kg. The subject stands next to the object keeping the back straight bending the knees and lifting the weight using the strength of the feet and not that of the back, avoiding turning or rotating during the weight lift. The weight must be kept at the level of the waist. When transferring a heavy object, it is preferable to push rather than to pull it and while carrying a weight to separate it evenly on both sides of the body. The abdominal muscles should be flexed, so that the back is in the correct position (Dionyssiotis Y., 2010 c).

Fig. 15. *The correct way for the osteoporotic patient to get up from chair:* The head and the chest must be in the upright position, the body must be bent forward using the hip joint and the base of the spine must be slightly bent with the help of abdominal muscle contraction. Standing up is achieved using the leg muscles. The subject should sit at the edge of the chair with feet slightly behind the knees, pushing forward by placing the weight on toes of the feet while getting up. If necessary the arm rests can be helpful in getting up from the chair. With this way subject is getting up keeping the back and the neck straight (Dionyssiotis Y., 2010 c).

3.2.6 Whole body vibration as antiosteoporotic intervention

Vibration platforms are used in rehabilitation of osteoporosis, based on the concept that non-invasive, short-duration, mechanical stimulation could have an impact on osteoporosis risk. The mechanical loading of bone can be done with application of non-physiological factors, such as vibrations that combine dynamic loads and high intensity loading on the skeleton (Dionyssiotis, 2008b). The implementation should be shortly and has specific indications, contraindications and adverse reactions. These machines cause whole-body vibration. The vibration is a mechanical stimulation of the whole body; the person is standing on the vibration platform trying to keep his head and body straight and upright. All the muscles that keep the body in this position are forced to react to the oscillating movements provided by the device. The duration of this exercise depends on the type of machine in order to have measurable results and benefits.

According to the mechanostat theory bones need great forces for their development. The mechanical loading of bone can be done either with usual exercise activities as those reported in subchapter 3.2 or by applying non-physiological factors, such as body vibration. With platforms goal is achieved safely, without injury and quickly. Mechanical loads are applied in a dynamic way with a high intensity defined by its frequency (hertz) and magnitude, where magnitude is expressed as vertical acceleration (g; 1g=9.8 m/s^2 acceleration due to gravity) or vertical displacement (millimeters). In the scientific world there is a debate about how exercise with vibrations develops bones. One theory holds that low vibration intensity but high frequency can cause osteogenic response by direct action on bone (Rubin et al., 2001). They support the following concept: because of small strains caused by this mechanism, there are benefits to bone without the risk of causing mechanical damage.

The credibility of this theory has been demonstrated in sheep, where one arm vibration caused a 34% increase in volumetric trabecular bone mineral density of the femur (Rubin et al., 2002). Moreover through this type of vibration trabecular bone density of the tibia in children with cerebral palsy was increased, whereas bone loss was expected without treatment (Ward et al., 2004). A recent study demonstrated benefits in postmenopausal women: an increase of 2.2% and 1.7% in bone density of the hip and spine respectively (Rubin et al., 2004). The second theory supports the concept of the important action of the muscles; vibrations make bones stronger through powerful muscular contractions (Rauch & Schoenau, 2001; Rittweger et al., 2000; Schiessl et al., 1998). In postmenopausal women, bone density increased by 1% after 6 months when vibration of static and dynamic knee-extensor exercises on a vibration platform (35-40 Hz, 2.28-5.09g) was performed which also increased muscle strength (Verschueren et al., 2004). However, these increases were also evident in the comparison group of women who performed traditional resistance exercises. A study performed on immobilized young men (Berlin bed rest study) concluded that a combination of vibration and resistance exercises prevent bone loss due to immobilization (Rittweger & Felsenberg, 2004). A systematic review and meta-analysis found significant but small improvements in BMD in postmenopausal women and children and adolescents, but not in young adults (Slatkovska et al., 2010).

Fig. 16. Galileo vibration platform (Novotec Medical GmbH, Pforzheim, Germany, with permission).

3.3 Exercise and bone density

The effect of aerobic exercise on bone density has been studied by review papers which report a decrease in bone loss at the spine and wrist but not at the hip (Bonaiuti et al., 2002; Martyn-St James & Carroll, 2008; Martyn-St James & Carroll, 2006). In meta-analysis studies which reviewed the effects of walking on bone density showed that walking has a small effect on sustaining bone density at the spine in postmenopausal women, however it has a significant positive effect on the femoral neck and concludes that other types of exercises which provide larger "targeted" weight bearing forces are needed to maintain bone density in this group (Martyn-St James & Carroll, 2006). In a review of 35 RCT's it was shown that in premenopausal women and in postmenopausal women intense exercise probably had a

positive effect on the femoral neck and in spinal lumbar bone density, where less intensive exercise also helped (Kerr et al., 1996). In one meta-analysis study it was found that systematic high intensity resistance training is required for the maintenance of spinal lumbar bone density in postmenopausal women; however weight bearing exercise is necessary to help bone density of the hip beyond any other therapeutic intervention (Kelley, 1998).
In a three year period during the EFOPS study (Erlangen Fitness Osteoporosis Study), which included a exercise protocol with a combined strengthening program, jumping and high intensity resistance training in early onset postmenopausal women, sustained the bone density in the spine, the hip and in the heel, however not in the forearm. A well planned study which compared muscle strengthening exercises with weights and with resistance exercises with repetitions showed that the weight used was more important than the number of repetitions in postmenopausal bone (Engelke et al., 2006). A similar analysis in men revealed similar results (Kelley et al., 2000). With respect to bone quality a review study which used peripheral quantitative computed tomography (pQCT) revealed that exercise possibly increased bone mass and geometry in postmenopausal women, changes which theoretically increase bone resistance. Specifically, the effects of exercise are moderate, area specific and act primarily on cortical rather than trabecular bone (Hamilton et al., 2010).

3.4 Combined exercise with calcium, bisphosphonates

A decreased rate of bone loss in postmenopausal women undergoing exercise and taking calcium supplements is reported in comparison with exercisers only suggesting that calcium deficiency reduces the efficacy of loading to improve bone mass (Prince et al., 2006). In another study included 1890 pre- and postmenopausal women measured by quantitative ultrasound (QUS) at the heel and assessed with validated questionnaire according to physical activity and daily calcium consumption (greater than or less than 800 mg/day) was found that systematically active premenopausal and postmenopausal women had significantly higher values of QUS parameters than their sedentary and moderately active counterparts. Moreover a statistically significant difference in QUS T-score between sedentary premenopausal women and those who exercise systematically was found suggesting that vigorous physical activity is a regulator of bone status during premenopausal years (Dionyssiotis et al, 2010a).
In a randomized, double-blind, placebo-controlled trial the primary endpoint was the 12-month change in bone mass and geometry of the effects of weight-bearing jumping exercise conducted in an average 1.6 ± 0.9 (mean ± SD) times a week and oral alendronate, alone or in combination, measured with dual-energy X-ray absorptiometry and peripheral computed tomography at several axial and limb sites. A total of 164 healthy, sedentary, early postmenopausal women were randomly assigned to one of four experimental groups:(1) 5 mg of alendronate daily plus progressive jumping exercise, (2) 5 mg alendronate, (3) placebo plus progressive jumping exercise, or (4) placebo. Alendronate daily was effective in increasing bone mass at the lumbar spine and femoral neck but did not affect other bone sites. Exercise alone had no effect on bone mass at the lumbar spine or femoral neck; it had neither an additive nor an interactive effect with alendronate at these bone sites. However, at the distal tibia the mean increase in the section modulus (a bone strength parameter) and in the ratio of cortical bone to total bone area were statistically significant in the exercise group compared to the non exercise group, indicating exercise-induced thickening of the bone cortex. The authors concluded that alendronate is effective in increasing bone mass at

the lumbar spine and femoral neck, while exercise is effective in increasing the mechanical properties of bone at some of the most loaded bone sites (Uusi-Rasi et al., 2003).
On the other hand the combined and separate effects of exercise training and bisphosphonate (etidronate) therapy on bone mineral in postmenopausal women were investigated in forty-eight postmenopausal women randomly assigned to groups that took intermittent cyclical etidronate; performed strength training (3 d/week) and received matched placebo; combined strength training with etidronate; or took placebo and served as non-exercising controls. Bone mineral was assessed by dual-energy X-ray absorptiometry before and after 12 months of intervention changes in bone mineral density (BMD) of the lumbar spine were greater in the subjects given etidronate compared with placebo, while exercise had no effect. No effect of etidronate or exercise on the proximal femur and there was no interaction between exercise and etidronate at any bone site was found (Chilibeck et al., 2002).

4. Modern orthoses in osteoporosis

Traditionally, spinal orthoses have been used in the management of thoracolumbar injuries treated with or without surgical stabilization. The vast majority of orthoses, however, are used in patients with low back pain (Perry, 1970). These orthoses, however, have never been tested under standardized conditions. Especially, no prospective, randomized, and controlled clinical trials are available to document efficacy according to the criteria of evidence-based medicine. Moreover, there is a lack of specific studies comparing various types of braces and orthoses. This is also the case for osteoporosis, in which approximately one-fourth of women above 50 years of age have one or more vertebral fractures (Melton, 1993).
Even though, it is widely accepted that spinal orthoses whether made of cloth, metal, or plastic, or whether rigid or flexible, relieve pain and promote the healing process by stabilizing the spine i.e. reducing the load applied on the anterior column and vertebral body by restraining any attempt of forward flexion. The most broadly used types of spinal orthoses use a three-point pressure system (Dionyssiotis et al., 2008; Mazanec et al., 2003): a) the TLSO type (Knight-Taylor, Jewett, CASH or Cruciform Anterior Sternal Hyperextension brace, Boston); that provides support to the thoracolumbosacral spine by making it adopt an anatomically correct position. The CASH or Jewett brace has been favoured for patients with acute vertebral fractures. The goal of these braces is to provide forces to encourage hyperextension. However, a drawback to these orthoses is the limited compliance because of their rigid configuration, b) the PTS (Posture Training Support) type, or the newer postural training support vest with weights (PTSW), two orthoses made of a softer material, gained popularity because of their improved comfort and increased compliance. The postural training support is worn over the shoulders similar to a mini-backpack and has a pocket into which small weights (total 1.75 lb) weights are added. The postural training support vest with weights is similar except that it is fashioned as a vest, with a Velcro attachment that fastens around the abdomen (Sinaki & Lynn, 2002), c) Spinomed and Spinomed active based on biofeedback theory (Pfeifer et al., 2004; Pfeifer et al., 2011); Spinomed consists of an abdominal pad, splint along the spine, back pad, and a system of belts with Velcro. The back orthosis consists of a back pad, which is workable as a cold material, and a system of belts with Velcro. This allows adjustments for individual sizes by an orthopedic technician. The orthosis weighs 450 g and is worn like a back pad and d) Osteomed, which is based upon

the gate control theory of pain (Vogt et al., 2008); the external appearance of the orthosis Osteomed resembles an item of clothing characterised by a constructively functional cut with Velcro tabs exerting pressure in the lumbosacral region as well as air chamber pads fixed in the paravertebral and lumbosacral areas which are filled with air to between 2/3 and ¾ of their maximum capacity (Vogt et al., 2008).

Fig. 17. Front, back and lateral view of the Spinomed (unpublished images of Dionyssiotis et al.)

Fig. 18. Front, back and lateral view of the Spinomed active orthosis for men and women (Medi-Bayreuth, Bayreuth, Germany, with permission).

In a controlled pilot study with a 4-week observation period the strength of the back extensors was reduced to below the initial value in 40% of female patients wearing a stable orthotic device pointed out that orthotic devices impose a risk of reduction in muscular strength (Kaplan et al., 1996). On the contrary, recently published results of women with established osteoporosis and/or an angle of kyphosis more than 55 degrees wearing Spinomed for at least 2 hours/day for 6 months showing significantly decreased back pain ($p=0.001$) (evaluation was performed using visual analogue scale at the beginning and 6 months follow up of the examination) and increased personal isometric trunk muscle strength (figure 19) (Dionyssiotis et al., 2010b). Moreover in another Spinomed study subjects separated in two groups, the control and orthosis group, who switched after 6 months. Wearing the orthosis resulted in a 73% increase in back extensor strength, a 58% increase in abdominal flexor strength, most likely because of increased muscular activity while wearing the orthosis, a 11% decrease in angle of kyphosis, a 25% decrease in body sway, a 7% increase in vital capacity, a 38% decrease in average pain, a 15% increase in well-being, and a 27% decrease in limitations of daily living (Pfeifer et al., 2004).

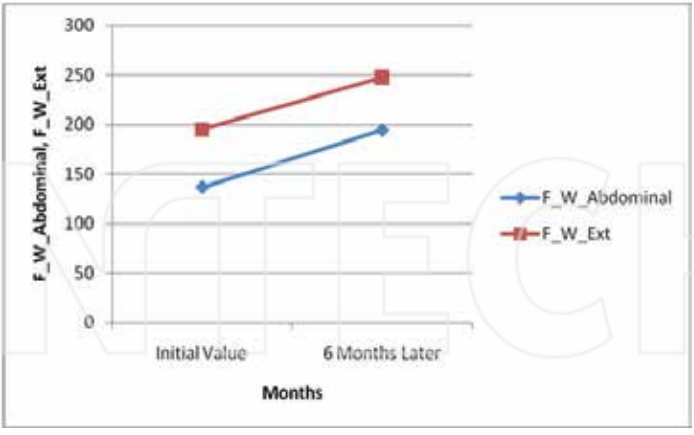

Fig. 19. Schematic presentation of differences in the values of personal isometric force: Force (F)/Weight (W) in abdominals and extensors muscles (F/W abdominals and F/W extensors, respectively, after 6 months wearing Spinomed orthosis (F: force in Newton, W: weight in Kg), measured with ISO-RACK device (Digimax, MechaTronic, Hamm, Germany). Figure adapted from Dionyssiotis et al., 2010b (with permission).

According to the results obtained from Osteomed studies, the orthosis brings an active erection of the spine of 60% on average of the deliberate maximum possible active erection. The wearing of the orthosis leads to an improvement of posture and statics (Vogt et al., 2005), a straightening of the spine of on average 46% of the conscious maximum achievable straightening (Vogt et al., 2008) and a statistically significant and clinically relevant reduction in chronic back pain by approximately 25% in female patients with osteoporosis worn it in a period of 2.5 months (Fink et al., 2007).

Fig. 20. a) Front view of the Osteomed osteoporosis orthosis (Osteomed, Thaemert Ltd, Germany), b) Dorsal view of the Osteomed osteoporosis orthosis (for demonstration purposes the air chamber pads are shown on the outside), c) View of the orthosis without air chamber pads, d) View of the placebo device (adapted from Fink et al., 2006, with permission).

Strengthening the back muscles not only maintains bone density in the spine but also reduces the risk of vertebral fractures. Ten years after a 2-year back exercise program in women fractures, both wedging and vertebral compression fractures, were significantly less (only 11% in the exercise group as compared to 30% in the control group) several years after the exercises were discontinued (Sinaki et al., 2002).

5. Prevention of falls and fall related fractures

An important issue in rehabilitation medicine is the prevention of falls and fall related fractures. Falls is a serious problem facing elderly persons. Falling results in increased mortality, morbidity, reduced functioning and premature nursing home admissions. Falls generally result from an interaction of multiple and diverse risk factors and situations, many of which can be corrected (Dionyssiotis et al., 2008a).

Falls can also result in deterioration of physical functioning and quality of life due to injury or due to fear of falling; 16% of fallers reported that they limited their usual activity because of fear of falling and one third of fallers reduced their participation in social activities (Nevitt et al., 1991). Fear of falling is reported by one in four older people in the community and can lead to distress and reduced quality of life, increased medication use and activity restriction, further decline in physical functioning, greater falling risk and admission to institutional care (Yardley et al., 2005). It is necessary to assess possible intrinsic and extrinsic risk factors for falls, as well as the exposure to individual's risk (Todd & Skelton, 2004).

Identifying risk factors is as important as appreciating the interaction and probable synergism between multiple risk factors because the percentage of persons falling increased from 27% for those with no or one risk factor to 78% for those with four or more risk factors (Tinetti et al., 1988). Important potentially modifiable risk factors for community-dwelling older adults are: mental status and psychotropic drugs, multiple drugs, environmental hazards, vision, lower extremity impairments, balance, gait status and for institution-dwelling older adults: mental status, depression, urinary incontinence, hypotension, hearing, balance, gait, lower extremity impairments, low activity level (exercise less than once a week), psychotropic drugs, cardiac drugs, analgesics and use of a mechanical restraint; non-modifiable risk factors (i.e. hemiplegia, blindness) also exist (Moreland et al., 2003).

Interventions to prevent falls may be planned to reduce a single internal or external risk factor of falling or be broadly focused to reduce multiple risk factors simultaneously (Sjösten et al., 2007). Single evidence based interventions include exercise, reassessment of medications and environmental modification (American Geriatrics Society [AGS], British Geriatrics Society [BGS], and American Academy of Orthopaedic Surgeons [AAOS], 2001; Tinetti, 2003). Although exercise has many proven benefits, the optimal type, duration and intensity of exercise for falls prevention remain unclear. Older people who have had recurrent falls should be offered long-term exercise and balance training (Dionyssiotis et al., 2008a).

5.1 Exercise for falls prevention

5.1.1 Balance exercises

Without good balance, there is always the danger of fracture. This type of exercise is the most important in falls prevention. Simple exercises for balance are walking heel to toe beside a wall or rail and balancing on one foot. The purpose of the exercises is the development of synchronized movements, resulting in balanced sitting and standing positions (Dionyssiotis, 2010c).

Fig. 21. Heel to toe exercise and balance standing on one foot: walking heel to toe beside a wall or rail for a short time. In alternative standing at the side of a chair (for safety) and leaning on the chair with one hand, whereas at the same time the opposite leg is raised with the knee bent as shown in the picture. Subjects perform the exercise, first with open and then with closed eyes and continue by changing side and leg of support. Ten repetitions for each leg are necessary (Dionyssiotis Y., 2010 c).

5.1.2 Coordination exercises

These exercises help the cooperation of muscle and nerves in order to avoid falls and fractures and should be done routinely every day for at least 5 minutes. This category includes exercises such as marching, walking around a chair and throwing and catching a ball.

Fig. 22. Marching (photo 1) and walking around a chair (photos 2 and 3). Marching is an excellent exercise for coordination. Training consists of the simultaneous movement of one arm and the opposite leg in turn. During the execution of the exercise, the head must look forward; the arms must be slightly bent on the elbows and must reach up to the height of the shoulders. Placing a chair in a room, to make it able to walk around it on all sides, walking clockwise and then counter clockwise, as fast as they can, (should stop before getting dizzy) and repeat for 5 times (Dionyssiotis Y., 2010 c).

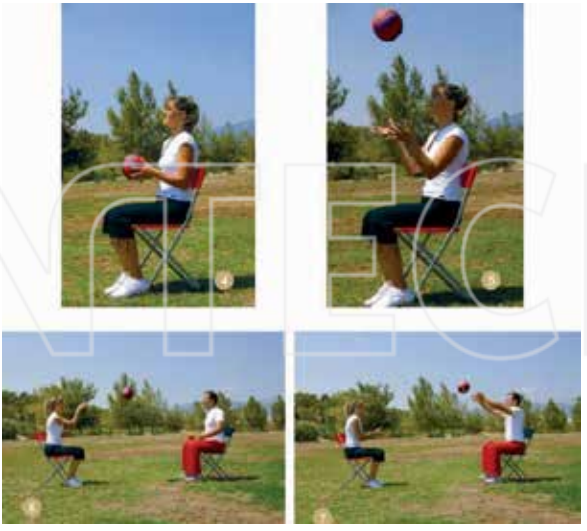

Fig. 23. Exercise balls. Throwing and catching a ball is a very good exercise for coordination. The exercise is performed for security, from the sitting position and the ball thrown at a low height (photos 4 and 5). After enough practice at the previous exercise and while still in the sitting position, the ball can be thrown to and from another person sitting opposite (photos 6 and 7), (Dionyssiotis Y., 2010 c).

Type Balance & Coordination	Target	Intensity Frequency Duration	Time to target
Execution in parallel bars or next to a wall or a chair, because it has to be safe, in order to avoid falls	Improving coordinated movements resulting an improve in balance in seated and standing position	medium intensity 5-7 times/week 5-10 min	2-4 weeks

Table 3. Balance and coordination exercises are important for falls prevention; the table summarises the following characteristics of this type of exercise: how we can do them, which are the targets, the intensity, frequency and duration of the program and when to expect the results (Dionyssiotis Y., 2010 c).

5.1.3 Tai Chi

Tai Chi is a promising type of balance exercise, although it requires further evaluation before it can be recommended as the preferred method for balance training (AGS, BGS, AAOS, 2001). Tai Chi which consists of slow, rhythmic movements emphasizing on the trunk rotation, weight shifting, coordination, and a gradual narrowing of the lower extremities position is thought to be an excellent choice of exercise for the elderly.There is experimental evidence from both cross-sectional and longitudinal studies that Tai Chi exercise has beneficial effects on balance control and that the postural stability is improved

more by Tai Chi than by other types of exercise (Graafmans et al., 1996). Although Tai Chi is probably the exercise programme we would least recommend to people who have previously suffered fractures because they show a level of frailty that means they could not fully participate in Tai Chi unless it was adapted so much it was no longer dynamic balance training (Skelton D, personal communication). From the most training studies after hip fracture it seems that combined training with task-specific and functionally based exercises may be a sensible way of retraining leg strength, balance and gait ability in elderly people after a hip fracture. The training thus may include a variety of gait exercises, step exercises, stair climbing, and rising from and sitting down on a chair (Sherrington et al., 2004; Hauer et al., 2002; Lindelοf et al., 2002).

5.1.4 Clinical trials and multifactorial intervention

A review about the effectiveness of interventions to prevent falls in older adults concluded that exercise programs help prevent falls with no differences between types of exercise (Chang et al., 2004).The results from the FICSIT trials (Frailty and Injuries: Cooperative Studies of Intervention Techniques) suggest that interventions that addressed strength alone did not reduce falls. On the other side balance training may be more effective in lowering falls risk than the other exercise components (Lord et al., 2007).

Others concluded that exercise programmes must be regular and sustainable to be effective but more trials are required to determine the exercise type, frequency, duration, and intensity that are most effective in lowering falls risk in different groups of older people (Gardner et al., 2000). However, as ageing is related with reduced physical functioning, exercise prescription for falls prevention, beyond balance and strength training, may include exercises to increase the functional capabilities in all elderly. The suggested guidelines especially for the Greek population are low intensity balance exercises (tandem walking and standing on one's foot) combined with coordination exercises. Individuals who are frail, severely kyphotic or suffer from pain or poor balance may benefit from water exercise (hydrotherapy). People are also advised to undergo strengthening exercises of the quadriceps, hip abductors/extensors, back extensors and the arm muscles (Dionyssiotis et al., 2008a)

Frequent fallers should have their medications reviewed. Studies have indicated that the use of medication is a potential cause for falls (Hartikainen et al., 2007). Central nervous system drugs, especially psychotropics warrant particular attention, since there is very strong evidence that use of these medications is linked to the occurrence of falls. Reducing the total number of medications to four or fewer, if feasible, has also been demonstrated to reduce the risk of falling (AGS, BGS, AAOS, 2001; Tinetti, 2003). Environmental hazards could be a cause of falls (Lord et al., 2007). In reducing environmental hazards, falls prevention programs may need to provide and install safety devices particularly in the homes (Wyman et al., 2007). Studies have shown that when older patients at increased risk of falls are discharged from the hospital, a facilitated environmental home assessment should be considered (AGS, BGS, AAOS, 2001; Tinetti, 2003).

There is emerging clinical evidence that alfacalcidol, a prodrug of D-hormone, improves muscle function (Runge & Schacht, 2005). In community dwelling elderly women and men with a total calcium intake of more than 500 mg daily and normal vitamin D serum levels 1 μg alfacalcidol daily reduced significantly the number of falls (-54%) and fallers (-55%) (Dukas et al., 2004). Other authors reported that cholecalciferol-calcium supplementation

reduces falls by 46% to 65% in community-dwelling older women, but has a neutral effect on falls in men (Bischoff-Ferrari et al., 2006). Prevention may be even more effective when multiple risk factors of falls are taken into account. Most multifactorial fall prevention programmes have been successful in reducing the incidence of falls and risk factors of falling, especially when prevention has been individually tailored and targeted to populations at high risk of falling (Moreland et al., 2003).
Multifactorial interventions should include: a) among community-dwelling older persons (i.e. those living in their own homes), gait training and advice on the appropriate use of assistive devices, review and modification of medication, especially psychotropic medication, exercise programs, with balance training as one of the components, treatment of postural hypotension, modification of environmental hazards and treatment of cardiovascular disorders, b) among older persons in long-term care and assisted living settings staff education programs, gait training and advice on the appropriate use of assistive devices and review and modification of medications, especially psychotropic medications (AGS, BGS, AAOS, 2001; Tinetti, 2003).

6. Rehabilitation of common osteoporotic fractures

Successful operative treatment of hip fracture victims is necessary for the optimization of post-injury mobility and the functional recovery of the patient (Koval, 2005). Two evidence-based clinical practice guidelines suggesting possible treatments and rehabilitation pathways for hip fracture patients, agree that it would be best if they underwent multidisciplinary rehabilitation (Scottish Intercollegiate Guidelines Network [SIGN], 2002; Chilov et al., 2003). Multidisciplinary rehabilitation can be defined as the combined and coordinated use of medical, social, educational and vocational measures for training or retraining the individual to the highest possible level of function (Cameron, 2005).
Hip fracture patients should start breathing exercises so that pulmonary secretions are drained, thus reducing the risk of atelectasies and other complications deriving from the pulmonary system. "Pump like" energetic exercises (ankle pumps) and dorsal/plantar flexion of the foot, knee joint flexion, exercises for the hip and thigh, abduction exercises for the gluteal muscles and exercises for the quadriceps are important. Exercises of the upper extremities and trunk must also be part of the rehabilitation program, so that the patient can move in bed, stand up from a chair and later on be able to mobilize himself by using crutches or a stick. Abdominal and dorsal muscles should also be exercised isometrically and then energetically, in order to minimize the risk of low back pain during weight-bearing exercises (a detailed rehabilitation program is published in Dionyssiotis et al., 2008a).
After a vertebral fracture a program of physical therapy is necessary and helps prevent deformity by strengthening anti-gravity muscles and promoting postural retraining. Breathing exercises promote thoracic expansion and improve the heavily degraded pulmonary function found in patients with spinal osteoporotic fractures (Pfeifer et al., 2004). Instruction on the proper way of lifting things, as well as how to appropriately use a walker or a cane, could be beneficial and thus is strongly recommended. Patients with fractures could perform low-intensity exercise and gentle strengthening programs (e.g., Tai Chi and hydrotherapy) and are strongly recommended to avoid high impact exercise or movements, so that they avoid suffering new vertebral fractures (Tosi et al., 2004). Forward bending of the spine or flexion exercises, especially in combination with twisting, should be avoided.

This includes several old favourite exercises which are now considered outdated, namely straight-leg toe touches and sit ups (or crunches) for strengthening the abdominal muscles (Bassey, 2001). The latter are associated with a dramatically increased rate of vertebral fracture in osteoporotic women (89% compared to 16% of those who did extension exercises) (Sinaki & Mikkelsen, 1984). As the acute fracture pain subsides, a walking program can begin with gentle strengthening exercises focusing on spinal extensor muscles (Bonner et al., 2003). A carefully supervised rehabilitation program should be started after 3 to 4 months, to strengthen the spinal extensor and abdominal muscles more aggressively (a detailed rehabilitation program is published in Dionyssiotis et al., 2008a).

Physical therapy after a Colles' fracture consists of muscle strengthening, motion range recovery, wound healing and scar adhesion. Early reduction of oedema is of primary importance in determining hand functions. Elevation of the hand above the heart's level and an active range of motion exercises are instructed to facilitate the pumping action of hand muscles to decrease swelling. Physical modalities and exercise programs consisting of passive and active range of motion; transverse scar massages, progressive resistive exercise, focusing on strengthening both extrinsic and intrinsic muscle groups of the hand are necessary (Morey & Watson, 1986; Dionyssiotis et al., 2008a). Physical therapy is followed by occupational therapy for 3 weeks (Christensen et al., 2001).

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Neurological Osteoporosis in Disabilities

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1. Introduction

Osteoporosis is characterized by low bone mass and destruction of the micro architecture of bone tissue, resulting in increased bone fragility and susceptibility to fractures (NIH 2001). The clinical usefulness of T-score at disabled people on the recognition of people with low BMD remains unclear according to ranking system of the World Health Organization (WHO 1994). Despite the increased number of risk factors in people with disabilities no guidelines are available on BMD measurements; so it would be more appropriate to use the term low bone mass instead of osteoporosis or osteopenia and also take into account the Z-score obtained from the measurement of bone densitometry which is the number of standard deviations above or below that normally expected for someone of similar age, sex, weight and race in question (Dionyssiotis, 2011c, 2011d).

In disabled subjects there are differences according to the type of injury (i.e. lesion with a level of injury vs. upper motor neuron pyramidal lesion), the type of lesion; complete (an absence of sensory or motor function below the neurological level, including the lowest sacral segment) vs. incomplete lesion (partial preservation of motor and/or sensory function below the neurological level, including the lowest sacral segment), the progression or not of the disease (i.e. progressive multiple sclerosis vs. complete paraplegia), life expectancy, the residual mobility and functionality, the ability to walk and stand (i.e. incomplete paraplegia vs. quadriplegia vs. high-low paraplegia), drug treatment (i.e. frequent corticosteroid therapy in multiple sclerosis vs. long-term therapy with anticoagulants in paraplegia), the degree of spasticity (i.e. flaccid vs. spastic paralysis) and it is necessary to take into account the issue of fatigue and muscle weakness. Depression in these subjects is usual; complicates the proposed treatments and limits mobility. Complete and incomplete disabled differ also in physical abilities. Moreover, subjects with complete injuries have greater bone loss than those with an incomplete injury (Garland et al., 1994) and as has already been shown in Brown-Sequard subjects (incomplete spinal cord lesion) where BMD of the more paretic knee was lower than that of the stronger knee (Lazo et al., 2001).

However, there are also similarities; for example the clinical equivalence of diseases with different physiopathology, location, evolution, etc. A severe form of multiple sclerosis (MS) can result in a wheelchair bound patient having a clinical figure equivalent to spinal cord injury paraplegia. One patient with MS may have better walking gait pattern in comparison with a patient with incomplete paraplegia but may also be unable to walk, bedridden and vice versa (Dionyssiotis, 2011c, 2011d).

In addition the role of factors which do not change, i.e.: race or gender is inadequately clarified. Studies in disabled women debate that bones are more affected compared to disabled men. In chronic spinal cord injured women a tendency to have lower bone mass than men (Coupaud et al., 2009) and higher rates of lower bone mass with lower T-scores compared to women with other disabilities have been reported (Smeltzer et al., 2005).

2. Spinal cord injury

Bone loss in spinal cord injury (SCI) is a multifactorial disease in acute and chronic phase and can be enhanced by the lack of weight bearing, muscular tension on bone or other neural factors associated with the injury. Moreover, differentiation of the sympathetic nervous system after SCI is leading to venous and capillary vascular stasis. Some additional non-mechanical factors to stimulate bone loss include poor nutritional adequacy, gonadal changes and other endocrine disorders (Chantraine 1978; Chantraine et al., 1979b; Jiang et al., 2007; Maimoun et al., 2006).

2.1 Bone mineral density

In individuals with SCI bone loss begins immediately after injury (Bauman et al., 1997; Uebelhart et al., 1995). SCI related bone impairment below the level of injury is much greater compared with other conditions (i.e. age, immobilization, bed rest, lack of gravity environment). A reduction of bone mineral content (BMC) during the first years after the injury of 4% per month in regions rich in cancellous bone, and 2% per month on sites containing mainly cortical bone is reported (Wilmet et al., 1995). According to another study 25 out of 41 patients with SCI (61%) met WHO's criteria for osteoporosis, eight (19.5%) were osteopenic and only eight (19.5%) showed normal values (Lazo et al., 2001). In SCI children (boys and girls) values for bone mineral density (BMD) at the hip were approximately 60% of normal, or had a Z-score that indicated a 1.6-1.8 SD reduction in BMD compared with age- and sex-matched peers (Lauer et al., 2007).

In studies with peripheral quantitative computed tomography (p QCT) in spinal cord injured subjects bone loss in the epiphyses was 50% in the femur and 60% in the tibia, while in the diaphyses of these bones was 35% and 25%, respectively, meaning that bone loss in the epiphyses almost doubled the loss in the diaphyses (Eser et al., 2004). This study also showed that bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses bone is lost due to the decrease in trabecular, while in diaphysis, the cortical bone density is maintained and bone is lost due to endocortical resorption. In line with the previous study another p QCT study, performed in complete paraplegics with high (thoracic 4-7) and low (thoracic 8-12) neurological level of injury at the tibia, found a loss of trabecular (57.5% vs. 51%, in high vs. low paraplegics, respectively) and cortical bone (3.6% and 6.5%, respectively), suggesting that trabecular bone is more affected during the years of paralysis in comparison with cortical bone (Dionyssiotis et al., 2007). In the same study both paraplegic groups had a similar loss of total BMD (46.90% vs. 45.15%, in high vs. low paraplegics, respectively) suggesting that a homogenously deficit pattern occurs in the epiphyseal area, especially in the group of low paraplegics because the central and the peripheral of the cross sectional area of bone were similarly affected. On the contrary, in high paraplegics' group trabecular bone loss was higher suggesting an increasing endocortical remodeling keeping the total BMD similar. Concerning cortical geometric properties the results had shown an increased endosteal circumference between

both paraplegic groups vs. controls leading to reduction of cortical thickness, 19.78% vs. 16.98% in paraplegic groups respectively, whereas periosteal circumference was comparable to controls (Fig. 1).

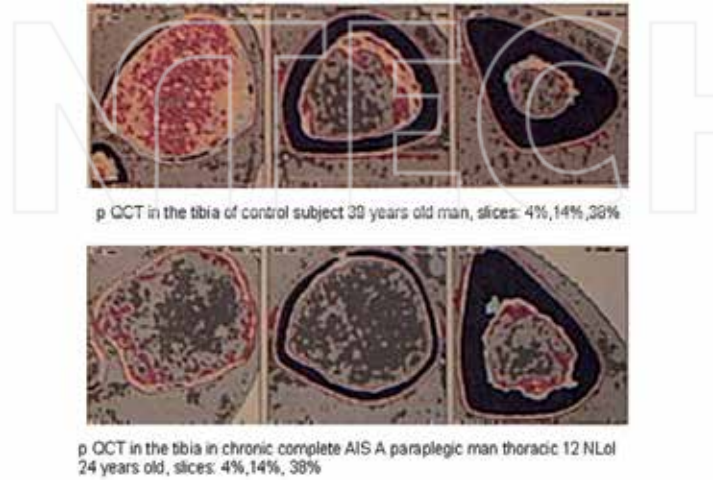

Fig. 1. Peripheral quantitative computed tomography (p QCT) tibia slices in control (a) and paraplegic subject (b), (scanner XCT 3000 Stratec, Medizintechnik, Pforzheim, Germany). Areas in red represent trabecular bone, while areas in grey represent fat; pQCT allows the measurements of true volumetric densities at a minimum exposure to X-rays, assess cortical and trabecular bone density separately as well as to evaluate the geometrical properties of long bones non-invasively, adapted from Dionyssiotis, 2011c, 2011d, with permission.

Regarding tetraplegic patients statistically significant differences were found in BMD of the spine, trochanteric region and upper limbs between paraplegic and tetraplegic patients but not in the femoral neck, pelvis, and lower extremities (Tzuzuku et al., 1999). Indeed, the effects on spinal BMD differed from previously published work in which the investigation was mainly focused in paraplegics (Biering-Sorensen et al., 1988, 1991; Leslie & Nance, 1993).
The importance of mechanical loading and site specificity to maintain or increase BMD is already shown (Lanyon, 1986). According to bone loss there are some interesting features in spinal cord injured subjects; demineralization is area dependent, occurs exclusively in the areas below the level of injury (Dauty et al., 2000), affecting mainly paralyzed extremities and increasing from proximal to distal regions i.e. in paraplegics weight bearing skeleton regions, as the distal end of femur and proximal tibia, which are rich in cancellous bone, while region of the diaphysis of the femur and tibia, rich in cortical bone is reserved (Eser et al., 2004; Kiratli et al., 2000; Dionyssiotis et al., 2007). Moreover, bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses is due to decrease in trabecular but in diaphysis cortical bone is maintained and bone is lost through endocortical resorption by reducing cortical wall thickness (Dionyssiotis et al., 2007; Eser et al., 2004).

Women with disabilities have a higher risk of losing bone mass compared to men because of the inevitable reduction in estrogen levels that occurs at menopause. Findings that women with serious disabilities have low bone density are not surprising and are probably related to the lack of activity (reduced mobility, reduced loading on bone) and worsening of the disability. Regarding women with complete SCI, the initial bone loss in the lumbar spine is negligible. Post injury over a period of years BMD in SCI women is maintained or increases compared with non-injured age-matched women, in whom BMD decreases during aging (Dionyssiotis, 2011c).

2.2 Duration of paralysis and bone steady state

The duration of paralysis affects the degree of bone loss in regions below the level of injury. A study of 21 men with SCI with an average duration of 10.6 years, using dual-energy X-ray absorptiometry (DXA), expressed at various levels of injury an inverse relationship between BMD in the legs and the duration of the lesion (Clasey et al., 2004), while others found a weaker relationship regarding the microarchitecture of the distal end of tibia (Modlesky et al., 2004).

In a study which included paraplegics with duration of paralysis of 14 ± 11.5 years a positive correlation between the duration of paralysis and the degree of bone loss was found (Eser et al., 2004). The length of immobilization in the acute posttraumatic period increased bone loss in the legs, particularly in the proximal tibia; over 50% of bone mass was lost (in the affected areas) in the period of ten years after the injury (Dauty et al., 2000). When subjects categorized depending on the length of the lesion (0-1, 1-5, 6-9, 10-19, 20-29, 30-39, 40-49, and 50-59 years after the injury), in all age groups bone loss to the hip area occurs a year after the injury (Szollar et al., 1998).

Using DXA and QUS (quantitative ultrasound) measurements in 100 men with SCI, aged 18 to 60 years, it was found that bone density decreases over time in all measured points, while bone loss followed a linear pattern in the femoral neck and distal epiphysis, stabilized within three years after the injury. On the contrary, Z-scores of the distal region of the diaphysis of the tibia continued to decrease even beyond ten years after the injury (Zehnder et al, 2004). Duration of paralysis related bone loss in the legs of monozygotic twins with chronic paraplegia in comparison with their able-bodied co-twins has been also reported (Bauman et al., 1999).

The results of a comparison of chronic complete paraplegic men vs. controls in another study found a reduction of BMD in paraplegics' legs independent of the neurological level of lesion. BMD of the legs was negatively correlated with the duration of paralysis in the total paraplegic group, but after investigation according to the neurological level this correlation was due to the strong correlation of high paraplegics' legs BMD with the duration of paralysis, suggesting a possible influence of the neurological level of injury on the extent of bone loss (Dionyssiotis et al., 2008). A significant inverse relationship between percentage-matched in BMD leg, arm and trunk values and time since injury was found when varying levels of SCI were analyzed (Clasey et al., 2004).

Studies are supporting the concept of a new bone steady state at 16-24 months after injury, especially for bone metabolic process (Bauman WA 1997; Demirel et al., 1998; Szollar et al., 1998), but BMD decreases over the years at different areas and is inversely related to the time of the injury, which means continuous bone loss beyond the first two years after the injury (Coupaud et al., 2009; Dionyssiotis et al., 2008; Eser et al., 2004) (Fig. 2).

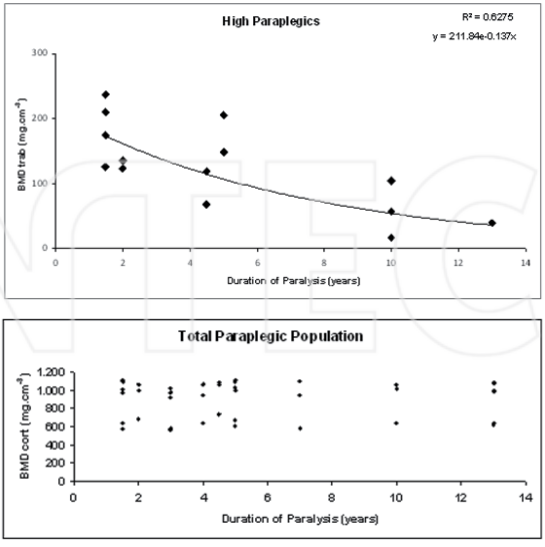

Fig. 2. The duration of paralysis was inversely related with trabecular bone loss in spinal cord injured subjects. Exponential correlation between volumetric trabecular bone mineral density BMD trab and duration of paralysis in high paraplegics was found to fit best. On the contrary no significant decrease in BMD cort of the diaphyses was found in total paraplegic group. BMD parameters were measured by pQCT in 31 paraplegic men in chronic stage (>1.5 years of injury). Spinal cord injury paraplegic men were allocated into 2 subgroups based on the neurological level of injury; subgroup A (n=16, Thoracic (T)4-T7 neurological level of injury) and subgroup B (n=15, T8-T12 neurological level of injury). BMDtrab: BMD trabecular; BMDcort: BMD cortical; (adapted from Dionyssiotis et al., 2011a, with permission).

The role played by factors such as race or gender of patients is not yet clear documented, but studies indicated more loss in women than men (Garland et al., 2001). Loss of bone is closing fracture threshold from 1 to 5 years after injury (Szollar et al., 1998) and risk factors for fractures after spinal cord injury are gender (women are more at risk than men), age and duration of injury (increasing age and duration of injury increases the risk of fracture with a statistically significant increase in 10 years after injury), the type of injury (complete SCI subjects have more fractures than incomplete), low body mass index (BMI) and low bone density in the tibia (Garland et al., 2004a,b; Garland et al., 1992; Lazo et al., 2001).

2.3. The role of central nervous system

2.3.1 Sympathetic denervation in SCI

Spinal cord injury is a dynamic process that is related to alterations in both the central and peripheral sympathetic nervous system (SNS). Sympathetic denervation in SCI may cause arteriovenous shunts and a slowdown of intraosseous blood flow, thus increasing bone resorption (Chantraine et al., 1979). With high-level spinal cord lesions the SNS is disproportionately involved when compared with the parasympathetic nervous system. In a complete high-level SCI, functioning in the isolated spinal cord below the lesion becomes

independent of supraspinal control and has been termed ˝decentralization˝ of the SNS (Karlsson et al., 1998).
Loss of supraspinal control leads to dysregulation of those homeostatic mechanisms normally influenced by the SNS through loss of facilitation or lack of inhibition (Teasell et al., 2000). Today there is clinical evidence that the sympathetic regulation of bone does exist in humans and plays a clinically important role in diseases characterized by excessive sympathetic activity (Schwartzman, 2000). The scientific finding about sympathetic innervations of bone tissue (Takeda et al., 2002; Kondo et al., 2005) and its role in the regulation of bone remodelling is of major interest in situations where uncoupling between osteoclasts and osteoblasts occurs (Levasseur et al., 2003).

2.3.2 Spasticity

Controversial results have also been reported regarding the effect of spasticity on BMD in SCI paraplegics. A cross-sectional study of 41 SCI paraplegics reported less reduction of BMD in the spastic paraplegics SCI patients compared to the flaccid paraplegic SCI patients (Demirel et al., 1998). Others reported that spasticity may be protective against bone loss in SCI patients, however, without any preserving effect in the tibia (Dionyssiotis et al., 2011; Eser et al., 2005). A possible explanation for that could lie in the fact that in the present study all paraplegics were above thoracic (T)12 level with various degrees of spasticity according to the Ashworth scale. In addition, muscle spasms affecting the lower leg would mainly be extension spasms resulting in plantar flexion thus creating little resistance to the contracting muscles. Furthermore, the measuring sites of the tibia did not include any muscle insertions of either the knee or the ankle extensor muscles (Dionyssiotis et al., 2011a; Dionyssiotis, 2011c). Other investigators also have not been able to establish a correlation between BMD and muscle spasticity (Lofvenmark et al., 2009).

3. Multiple sclerosis

Reduced mobility has been implicated as an important factor in bone loss in patients suffering from multiple sclerosis (MS) and it seems to greatly influence the BMD of the femur. However, the high proportion of ambulatory patients with bone loss suggest additional non-mechanical factors (Cosman et al., 1998; Dionyssiotis, 2011b).
There is a high incidence of vitamin D deficiency in MS patients and is determined by levels of 25-hydroxy vitamin D <20ng/ml (Nieves et al., 1994). The reasons might be due to a combination of low dietary vitamin D intake and avoiding of sun exposure, and that because of MS symptoms may worsen after sun exposure (fatigue-related heat) leading these patients to avoid sun. Low testosterone alone in these populations does not explain bone loss and no clear effect of smoking or alcohol abuse to decreased bone mass could be established (Weinstock-Guttman et al., 2004).
Glucocorticoid (GC)-induced osteoporosis (OP-GC) is the main type of secondary osteoporosis (Canalis et al., 2004; Canalis et al., 2007; Lakatos et al., 2000; Mazziotti et al., 2006; Schwid et al., 1996; Shuhaibar et al., 2009). The mechanism is that excess GC causes a rapid and significant damage to bone quality. Now days we know that GCs act direct on bone mainly to the stromalosteoblastic lineage and at high concentrations alter differentiation, survival, and function of them causing a shift from osteoblastic to adipocytic differentiation of precursors; inducing apoptosis of mature osteoblasts; and inhibition of

synthesis and secretion of bone components (Manolagas, 2000; Pereira et al., 2002). Finally, GCs promote ostoclasts and stimulate bone resorption (Weinstein et al., 2002). The mechanisms of GCs action in bone has been studied extensively. In patients receiving chronic per os GC, bone loss is admitted rapidly and is evident within 6 or even 3 months (Cosman et al., 1998). A study investigated the effect of intravenously (i.v.) administration of glucocorticoids in MS patients found no clear effect on bone loss: on the contrary they reported an increase in BMD of the lumbar spine (Schwid et al., 1996). Prolonged treatment with glucocorticoids results in increased risk of fractures, evident at 3 months, regardless of changes in BMD. High dose, short-term i.v. treatment with GCs leads directly to reduction of bone formation and increased bone resorption, as indicated by markers of bone turnover (De Vries et al. 2007; Van Staa et al., 2000). Osteopenia not osteoporosis was significantly more frequent in patients with MS compared with controls, especially in women who received high dose methylprednisolone pulses (HDMP) in relapses period making important the regularly monitoring of BMD in these patients. The authors concluded that disability and the subsequent immobilization osteoporosis is the more serious factor in this group and treatment with repeated HDMP pulses did not cause osteoporosis in MS subjects followed-up for almost 8 years unlike chronic corticosteroid therapy which induces osteoporosis and/or recovery of BMD is permitted without permanent skeletal damage (Zorzon et al., 2005). The lack of physical activity exacerbates osteoporosis. All MS patients should be considered high risk for osteoporosis. Prevention with calcium rich foods and dietary supplements containing vitamin D and antiosteoporotic drugs is necessary for these patients. Particular attention should be paid to transfers and falls prevention in this population to prevent fractures which occur easily and heal slowly (Cattaneo et al., 2007; Dionyssiotis, 2011b).

In osteoporosis molecular mechanisms leading to bone loss are inadequately explained. There is evidence of interaction between bone and immune system. T cells' activity could stimulate bone loss under certain circumstances such as estrogen deficiency. Women with post-menopausal osteoporosis have higher T cell activity than healthy post-menopausal subjects which could be also the case in inflammatory or autoimmune disorders like MS: receptor activator of nuclear factor kappa B ligand (RANKL) stimulates osteoclastogenesis and the same do cytokines, such as TNF-*a*, IL-1, or IL-11, all produced by T-cells activation, leading to bone destruction. On the contrary osteoprotegerin (OPG) is an osteoclastogenesis inhibitory factor preventing the function from RANKL. A balanced system of RANKL/OPG regulates bone metabolism. In MS this system is disturbed in favour of RANKL (Zhao et al., 2008; Kurban et al., 2009).

4. Stroke

Disuse has been suggested as the main cause for loss of bone mass in patients immobilized because of stroke (Takamoto et al., 1995). However, this was not confirmed in a prospective study, in which only weak associations between bone loss and motor function, activities of daily living (ADL), or ambulation were found (Ramnemark et al., 1999a). This could be explained by the selected severely affected patients, but it does raise questions about other risk factors for the development of hemiosteoporosis apart from paresis and immobilization (Ramnemark et al., 1999b).

The critical role in pathogenesis of osteoporosis is attributed to hormonal processes and osteoporosis itself is often defined as generalized skeletal disorder. Findings of tibial bone

changes in hemiplegic patients are not compatible with this view. The adaptations are found in trabecular bone in the epiphysis as well as in cortical bone in the diaphysis. They represent an individually different distribution of local changes which can be explained by the feedback principles of the muscle-bone-unit, in which bone strength is controlled by the muscle forces that act upon the bone. Muscle forces acting habitually on the paretic limb are considerably less than on the opposite side. This reduction of forces reduces the strain on bones. This leads to loss of bone mass and bone strength (Runge et al., 2004).

Determinants of bone mineral loss have been identified as duration of hemiplegia-induced immobilization and severity of palsy (Sato, 1996). A rapid and pronounced loss of BMD in the paretic extremities that progressed during the first year after stroke (Ramnemark et al., 1999a) more pronounced during the first few months after stroke onset (Hamdy et al., 1993). The lower extremities lost BMD bilaterally, but the losses were significant after 12 months in the affected femur, proximal femur and trochanter. In immobile patients, this could explain the loss of BMD in the nonaffected leg as compared with the nonaffected arm, which even increased in BMD, probably due to increased compensatory activity (Ramnemark et al., 1999a).

Hemiosteoporosis has previously been described as being caused by disuse and vitamin D deficiency (Sato et al, 1996), and in a randomized study a significant decrease in the rate of bone loss in stroke patients with a mean duration of 4.8 years after stroke when supplemental vitamin D was given (Sato et al., 1997). Bone mineral loss was more pronounced in the upper than in lower limbs, and the difference between sides was more marked in long-standing poststroke hemiparesis. The upper versus lower difference may reflect that hemiparesis from stroke is commonly more severe in the upper limb. Notably, BMD on the nonhemiplegic side is intermediate between that for the hemiplegic side and that in control subjects. The decrease in mobility of the intact limb, resulting from stroke-related need for assistance with activities of daily living, presumably results in mild osteoporosis paralleling the patient's overall degree of immobilization (Sato et al., 1998, 2000).

5. Myelomeningocele and cerebral palsy

Previous studies suggest that the level of neurological injury and mobility affect BMD in myelomeningocele (MMC). Studies concluded that loading of the lower limbs rather than child's potential ability to walk because of the level of neurological lesion or residual motor capacity of lower limbs is a prognostic criterion for the BMD (Apkon et al., 2009; Ausili et al., 2008; Quan et al., 1998). This theory is probably challenged by other studies that revealed low values of forearm BMD in individuals and indicate that in this patient osteoporosis can be caused by neurogenic and metabolic mechanisms. The fact is that these patients are loading the arms through the use of crutches and wheelchairs and BMD values in the upper extremities are expected to be higher in relation to immobilized people (Quan et al., 1998). Subjects with MMC may have hypercalciuria associated with immobilization and an additional risk factor for osteoporosis in these patients group (Quan et al., 2003). Others support that low-energetic fractures in MMC children may result from metabolic disturbances that are a consequence of excessive renal calcium loss or excessive fatty tissue content (Okurowska-Zawada et al., 2009).

Children with cerebral palsy (CP) are growing slowly. The impact of this altered growth on skeletal development and bone density is a difference in linear growth which becomes more accentuated over time compared with their typically growing peers. In addition, as growth slows, the bone mineral density also falls further outside the normal range (Houlihan et al., 2009). Significantly decreased bone density is virtually universal in non-ambulatory children with moderate to severe CP after the age of 10 years (Henderson et al., 2002); Bone-mineral content and density were measured in a study by dual energy X-ray absorptiometry in the proximal femur, femoral neck, and total body of nutritionally adequate children (n=17; 11 girls, six boys; aged 7.6 to 13.8 years) with spastic cerebral palsy (CP) and found that non-independent ambulators had lower z scores for total body BMD, femoral neck BMD, and BMC than independent ambulators (Chad et al., 2000). The potential causes of deficient bone mineralization in this population are multiple, including poor nutrition and abnormal vitamin D metabolism. Findings from recent studies (Shaw et al. 1994, Henderson et al. 1995, Wilmhurst et al. 1996) suggest that non-nutritional factors, such as ambulation, may contribute to the alterations in body composition observed in children with CP.

5.1 Interventions to prevent bone loss

5.1.1 Weight bearing activities-cycling-body weight supported treadmill

The effect of standing in bone after SCI has been investigated by many researchers. A beneficial effect on bone mass using passive mechanical loading has been shown on preservation of bone mass in the region of the femoral shaft, but not at the proximal hip of standing and non-standing patients and relatively better-preserved densities in patients standing with braces than in those using a standing frame or standing wheelchair (Goemaere et al., 1994). A slower rate of bone loss in paraplegic subjects who did standing was expressed in a prospective study of 19 patients in acute SCI phase participated in early standing training program showed benefits concerning the reduction of cancellous bone loss compared to immobilized subjects (de Bruin and others 1999; Frey-Rindova and others 2000), while no correlation for passive standing-training to bone status was found in another p QCT study (Eser et al., 2005). Protection afforded by standing in the femoral diaphysis stands in contrast with the loss of bone in the proximal femur. This suggests that the transmission of forces through trabecular and cortical bone varies; so the less effective strain for the initiation of bone remodeling reaches faster cortical bone (Frost, 1992, 2001, 2003). Others also supported the concept of different strain thresholds bone remodeling control (Gutin & Kasper, 1992; LeBlanc et al., 2007; Smith et al., 2009). There is level 2 evidence (from 1 non-randomized prospective controlled trial) that Functional Electrical Stimulation (FES) - cycling did not improve or maintain bone at the tibial midshaft in the acute phase (Eser et al., 2003). Moreover, there is level 4 evidence (from 1 pre-post study) that 6 months of FES cycle ergometry increased regional lower extremity BMD over areas stimulated (Chen et al., 2005). Body weight supported treadmill training (BWSTT) did not alter the expected pattern of change in bone biochemical markers over time and bone density at fracture-prone sites (Giangregorio et al., 2009).

5.1.2 Whole body vibration

At a meeting of the American Society for Bone and Mineral Research results of a small randomised, placebo-controlled study among 20 children with cerebral palsy who used a similar, commercially available vibrating platform for 10 min per day, 5 days per week for 6 months were reported (Ward et al., 2001). A significant increase in tibial, but not lumbar-

spine bone density in the treated group was found despite the simplicity, short duration of the "vibration", the young age of the children and the poor compliance (Eisman, 2001).

Fig. 3. Weight bearing in disabled subjects; using standing frames, functional walking with orthoses between bars and crutches, even push-ups in the wheelchair (in case of multiple sclerosis with a clinical equivalent like tetraplegia) bone can be loaded and bone loss rate would be slower (unpublished photos of Dionyssiotis Y).

After 6 months of whole body vibration (WBV) therapy in twenty children with cerebral palsy (age 6.2 to 12.3 years; 6 girls) randomized to either continue their school physiotherapy program unchanged or to receive 9 minutes of side-alternating WBV (Vibraflex Home Edition II®, Orthometrix Inc) not effect on areal BMD at the lumbar spine was observed, while areal BMD seemed to decrease somewhat in the cortical region of the femoral diaphysis. Authors explained that mechanical stimulation increases intracortical bone remodeling and thereby cortical porosity; moreover changes occurred in ways that are not reflected by areal BMD, but might be detectable by more sophisticated techniques such as such as peripheral quantitative computed tomography (Ruck et al., 2010). Low-intensity vibration (LIV) has shown to be associated with improvement in bone mineral density in post-menopausal women and children with cerebral palsy. Seven non-ambulatory subjects with SCI and ten able-bodied controls underwent transmission of a plantar-based LIV signal (0.27 +/- 0.11 g; 34 Hz) from the feet through the axial skeleton as a function of tilt-table angle (15, 30, and 45 degrees). SCI subjects and controls demonstrated equivalent transmission of LIV, with greater signal transmission observed at steeper angles of tilt which supports the possibility of the utility of LIV as a means to deliver mechanical signals in a form of therapeutic intervention to prevent/reverse skeletal fragility in the SCI population (Asselin et al., 2011).

Fig. 4. The Galileo Delta A TiltTable offers a wide variety of applications from relaxation to muscle training for a diverse range of patients who are unable to stand without support. The motor driven adjustable tilt angle of the Galileo Delta TiltTable (90°) allows vibration training with reduced body weight from 0 to 100%. This is ideal for deconditioned and disabled patients for gradually increasing training weights up to full body weight. System for application in adults (max. body height: 1.90 m) and children (max. body height: 1.50 m).The Galileo Delta A TiltTable is exclusively available from the manufacturer Novotec Medical GmbH., (with permission).

5.1.3 Drugs

Calcitonin in varying doses and methods of administration has given variable results in paraplegia (preferred dosage regimen, treatment duration, and administration route for adequate efficacy in SCI patients' remains unclear) (Chantraine et al., 1979a; Minaire, 1987). Likewise, the outcome using bisphosphonates has been variable. Etidronate produced long-term benefit in lower limb bone mineral density (BMD) in selected walking SCI patients (Roux et al., 1998); whereas tiludronate appeared effective in reducing bone resorption and preserving bone mass in a histomorphometric study in 20 paraplegic patients (Chappard et al., 1995). Intravenous pamidronate has been shown to attenuate bone loss in SCI and normalize serum calcium in immobilization hypercalcemia (Bauman et al., 2005). Alendronate (1000 times more potent than etidronate), in an open observational study, reversed BMD loss in men with established SCI increased both axial and trabecular bone density and has proven efficacy and safety in men treated for osteoporosis, prevents hypercalciuria and bone loss after bed rest and lower leg fracture (Moran de Brito et al., 2005; Zehnder et al., 2004). Six months after using zolendronic acid in the treatment group BMD showed differences in the response to treatment between the mixed trabecular/

cortical regions (narrow neck and intertrochanteric) and the purely cortical shaft. With respect to cross-sectional geometry, bone cross-sectional area and sectional modulus (indices of resistance to axial and bending loads, where higher values would indicate a positive effect of treatment) increased at the hip and buckling ratio (an index of the instability of thin-walled cross sections, where lower values would suggest that the treatment is improving stability) decreased consistent with improved bone outcomes; at 12 months, narrow-neck femur values declined and intertrochanteric and femoral shaft BMD was maintained vs. placebo group which showed a decrease in bone outcomes and an increase in buckling ratio at the hip at 6 and 12 months, while with respect to bone prevention 4 mg i.v. were effective and well-tolerated to prevent BMD loss at the total hip and trochanter for up to 12 months following SCI (Bubbear et al; Shapiro et al., 2007).

Clinical examination and management of bone loss in SCI	
• history of the patient (co morbidities, neurologic complications, use of drugs which impair bone metabolism, alcohol, smoking and information about the level of injury, duration of paralysis, immobilization period, onset of rehabilitation, use of assistive devices and orthoses).	• pharmacological treatment with bisphosphonates p.os and i.v. that have been studied in patients with spinal cord injuries and had positive effects on bone parameters. • Use of calcium supplements (monitoring renal function) and vitamin D.
• anthropometric parameters (age, weight, body mass index, BMI) • clinical examination (level of injury according to American Spinal Injury Association Impairment Scale, AIS) and assessment of spasticity)	• Education on falls prevention • Counseling regarding osteoporosis and related factors and identification of fractures in regions of impaired sensation.
• imaging (bone densitometry by DXA at the hip and spine, and if possible, p QCT at the the tibia or femur)	• physical therapy including: a) range of motion exercises, b) loading of the skeleton to reduce bone loss, d) therapeutic standing-walking with orthoses, e) passive-active cycling
• measurement of bone turnover indices in the serum (parathyroid hormone, alkaline phosphatase, calcium, vitamin D, PINP molecule, osteocalcin) and urinary excretion of 24 hour (calcium, hydroxyproline, aminoterminal (NTx) and carboxylterminal (CTx) intermolecular cross-linking domain of bone type-1 collagen), which provide a good indicator of bone resorption.	• dietary interventions to improve dietary intake of calcium and nutrition indices.

Table 1. An algorithm for the screening and management of osteoporosis in subjects with spinal cord injury (should be read top to bottom starting with the left column); adapted from: Dionyssiotis Y. (2009). Bone loss in paraplegia: A diagnostic and therapeutic protocol. Osteoporos Int Vol. 20 (Suppl 1):S23-S176 (with permission).

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Body Composition in Paraplegia

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Additional information is available at the end of the chapter

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1. Introduction

Paraplegia leads to immobilisation associated with profound changes in body composition. The potential risks involved with these changes i.e. loss of lean tissue mass (LM) and bone mineral density (BMD) vs. gain in fat mass (FM) in body composition have implications for the health of the disabled individuals [1]. Body fat has been identified as a significant predictor of mortality in humans making body composition measurement to quantify nutritional and health status an important issue for human health [2-4]. Moreover, some disorders such as carbohydrate intolerance, insulin resistance, lipid abnormalities, and heart disease occur prematurely and at a higher prevalence in disabled populations may be related to adverse changes in body composition that result from immobilization and skeletal muscle denervation [5]. To standardize or index physiological variables, such as resting metabolic rate and power fat free mass (FFM) is usually used [4]. Skeletal muscle represents 50% of the non fat component in the total body [6, 7] and exact quantification of the amount of skeletal muscle is important to assess nutritional status, disease risk, danger of illnesses, physical function, atrophic effects of aging, and muscle-wasting diseases [8, 9].

A paraplegic subject could be wheelchair bound, may have an alternated walking gait pattern but may also be unable to walk at all [10, 11]. In addition to these differences and according to osteoporosis the role of factors which do not change, such as race or gender of patients has not been yet clarified, although there are few studies in women debating that bone mass in women with paraplegia is more affected than men [12, 13]. Similar findings of reduced muscle mass and increased intramuscular fat have been also published in individuals with incomplete spinal cord injury (SCI) [14].

Therefore, the purpose of this chapter was to present the bone-mineral density, bone-mineral content, and bone-mineral-free lean and fat tissue mass alterations of ambulatory and non-ambulatory subjects with paraplegia.

2. Body composition measurements

2.1. Anthropometric and various techniques of body composition measurements

Similar body mass indices were found between paraplegics and controls; although there were significant decreases in the lean muscle mass of the paraplegics (16% less). The analysis of body composition with dual-energy X-ray absorptiometry (DXA) has also revealed large increases in fat in people who do not appear to be obese, yet they carry large amounts of fat tissue and in the group of paraplegic subjects fat mass was 47% higher [15]. Furthermore, where authors performed a research in the usage of the body mass index (BMI) in anthropometric measurements, the conclusion was that BMI, widely used as an obesity measurement tool, is not capable of distinguishing the weight components among people so that the fat percentage is degraded in the population of paraplegic in comparison to the control group [16].

In a study which investigated a chronic paraplegic population the values of BMI did not present statistical significance in relation to the controls, which is a finding in line with the literature [17, 18, 19]. Moreover, the values of BMI in both paraplegics and controls were below values consider to signify obesity (BMI>27.8) [19, 20, 21]. This finding could be acceptable for the population of the controls, but raises questions regarding the paraplegics. It is known from literature that paraplegics are obese [22]. Nevertheless, there are studies which demonstrate the usefulness of BMI as an indicator of obesity, in body composition in people with spinal cord injury [23]. These studies, however, included in their sample both tetraplegics and middle-aged people unlike the Greek one which included relatively young individuals [19]. Whether the criteria of BMI may assess obesity in people with spinal cord injury the latest studies show the opposite [24].

Similarly to the healthy population values of BMI are positively correlated with obesity. This emerged from a study, conducted by whole body DXA Norland X-36, only when the findings of total fat in paraplegics were correlated with BMI. Employing whole body DXA Norland XR-36 it was found that the total fat mass was statistically significantly higher for any given BMI value in paraplegics compared with controls [19], finding that strongly supports the studies held by the whole body DXA Hologic QDR-2000 method [5, 25].

The studies illustrated statistically significantly higher total fat mass and fat percentages for any given unit of body mass index in paraplegics in comparison to controls. Increased fat per body mass index unit was found in a study of monozygotic twins, one with SCI compared with a non-SCI co-twin by the above authors also [25]. Adjustments in classifications of normal, overweight, obese, and morbid obesity by BMI are needed for persons with SCI [26].

In addition, by analysis between paraplegics with high and low neurological level injuries not statistically significant differences in BMI were highlighted. However, when data from the analysis undertaken in areas measured by the method of whole body DEXA were compared in the same patients there were differences between paraplegics with high and low neurological level of injury. This finding is new and reinforces those views on the inability of BMI usage in the analysis of body composition of paraplegics [19].

BMI of the male paraplegic group was slightly greater than that of the male tetraplegic group (25.2 vs. 24.7 kg/ m^2; $p<0.01$). Proportion of overweight or obese was comparable between men with SCI and that observed in men in the US general population. Distribution of BMI by level of injury was similar with 37.5% and 40.5% of the male tetraplegic and male paraplegic groups, respectively, falling into the recommended BMI range. Approximately 50% in each male group were overweight by BMI, and 12.5% and 10.8%, respectively, were classified as obese. Overall, when compared with the general population-observed distribution by BMI, a greater proportion of men with SCI fell into the desirable BMI range and fewer fell into the obese category [26].

No differences were found in BMI between paraplegics in the acute phase of injury and controls, which is a finding in accordance with other studies reported in chronic paraplegic patients and controls, in which despite the same BMI the body composition and the distribution of fat and fat free mass were alterated in patients with spinal cord damage, with the fat free mass being statistically significantly lower in paraplegic patients in total body composition and in the lower, but not the upper limbs. As far as the fat mass is concerned, it was statistically significantly higher (kilograms and %) in the total body composition in the upper and lower limbs [27].

These findings show that using the BMI does not contribute substantially in determining the body composition of paraplegics and lowers the percentage of fat in this population, finding that agrees with other studies and shows that the anthropometric measurement with BMI in paraplegics, underestimates fat in body composition when measurements are compared with healthy subjects [1].

Changes in body composition in spinal cord injured subjects can be assessed with various techniques including isotope-labelled water [1] total body potassium counting (Lussier et al 1983; Spungen et al 1992) anthropometric measures [16] hydrodensitometry [28] dual photon absorptiometry (DPA) [29] and dual energy X-ray absorptiometry (DXA) [1]. However, some of these methods are not particularly suitable for use in the SCI population.

The hydrodensitometric model was regarded as the "gold standard" for body composition assessment. This model partitions the body into two compartments of constant densities [fat mass: 0.9007 g/cm^3 and FFM: 1.100 g/cm^3] and assumes that the relative amounts of the FFM components [water, protein, protein, bone mineral (BM), and non-BM] are fixed [4]. Hydrodensitometry is clearly inappropriate for individuals who deviate from these fixed and/or assumed values (e.g., children, elderly, blacks, obese), and its application is, therefore, somewhat limited [30, 31].

Bioelectrical impedance analysis has been used to measure cerebral palsy subjects. However, the inclusion of weight in the BIA predictive equation may reduce its accuracy in determining change in lean body mass. The inability of BIA to accurately predict percentage body fat in the sample may be related to several factors. In the BIA method where the impedance of a geometrical system (i.e., the human body) is dependent on the length of the conductor (height) and its configuration, it is almost impossible to measure accurately height in subjects with CP because of their muscle contractures. An over-or underestimation of height by 2.5 cm can result in a l.0-L error in the estimation of TBW, producing a small error in the estimation of percentage

body fat (< 5%). The second major problem is body asymmetry which renders the assumption of a symmetrical configuration of the human body invalid in this case [20, 32].

Isotope dilution measures the water compartment of the whole body rather than a single area assumed to mimic the composition of the whole body. Thus, the use of a stable isotope to measure body composition is ideal for people with CP because it is non-invasive, does not require the subject to remain still for the measurement, and is independent of height and body symmetry. However, the prohibitive cost of the isotopes and the need for a mass spectrometry facility and highly trained technicians make this method impractical for routine clinical use [32].

To determine whether bioelectrical impedance analysis (BIA) and anthropometry can be used to determine body composition for clinical and research purposes in children with cerebral palsy 8 individuals (two female, mean age=10 years, mean gross motor function classification=4.6 [severe motor impairment]) recruited from an outpatient tertiary care setting underwent measurement of fat mass, fat-free mass, and percentage body fat using BIA, anthropometry (two and four skinfold equations), and dual-energy x-ray absorptiometry. Correlation were excellent for determination of fat-free mass for all methods (i.e., all were above 0.9) and moderate for determination of fat mass and percent body fat (range=0.4 to 0.8). Moreover, skinfolds were better predictors of percent body fat, while bioelectrical impedance was a better predictor for fat mass [33]. On the contrary another study investigated the pattern of body composition in 136 subjects with spastic quadriplegic cerebral palsy, 2 to 12 years of age, by anthropometric measures, or by anthropometric and total body water (TBW) measures (n=28), compared with 39 control subjects. Body composition and nutritional status indicators were significantly reduced. Calculation of body fat from two skinfolds correlated best with measures of fat mass from TBW [34].

Magnetic resonance imaging (MRI) provides remarkably accurate estimates of skeletal muscle in vivo [7]. MRI and also quantitative computed tomography (QCT) have been validated in studies of humancadavers in the assessment of regional skeletal muscle [35]. Although, these devices have disadvantages of high radiation exposure and are expensive.

2.2. Dual-energy X-ray absorptiometry (DXA)

Recently, dual-energy X-ray absorptiometry (DXA) has gained acceptance as a reference method for body composition analysis [36, 37]. Originally designed to determine bone density, DXA technology has subsequently been adopted for the assessment of whole body composition and offers estimation rapidly, non-invasively and with minimal radiation exposure [4, 19]. Moreover, is well tolerated in subjects who would be unable to tolerate other body composition techniques, such as underwater weighing (hydro-densitometry). DXA software determines the bone mineral and soft tissue composition in different regions of the body being a three-compartment model that quantifies: (i) bone mineral density and content (BMD, BMC), (ii) fat mass (FM); and (iii) lean mass (LM), half of which is closely correlated with muscle mass and also yields regional as well as total body values [38] for example in the arms, legs, and trunk (figure 1).

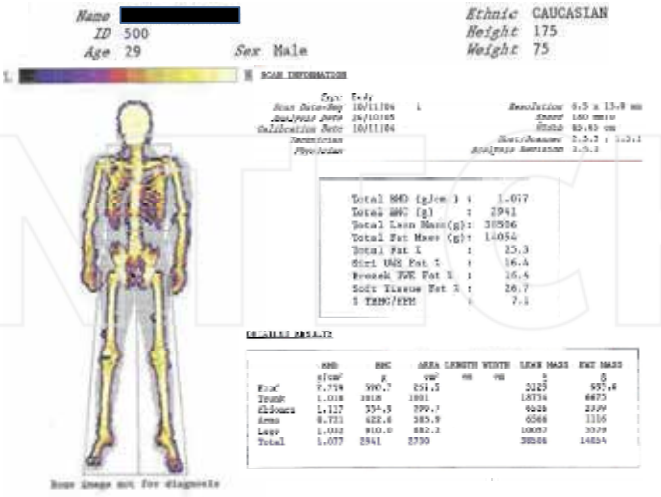

Figure 1. Whole body and regional distribution of fat mass, lean mass, bone mineral content (BMC) and bone mineral density (BMD) from paraplegic subject thoracic 6 using whole body DXA (Norland X-36, Fort Atkinson, Wisconsin, USA) and values of measured parameters. Modified and translated with permission from Dionyssiotis Y, Doctoral Dissertation, Laboratory for Research of the Musculoskeletal System, University of Athens, 2008 [39].

DXA analyzes differently the dense pixels in body composition. Soft tissue pixels are analyzed for two materials: fat and fat-free tissue mass. Variations in the fat mass/fat free tissue mass composition of the soft tissue produce differences in the respective attenuation coefficients at both energy levels. The ratio at the two main energy peaks is automatically calculated of the X-ray attenuation providing separation of the soft tissue compartment into fat mass and fat-free tissue mass (lean mass) [40, 41]. A bone-containing pixel is analyzed for "bone mass" (bone mineral content, BMC) and soft tissue as the two materials. Thus, the fat mass/fat free tissue mass of the soft tissue component of the bone pixels cannot be measured, but only estimated [42].

The important issue on this the investigation of distribution of bone mineral, fat and mass throughout the body. These changes induce the risk for diseases such as diabetes, coronary heart disease, dyslipidaimias and osteoporosis [22, 43, 44, 45]. There is a need to quantify the alterations in body composition to prevent these diseases and their complications. Studies also reported that bone density measurements at one site cannot usefully predict the bone density elsewhere [46] because different skeletal regions, even with similar quantities of trabecular or cortical bone, may respond variably in different physiopathological conditions [47].

In disabled conditions the accuracy of skeletal muscle measured by DXA may be compromised when muscle atrophy is present. A lower ratio of muscle to adipose-tissue-free mass indicates a lower proportion of muscle in the fat-free soft tissue mass. Cross-sectional area of skeletal muscle in the thighs after SCI is extensively reduced [48]. If this is the case

muscle mass would be overestimated by prediction models that assume that muscle represents all or a certain proportion of the fat-free soft tissue mass, i.e. in spinal cord injured subjects [7]. DXA technique has been used in assessment of SCI and appears to be tolerated well by this population [49, 50, 51].

Total BMD (g/cm)	1.256
Total BMC (g)	3527
Total Lean Mass(g)	79838
Total Fat Mass (g)	40884
Total Fat %	32.9
Siri UWE Fat %	29.6
Brozek UWE Fat %	28.6
Soft Tissue Fat %	33.9
% TBMC/FFM	4.2

	BMD g/cm²	BMC g	AREA cm²	LENGTH cm	WIDTH cm	LEAN MASS g	FAT MASS g
Head	2.218	588.9	264.6			4141	1035
Trunk	1.256	1181	942.0			40751	24109
Abdomen	1.342	564.3	365.8			17188	12251
Arms	0.781	454.0	583.7			8784	4305
Legs	1.280	1302	1017			26661	11596
Total	1.256	3527	2807			79838	40884

Figure 2. Whole body and regional distribution of fat mass, lean mass, bone mineral content (BMC) and bone mineral density (BMD) from controls male subject using whole body DEXA Norland X-36 and values of measured parameters. Modified and translated with permission from Dionyssiotis, Doctoral Dissertation, Laboratory for Research of the Musculoskeletal System, University of Athens, 2008 [39].

3. Physiopathological context

Spinal cord injury (SCI) always results in substantial and rapid bone loss predominately in areas below the neurological level of injury. The predominant finding of SCI on bone is a large loss of bone during the first year of injury [5] and an ongoing demineralisation 3 years after trauma in tibia [52] with a progressive bone loss over 12 to 16 months prior to stabilizing [53] was demonstrated.

Cancellous bone is more affected than cortical bone after SCI. In a prospective study, six acute tetraplegics were followed up for 12 months, and the trabecular and cortical BMD's of the tibia were found to be decreased by 15 and 7% [54], while in paraplegics trabecular metaphysical-epiphyseal areas of the distal femur and the proximal tibia are the most affected sites [55]. A cross-sectional study [56] in SCI subjects demonstrated a significant demineralization at the distal femur (-52%) and the proximal tibia (-70%), respectively.

There is no demineralization of the upper limbs in paraplegics. On the contrary, a minor increase of BMD (6%) in the humerus was reported in a cross-sectional study of 31 male chronic

paraplegics 1 year post injury. With reliance on the upper limbs to provide movement for activities of daily living in the SCI population, this area could be subjected to greater site-specific loading, and thus increasing osteogenesis, than in the corresponding able-bodied population. At the lumbar spine, the trabecular bone demineralization remains relatively low compared to the cortical bone demineralization of long bones [56]. Normal [52, 57] or even higher than normal [58] values of BMD in the lumbar spine have been reported a phenomenon is named "dissociated hip and spine demineralization" [54]. One reason for preservation of bone mass in the vertebral column is because of its continued weight-bearing function in paraplegics. In a cross-sectional study of 135 SCI men, BMD in the lumbar spine was found to be stable with an insignificant decline in the tetraplegic population at 1±5 years post injury in the 20–39-year age group, whereas in the 40-59-year age group and the 60+-year age group, bone mass in the lumbar spine remained unchanged or even increased with age [49]. However, several factors may affect the results of BMD measurement: lumbar spine arthrosis, bone callus, vertebral fracture, aortic calcification, osteosynthesis material, etc. Degenerative changes in the spine may be the most possible reason to give falsely higher values of BMD [56]. An interesting question is why we don't see osteoporotic vertebral fractures in SCI patients to the extent it occurs in post-menopausal osteoporotic women or senile osteoporotic men?

Figure 3 depicts the analysis of bone mineral density (BMD) in high and low level paraplegics and controls. A statistically significant reduction in total BMD ($p<0.001$) and lower limbs BMD in body composition compared to able-bodied males was observed. On the contrary, upper limbs BMD was higher in low paraplegics and controls, an unexpected finding explained in the paper of Dionyssiotis et al. [19].

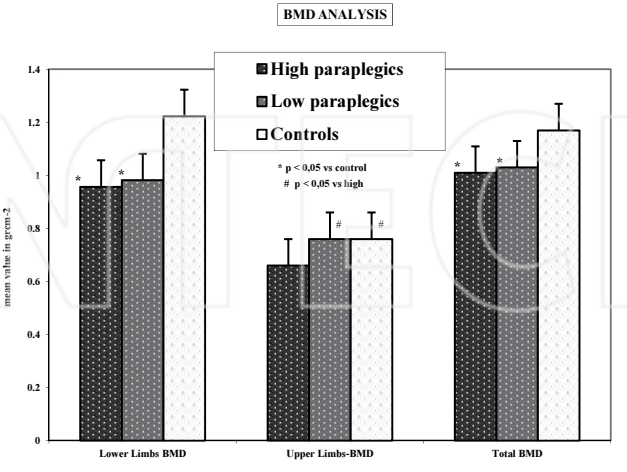

Figure 3. Analysis of bone mineral density (BMD) in high and low level paraplegics and controls. Diagram modified and translated from Dionyssiotis Y [39].

The neurological level of the lesion i.e. the extent of impairment of motor and sensory function is important, because tetraplegics are more likely to lose more bone mass throughout the skeleton than paraplegics [60]. In paraplegics legs' BMC was reduced vs. controls, independently of the neurological level of injury and negatively correlated with the duration of paralysis in total paraplegic group, but after investigation according to the neurological level of injury this correlation was due to the strong correlation of high paraplegics' legs BMC with the duration of paralysis, meaning that the neurological level of injury determines the extent of bone loss [61]. The similar severity of demineralization in the sublesional area was shown between paraplegics and tetraplegics, and the extent of the bone loss may be variable [56, 60, 62].

In addition, in those SCI individuals with complete lesions (an absence of sensory or motor function below the neurological level, including the lowest sacral segment) bone loss is more severe than subjects with incomplete lesions (partial preservation of motor and/or sensory function below the neurological level, including the lowest sacral segment) [62, 63]. In a cross-sectional study of 11 patients with complete SCI and 30 patients with incomplete SCI noticed a significant osteopenia in patients with complete SCI than in patients with incomplete SCI [62].

The duration of paralysis has an inverse relationship with leg percentage-matched BMD and trunk percentage-matched BMD [64]. In addition in complete paraplegics, with high (thoracic 4-7) and low (thoracic 8-12) neurological level of injury, upper limbs FM and lower limbs BMD were correlated with the duration of paralysis in total paraplegic group but after investigation according the neurological level of injury this correlation was due to the strong correlation of high paraplegics' lower limbs BMD with the duration of paralysis. The explanation of this strong correlation could possibly lie on higher incidence of standing in the group of low paraplegics and direct effect of loading lower limbs while standing and walking with orthotic equipment. Moreover, the association of the duration of paralysis with parameters below and above the neurological level of injury (upper limbs FM) raises the question of the existence of a hormonal mechanism as an influential regulator in paraplegics' body composition [19, 61, 65].

Is there a time after injury where bone loss ceases? Some authors reported that approximately 2 years after SCI, a new steady state level between bone resorption and formation would be re-established [52, 57], whereas others [66] found that there was no sign of a new steady state in bone formation in the lower extremities 2 years after the SCI. If a new steady state of bone remodelling is re-established after SCI still remains controversial.

Inconsistent results have been reported regarding the effect of muscle spasms on BMD in SCI patients. Those with spasticity were found with higher BMD when compared with flaccid individuals [62], and a significant correlation between the degree of spasticity measured with modified Ashworth scale and BMD was reported. Thus, it was concluded that spasticity may be protective against bone loss in SCI patients [67]; however, without any preserving effect in the tibia [65, 67]. A possible explanation for that could lie in the fact paraplegics to be above thoracic (T)12 level with various degrees of spasticity according to the Ashworth scale. In addition, muscle spasms affecting the lower leg would mainly be extension spasms resulting in plantar flexion thus creating little resistance to the contracting muscles. Furthermore, the measuring sites of the tibia did not include any muscle insertions of either the knee or the ankle

extensor muscles [65]. Other investigators have not established a correlation between BMD and muscle spasticity [68].

Studies also emphasize the contribution of aging to bone loss in complete SCI patients. Moderate correlation between age and femoral BMD was observed in a cross-sectional study of 30 patients with SCI of 1-year duration or less [69]. On the other side bone loss in eight pairs of identical male twins with SCI of duration ranging from 3 to 26 years appeared to be independent of age [70].

Muscular loading of the bones has been thought to play a role in the maintenance of bone density. The ability to stand or ambulate itself does not improve BMD and does not prevent osteoporosis after SCI, although exercise increases site-specific osteogenesis in able-bodied individuals [71]. There was only one study demonstrating that standing might reduce the loss of trabecular bone after SCI. In this prospective study of 19 acute SCI patients, the patients involved in early loading intervention exercise lost almost no bone mineral, whereas the immobilization patients lost 6.9 to 9.4% of trabecular bone [66].

Muscles rather than body weight are causing the greatest loads on bone [72]. It is difficult to translate in vivo bone strains from animal work to a gross loading environment for humans. However, the pioneering work in animal models [73] suggests that if the active–resistive standing exercise can indeed transmit loads at an appropriate frequency and strain-rate, compressive loads approaching 240 % body weight may have the potential to be osteogenic [73, 74].

FES cycling [75] and quadriceps muscle training [76] have been able to increase force-generating capability and to improve muscular endurance with training after SCI [75]. Conversely, cycling with FES has been reported to induce only small improvements in BMD [77, 78] as well as have no effect [78] on lower extremity BMD measurements in individuals with SCI. Additionally, neither passive standing, ambulation with long-leg braces, nor ambulation with FES have yet to exhibit any improvement in lower extremity BMD in chronically injured subjects [79]. The subject populations of previous BMD studies were comprised almost exclusively of individuals with chronic rather than acute SCI. these interventional BMD studies may have utilized sub-threshold mechanical stimuli. The use of relatively low bone loading regimens is not unexpected due to the extensive atrophy of chronically paralyzed muscle [80, 81] and concerns of fracture, which have been reported to occur with physical interventions [82, 83].

The role of leptin: The hormone leptin is secreted by fat cells and help regulate body weight and energy consumption [84]. The amount of leptin in the circulation is positively correlated with the percentage of fat in people [85]. In paraplegics, when compared with healthy subjects, higher levels of leptin have been found, possibly due to greater fat tissue storage [86, 87]. Leptin activates the sympathetic nervous system (SNS) through a central administration. The disruption of the sympathetic nervous system may modify the secretion and activity of the leptin, because the sympathetic preganglionic neurons become atrophic in high paraplegics [88, 89]. The irritation thus, below the neurological level of injury, from the leptin is disturbed. In addition, extensive obesity is known to reduce lipolytic sensitivity [89, 90, 91]. Given that

in the high level of neurological paraplegia there is a problem of disorder of the autonomic nervous system and in combination with the existence of scientific evidence that the hormone leptin activates the sympathetic nervous system through central control, was formulated, that the closure <of paths> of the central nervous system disrupts the effect of leptin and possibly increases the risk of obesity in paraplegic patients with high-level injury [92, 93].

However, after separation of SCI subjects into those with an injury above or below Thoracic (T) 6, leptin levels were significantly higher in the former group. T6 appears to be the lowest level of injury in most patients with SCI to develop autonomic dysreflexia. With SCIs above the level of T6, there is reduced SNS outflow and supraspinal control to the splanchnic outflow and the lower-extremity blood vessels. Multiple regression analysis showed that serum leptin levels in men with SCI correlated not only with BMI but also with the neurologic deficit. This finding supports the notion that decentralization of sympathetic nervous activity relieves its inhibitory tone on leptin secretion, because subjects with tetraplegia have a more severe deficit of sympathetic nervous activity [94].

Actually, little is known regarding the nature and time frame of the influence of complete SCI on human skeletal muscle because published data are coming from cross-sectional studies, where different groups with few subjects have been examined at different times, usually in the chronic phase of paralysis. Disuse was thought to be the mechanism responsible for the skeletal muscle atrophy in paraplegics, but muscle fibres following SCI begin to change their functional properties early post injury. Muscle fiber cross-sectional area (CSA) has been suggested to decline from 1 to 17 months after injury and thereafter to reach its nadir. Conversion to type II fibers has been suggested to occur between 4 months and 2 years after injury, resulting in even slow-twitch muscle becoming predominantly fast twitch thereafter (Castro et al 1999). Metabolic enzymes levels in skeletal muscle might be expected to be reduced after SCI because of inactivation. In support of this contention, succinic dehydrogenase (SDH) activity, a marker of aerobic-oxidative capacity, has been reported to be 47–68% below control values in fibers of tibialis anterior muscle years after injury in support of this contention [95].

The muscle atrophy in SCI is of central type and depends on the disuse and loss of upper connections of the lower motor neuron, sometimes associated to the loss of anterior horn cells and transinaptic degeneration. The last alteration may be responsible for the denervation changes seen in early stages post SCI. In the later stages (10-17 months post SCI) diffuse muscle atrophy with reduction of the muscle fascicle dimension is associated to fat infiltration and endomysial fibrosis. In all stages post SCI, almost all patients showed myopathic changes, as internal nuclei, fibre degeneration and cytoplasmic vacuolation due to lipid accumulation [95].

It is evident that other co-factors as spasticity and microvascular damage, contribute to the induction of the marked morphological and enzyme histochemical changes seen in the paralyzed skeletal muscle [95]. Small fibers, predominantly fast-twitch muscle, and low mitochondrial content have been reported years after injury in cross-sectional studies. These data have been interpreted to suggest that human skeletal muscle shows plasticity [48].

On the contrary, force loss during repetitive contractions evoked by surface electrical stimulation (ES) of skeletal muscle in humans does not appear to be altered within a few months of

injury [80] but it is greater a year or more after SCI (Hillegass and Dudley, unpublished observations). The greater fatigue, when evident, was partially attributed to lower metabolic enzyme levels [95].

Muscular loading of the bones has been thought to play a role in the maintenance of bone density [65, 66]. However, the ability to stand or ambulate itself does not improve BMD or prevent osteoporosis after SCI.

4. Conclusions

Other important issues according alterations of body composition are the completeness of lesions (an absence of sensory or motor function below the neurological level, including the lowest sacral segment), because body composition seems to be worse than subjects with incomplete lesions (partial preservation of motor and/or sensory function below the neurological level, including the lowest sacral segment) and aging which contributes to major alterations of body composition [62, 63].

In disabled subjects the most important issue according to body composition is how to promote optimal body weight to reduce risk of diseases such as coronary heart disease, non-insulin dependent diabetes mellitus, lipid abnormalities and fractures because of bone loss. Dietary changes, individualized physical activity programs and medication should be taken in mind in therapy when we deal with this subgroup of subjects. However, self-management of dietary changes to improve weight control and disease should be the case, which means they need to follow diets with lower energy intake and at the same time to eat regularly foods rich in nutrients [26].

We need to take in mind that healthy BMI values often underestimate body fat and may mask the adiposity and spasticity did not defend skeletal muscle mass and bone, supporting the concept that in neurologic disabilities the myopathic muscle could not recognize correctly the stimulation because of the neurogenic injury. Moreover, disabled subjects mostly transfer much of the weight-bearing demands of daily activities to their upper extremities reducing the weight-bearing of the affected paralyzed muscles triggering a cycle of added muscle atrophy which interacts with the continuous catabolic action caused by the neurogenic factor. Finally, an irreversible (once established) decline in bone mineral density, bone mineral content as well as geometric characteristics of bone is expected and the duration of lesion-injury is positively correlated with the degree of bone loss.

Further research about body composition is needed in all physical disabilities and more longitudinal studies to quantitate and monitor body composition changes and to modify our therapeutic interventions. However, prevention rather than treatment may have the greatest potential to alleviate these major complications. Therapies should focus on how to perform weight bearing, standing or therapeutically walking activities early in the rehabilitation program to gain benefits according to muscles and bones.

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INTECH

Paraplegia Related Osteoporosis

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Additional information is available at the end of the chapter

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1. Introduction

Osteoporosis is characterized by low bone mass and destruction of the micro architecture of bone tissue, resulting in increased bone fragility and susceptibility to fractures. [1]

The World Health Organisation (WHO) created an operational definition of postmenopausal osteoporosis based on a bone mineral density (BMD)-based T-score measurement. The most widely validated technique to measure BMD is dual energy X-ray absorptiometry (DXA), and diagnostic criteria based on the T-score for BMD are a recommended entry criterion for the development of pharmaceutical interventions in osteoporosis. (2) The ranking system of the WHO is commonly used in the literature and in all discussions with respect to bone diseases. According to WHO criteria, the general categories for making a diagnosis are the following: 1) normal: BMD of not less than one standard deviation (SD) than the average young adult (T-score>-1), 2) osteopenia: BMD between one and 2.5 SD below the average for young adults (-1<T-score<-2.5), 3) osteoporosis: BMD 2.5 SD or more below the average for young adults (T-score>-2.5) and 4) severe or established osteoporosis: BMD 2.5 SD or more below the average for young adults and the presence of one or more fractures. [2, 3]

Because of the unique and individually-based approach needed in the management of each disabled subject with a spinal cord lesion and their complications according to bone loss the new term "paraplegia-related bone impairment, (Para-related BI)" is used throughout this chapter. The term bone impairment is more appropriate than bone disorder because includes terminology from Rehabilitation Science a specialty which interferes with all complications of spinal cord injury (SCI) and follows these patients during aging with paralysis. It is not used here for the 1st time. Very experienced scientists and researchers chose this term to describe "osteoporosis" in SCI. [4]

2. Paraplegia related bone impairment

2.1. Epidemiology

According to the literature, spinal cord injury-related bone impairment (SCI-related BI) occurs in 75% of patients with complete SCI. [5] Twenty five out of 41 patients with SCI (61%) met WHO criteria for osteoporosis; eight (19.5%) were osteopenic and only eight (19.5%) showed normal values.[6] In SCI children (boys and girls), values for BMD at the hip were approximately 60% of normal, or had a Z-score that indicated a 1.6-1.8 SD reduction in BMD compared with age-and sex-matched peers. [7] The decrease in BMD was probably the dominant cause for the high prevalence of SCI-related BI in the long femur or proximal tibia and explains why these areas are often fracture site. [6, 8, 9] For example, a reduction in bone mineral density in the femoral neck of about 0.1 g/cm^2 increases fracture risk by 2.2 times. This decrease in bone mass is associated with alterations in bone material, reduced bone elasticity and is connected to the origin of pathological fractures with minimal injury, in which these patients are vulnerable and exposed. [8, 9]

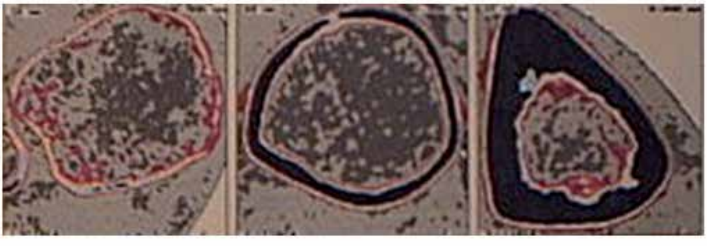
2.2. Bone mineral density

In individuals with SCI bone loss begins immediately after injury. [10, 11] SCI-related BI below the level of injury is much greater compared with other conditions (i.e. age, immobilization, bed rest, lack of gravity environment). A reduction of bone mineral content during the first years after the injury of 4% per month in regions rich in cancellous bone, and 2% per month on sites containing mainly cortical bone is reported. [12] According to another study 25 out of 41 patients with SCI (61%) met WHO's criteria for osteoporosis, eight (19.5%) were osteopenic and only eight (19.5%) showed normal values. [6] In SCI children (boys and girls) values for BMD at the hip were approximately 60% of normal, or had a Z-score that indicated a 1.6-1.8 SD reduction in BMD compared with age-and sex-matched peers. [7]

Bone loss measured with peripheral quantitative computed tomography (p QCT) in SCI subjects in the femur's and tibia's epiphyses was 50% and 60% vs. 35% and 25% in the diaphyses, respectively, meaning that bone loss in the epiphyses almost doubled the loss in the diaphyses. [13] This study also showed that bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses bone is lost due to the decrease in trabecular, while in diaphysis, the cortical bone density is maintained and bone is lost due to endocortical resorption. In line with the previous study, another p QCT study, performed in complete paraplegics with high (thoracic 4-7) and low (thoracic 8-12) neurological level of injury at the tibia, found a loss of trabecular (57.5% vs. 51%, in high vs. low paraplegics, respectively) and cortical bone (3.6% and 6.5%, respectively), suggesting that trabecular bone is more affected during the years of paralysis in comparison with cortical bone. [14] In the same study both paraplegic groups had a similar loss of total BMD (46.90% vs. 45.15%, in high vs. low paraplegics, respectively) suggesting that a homogenously deficit pattern occurs in the epiphyseal area, especially in the group of low paraplegics because the central and the peripheral of the cross sectional area of bone were similarly affected. On the contrary, in high paraplegics' group trabecular bone loss was higher suggesting an increasing endocortical

remodeling keeping the total BMD similar. Concerning cortical geometric properties the results had shown an increased endosteal circumference between both paraplegic groups vs. controls leading to reduction of cortical thickness, 19.78% vs. 16.98% in paraplegic groups respectively, whereas periosteal circumference was comparable to controls (Fig. 1).

p QCT in the tibia of control subject 38 years old man, slices: 4%,14%,38%



p QCT in the tibia in chronic complete AIS A paraplegic man thoracic 12 NLol 24 years old. slices: 4%,14%, 38%

Figure 1. Peripheral quantitative computed tomography (p QCT) tibia slices in control (a) and paraplegic subject (b), (scanner XCT 3000 Stratec, Medizintechnik, Pforzheim, Germany). Areas in red represent trabecular bone, while areas in grey represent fat; pQCT allows the measurements of true volumetric densities at a minimum exposure to X-rays, assess cortical and trabecular bone density separately as well as to evaluate the geometrical properties of long bones non-invasively, adapted from: Dionyssiotis Y. (15) (with permission).

Regarding tetraplegic patients statistically significant differences were found in BMD of the spine, trochanteric region and upper limbs between paraplegic and tetraplegic patients but not in the femoral neck, pelvis, and lower extremities. [16] Indeed, the effects on spinal BMD differed from previously published work in which the investigation was mainly focused in paraplegics. [17-19]

The importance of mechanical loading and site specificity to maintain or increase BMD is already shown. [20] According to bone loss there are some interesting features in spinal cord injured subjects; demineralization is area dependent, occurs exclusively in the areas below the level of injury, affecting mainly paralyzed extremities and increasing from proximal to distal regions i.e. in paraplegics weight bearing skeleton regions, as the distal end of femur and proximal tibia, which are rich in cancellous bone, while region of the diaphysis of the femur

and tibia, rich in cortical bone is reserved. [13, 14, 21] Moreover, bone loss between trabecular and cortical bone compartment differs in mechanism, i.e. in the epiphyses is due to decrease in trabecular but in diaphysis cortical bone is maintained and bone is lost through endocortical resorption by reducing cortical wall thickness. [13, 14]

2.2.1. The additional risk factor of feminine gender

Women with disabilities have a higher risk of losing bone mass compared to men because of the inevitable reduction in estrogen levels that occurs at menopause. Findings that women with serious disabilities have low bone density are not surprising and are probably related to the lack of activity (reduced mobility, reduced loading on bone) and worsening of the disability. [22] Regarding women with complete SCI, the initial bone loss in the lumbar spine is negligible. Post injury over a period of years BMD in SCI women is maintained or increases compared with non-injured age-matched women, in whom BMD decreases during aging.

2.2.2. Biochemical changes in bone after spinal cord injury

After SCI, osteoblast activity slightly increases, while a significant increase in osteoclast activity within a maximum of 10 weeks after injury and at level up to 10 times greater than normal is present. The imbalance between bone resorption and bone formation below the level of the lesion or injured area may be due to decreased blood flow and venous stasis, arteriovenous anastomoses and tissue oxidation. [23] SCI-related BI can be enhanced by a lack of muscular tension on bone or other neuronal factors associated with the lesion. The parathyroid glands are inactive with low levels of parathyroid hormone (PTH) observed up to one year after injury. The hypercalcemia that occurs immediately after injury is responsible for low levels of PTH. Gradually, in a range of one to nine years after injury, the function of the parathyroid is restored. The result is an increase in bone resorption associated with dysfunction of the parathyroid glands in the chronic phase of injury. This mechanism of SCI-related BI during the chronic phase tends to be balanced by an increase in bone mineral density (BMD) in areas of the body with increased loading (upper limbs, spinal column) and adds bone density (transferring bone mineral) compared to a loss in the chronic non-loadable areas of the skeleton (pelvis, lower limbs and upper limbs in tetraplegics). Hormonal changes (parathyroid hormone, glucocorticoids and calcitonin) and metabolic disorders (increased alkaline phosphatase, hypercalcemia/hypercalciuria and hydroxyproline excretion) may be secondary to the loss of bone density. [10, 24] Hypercalciuria is seen in the first 10 days after neurological injury and reaches its maximum value after one to six months and is two to four times greater that the hypercalciuria observed after prolonged bed rest. The significant increase of calcium in the urine is the result of an imbalance between bone formation and bone resorption. [25] The rate of formation or resorption of bone matrix can be determined by quantifying the enzyme activity of bone cells or by measuring the components of the matrix that are released into the circulation during the process of absorption. It should be noted that these indices of bone activity are somewhat non-specific. The intact procollagen I N-terminal propeptide (PINP) molecule is the amino end of type I procollagen before excision and the formation of fibrils and is a measure of the total synthesis of collagen in the body, all of which is related to

bone matrix. Osteocalcin is a non-collagen protein which is a primary constituent of osteoblasts, and may also be released during apoptosis of osteoclasts and indicates either formation when resorption and formation are coupled or turnover in decoupling. [26, 27] Urinary excretion of cross-linked pyridoline type I collagen is recognised as a sensitive marker of bone resorption, and pyridoline quality tests including measurement of the aminoterminal (NTx) and carboxyterminal (CTx) intermolecular cross-linking domain of bone type-1 collagen provide a good indicator of bone resorption. [28, 29] Others studied markers of bone metabolism for six months after acute spinal cord injury and observed an increase in ionised serum calcium above the upper limit of normal and suppression of serum PTH. [30] The indices of bone resorption (total pyridoline, deoxypiridoline [total and free] and NTx) recorded a significant increase (even 10 times above the upper limit of normal) after acute immobilisation, with the highest values found 10 to 16 weeks after injury. The markers of bone formation (total alkaline phosphatase and osteocalcin) showed an insignificant increase, which remained within the normal limits. [10] Moreover, Nance et al. observed that values of NTx in the urine were lower during the first months in patients receiving pamidronate compared with the control group, but this finding did not reach significance. [31] Regarding the lack or insufficiency of vitamin D, it has been reported that 64% of paraplegics are deficient (<15ng/ml). [32]

Mechanical unloading (paralysis) in acute SCI subjects causes greater sclerostin levels than those observed in the able bodied. This increase is associated with reduced bone formation during the acute phase of SCI. The ability to walk (mechanical loading) modulates the response of bone to paralysis by causing a smaller increase in sclerostin levels, thereby partially protecting against bone loss. In the chronic phase, bone wasting results in lower sclerostin levels than those observed in the able bodied. This effect is due to the reduction of sclerostin-producing osteocytes in the osteoporotic bone. In the chronic phase, similar to the acute phase, the ability to walk partially protects against bone loss. Sclerostin causes up-regulation of RANKL (key factor that promotes the differentiation of osteoclasts) and down regulation of osteoprotegerin (a key inhibitor of osteoclast differentiation) expression in osteocytes, which leads to increased osteoclast activity and bone resorption. [33]

2.2.3. Duration of paralysis and bone steady state

The duration of paralysis affects the degree of bone loss in regions below the level of injury. A study of 21 men with SCI with an average duration of 10.6 years, using DEXA, expressed at various levels of injury an inverse relationship between BMD in the legs and the duration of the lesion, while others found a weaker relationship regarding the microarchitecture of the distal end of tibia. [34, 35]

In a study which included paraplegics with duration of paralysis of 14 ± 11.5 years a positive correlation between the duration of paralysis and the degree of bone loss was found. [13] The length of immobilization in the acute posttraumatic period increased bone loss in the legs, particularly in the proximal tibia; over 50% of bone mass was lost (in the affected areas) in the period of ten years after the injury. [21] When subjects categorized depending on the length of the lesion (0-1, 1-5, 6-9, 10-19, 20-29, 30-39, 40-49, and 50-59 years after the injury), in all age

groups bone mineral density of the proximal femur declined and was detected a year after the injury. [24]

Using DXA and QUS (quantitative ultrasound) measurements in 100 men with SCI, aged 18 to 60 years, it was found that bone density decreases over time in all measured points, while bone loss followed a linear pattern in the femoral neck and distal epiphysis, stabilized within three years after the injury. On the contrary, Z-scores of the distal region of the diaphysis of the tibia continued to decrease even beyond ten years after the injury. [36] Duration of paralysis related bone loss in the legs of monozygotic twins with chronic paraplegia in comparison with their able-bodied co-twins has been also reported. [37]

The results of a comparison of chronic complete paraplegic men vs. controls in another study found a reduction of BMD in paraplegics' legs independent of the neurological level of lesion. BMD of the legs was negatively correlated with the duration of paralysis in the total paraplegic group, but after investigation according to the neurological level this correlation was due to the strong correlation of high paraplegics' legs BMD with the duration of paralysis, suggesting a possible influence of the neurological level of injury on the extent of bone loss. [38] A significant inverse relationship between percentage-matched in BMD leg, arm and trunk values and time since injury was found when varying levels of SCI were analyzed. [34]

Studies are supporting the concept of a new bone steady state at 16-24 months after injury, especially for bone metabolic process, but BMD decreases over the years at different areas and is inversely related to the time of the injury, which means continuous bone loss beyond the first two years after the injury (Fig. 2). [11, 13, 14, 24, 38-41]

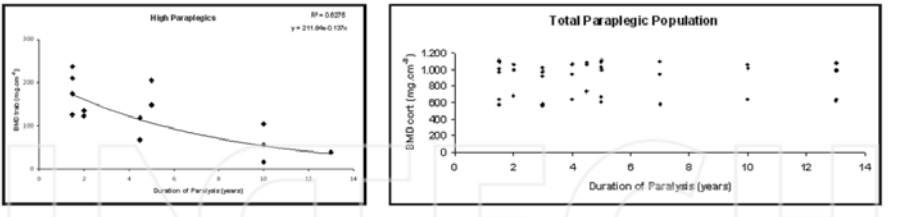


Figure 2. The duration of paralysis was inversely related with trabecular bone loss in spinal cord injured subjects. Exponential correlation between volumetric trabecular bone mineral density BMD trab and duration of paralysis in high paraplegics was found to fit best. On the contrary no significant decrease in BMD cort of the diaphyses was found in total paraplegic group. BMD parameters were measured by pQCT in 31 paraplegic men in chronic stage (>1.5 years of injury). Spinal cord injury paraplegic men were allocated into 2 subgroups based on the neurological level of injury; subgroup A (n=16, Thoracic (T) 4 –T 7 neurological level of injury) and subgroup B (n=15, T8-T12 neurological level of injury). BMDtrab: BMD trabecular; BMDcort: BMD cortical; (adapted from Dionyssiotis et al. [41] with permission).

The role played by factors such as race or gender of patients is not yet clear documented, but studies indicated more loss in women than men. [42] Loss of bone is closing fracture threshold from 1 to 5 years after injury and risk factors for fractures after spinal cord injury are gender (women are more at risk than men), age and duration of injury (increasing age and duration of injury increases the risk of fracture with a statistically significant increase in 10 years after

injury), the type of injury (complete SCI subjects have more fractures than incomplete), low body mass index (BMI) and low bone density in the tibia. [6, 24, 43]

2.2.4. The role of central nervous system

2.2.4.1. Sympathetic denervation in SCI

Spinal cord injury is a dynamic process that is related to alterations in both the central and peripheral sympathetic nervous system (SNS). Sympathetic denervation in SCI may cause arteriovenous shunts and a slowdown of intraosseous blood flow, thus increasing bone resorption. [44] With high-level spinal cord lesions the SNS is disproportionately involved when compared with the parasympathetic nervous system. In a complete high-level SCI, functioning in the isolated spinal cord below the lesion becomes independent of supraspinal control and has been termed ″decentralization″ of the sympathetic nervous system. [45]

Loss of supraspinal control leads to dysregulation of those homeostatic mechanisms normally influenced by the SNS through loss of facilitation or lack of inhibition. [46] Today there is clinical evidence that the sympathetic regulation of bone does exist in humans and plays a clinically important role in diseases characterized by excessive sympathetic activity. [47] The scientific finding about sympathetic innervations of bone tissue and its role in the regulation of bone remodelling is of major interest in situations where uncoupling between osteoclasts and osteoblasts occurs. [48-50]

2.2.4.2. Spasticity

So far, spasticity has been considered by many researchers as a prophylactic factor for bone. It is well known that voluntary muscle contraction is effective in the prevention of osteoporosis. [51, 52] Although muscle loading plays a vital role in maintaining bone density, conflicting results regarding the effect of muscle spasms in the form of spasticity have been reported in SCI patients. [53-56] Controversial results have also been reported regarding the effect of spasticity on BMD in paraplegics. A cross-sectional study of 41 paraplegics reported less reduction of BMD in the spastic compared to the flaccid paraplegic SCI patients. [53-55] Other investigators suggested that muscle spasms can slow bone loss based on the theory of a single basic muscle/bone unit. [56] Muscle spasms and muscle tension in the presence of spasticity put force on bone. This is likely to play a regulatory role in maintaining bone density. These studies concluded that spasticity may be a protective factor against bone loss in SCI. Other researchers, however, could not find a correlation between bone density and spasticity. [55] Moreover, in 18 motor complete SCI men matched for time since injury, gender and age (nine had severe spasticity and nine had spasticity that was either mild or not present) no difference was found in BMD depending on the level of spasticity. [57] A pQCT study investigating the tibia in complete paraplegics above the thoracic 12 (T12) level with various degrees of spasticity according to the Ashworth scale found no effect on volumetric BMD measurements.[41] Others have reported that spasticity may be protective against bone loss in SCI patients, however, without any preserving effect on the tibia. [55] A possible explanation for this could lie in the fact that studies include various SCI subjects with various degrees of spasticity. In addition,

in studies examining the lower leg, muscle spasms affecting the lower leg would mainly be extension spasms resulting in plantar flexion, thus creating little resistance to the contracting muscles. Furthermore, the measuring sites of the tibia did not include any muscle insertions of either the knee or the ankle extensor muscles. Patients without spasticity usually have more fractures. At the same time, excessive spasticity may cause fractures through uncontrolled limb movements, i.e. in a wheelchair. Therefore, the effect of spasticity on bone is probably two-sided: a low grade of spasticity is beneficial while a high grade is harmful. [41]

3. Interventions for prevention of bone impairment

3.1. Weight bearing activities – Body weight supported treadmill – Cycling

The effect of standing in bone after SCI has been investigated by many researchers. A beneficial effect on bone mass using passive mechanical loading has been shown on preservation of bone mass in the region of the femoral shaft, but not at the proximal hip of standing and non-standing patients and relatively better-preserved densities in patients standing with braces than in those using a standing frame or standing wheelchair. [58] A slower rate of bone loss in paraplegic subjects who did standing was expressed in a prospective study of 19 patients in acute SCI phase participated in early standing training program which showed benefits concerning the reduction of cancellous bone loss compared to immobilized subjects, while no correlation for passive standing-training to bone status was found in another p QCT study. [59, 60] Protection afforded by standing in the femoral diaphysis stands in contrast with the loss of bone in the proximal femur. This suggests that the transmission of forces through trabecular and cortical bone varies; so the less effective strain for the initiation of bone remodeling reaches faster cortical bone. [61] Others also supported the concept of different strain thresholds during bone remodeling control. [62-64] There is level 2 evidence (from 1 non-randomized prospective controlled trial) that Functional Electrical Stimulation (FES)-cycling did not improve or maintain bone at the tibial midshaft in the acute phase. [65] Moreover, there is level 4 evidence (from 1 pre-post study) that 6 months of FES cycle ergometry increased regional lower extremity BMD over areas stimulated. [66] Body weight supported treadmill training (BWSTT) did not alter the expected pattern of change in bone biochemical markers over time and bone density at fracture-prone sites. [67]

3.2. Whole body vibration

At a meeting of the American Society for Bone and Mineral Research the results of a small randomised, placebo-controlled study among 20 children with cerebral palsy who used a similar, commercially available vibrating platform for 10 min per day, 5 days per week for 6 months, reported a significant increase in tibial, but not lumbar-spine bone density in the treated group despite the simplicity, short duration of the “vibration, the young age of the children and the poor compliance. [68, 69]

After 6 months of whole body vibration (WBV) therapy in twenty children (14 boys-6 girls) with cerebral palsy (age 6.2 to 12.3 years) randomized to either continue their school physio-

Figure 3. Weight bearing in disabled subjects; using standing frames, functional walking with orthoses between bars and crutches, even push-ups in the wheelchair (in case of multiple sclerosis with a clinical equivalent like tetraplegia) bone can be loaded and bone loss rate would be slower (unpublished photos of Dionyssiotis Y).

therapy program unchanged or to receive 9 minutes of side-alternating WBV (Vibraflex Home Edition II®, Orthometrix Inc) no effect on areal BMD at the lumbar spine was observed, while areal BMD seemed to decrease somewhat in the cortical region of the femoral diaphysis. Authors explained that mechanical stimulation increases intracortical bone remodeling and thereby cortical porosity; moreover changes occurred in ways that are not reflected by areal BMD, but might be detectable by more sophisticated techniques such as such as peripheral quantitative computed tomography. [70] Low-intensity vibration (LIV) has shown to be associated with improvement in bone mineral density in post-menopausal women and children with cerebral palsy. Seven non-ambulatory subjects with SCI and ten able-bodied controls underwent transmission of a plantar-based LIV signal (0.27+/-0.11 g; 34 Hz) from the feet through the axial skeleton as a function of tilt-table angle (15, 30, and 45 degrees). SCI subjects and controls demonstrated equivalent transmission of LIV, with greater signal transmission observed at steeper angles of tilt which supports the possibility of the utility of LIV as a means to deliver mechanical signals in a form of therapeutic intervention to prevent/reverse skeletal fragility in the SCI population. [71]

Figure 4. The Galileo Delta A TiltTable offers a wide variety of applications from relaxation to muscle training for a diverse range of patients who are unable to stand without support. The motor driven adjustable tilt angle of the Galileo Delta TiltTable (90°) allows vibration training with reduced body weight from 0 to 100%. This is ideal for deconditioned and disabled patients for gradually increasing training weights up to full body weight. System for application in adults (max. body height: 1.90 m) and children (max. body height: 1.50 m).The Galileo Delta A TiltTable is exclusively available from the manufacturer Novotec Medical GmbH. (published with permission).

3.3. Pulsed Electromagnetic Fields (PEMF)

Huang et al recently reviewed the effects of low-frequency pulsed electromagnetic fields (PEMFs) on chronic bony pain, bone mineral density (BMD), bone strength and biochemical markers of bone metabolism in the patients of osteoporosis. [72] Two studies are analyzed in SCI subjects: In a study that consisted of 6 male patients with complete spinal cord injury of a minimum of 2 years duration the time of therapy of PEMFs continued for 6 months and at 3 months BMD increased in the stimulated knees by 5.1% and declined in the control knees by 6.6% (P <0.05 and P <0.02, respectively). By 6 months the BMD returned to near baseline values and at 12 months both knees had lost bone at a similar rate. It was demonstrated that PEMFs can delay bone loss and there may exist both a local and a systemic response. [73] Another study consisted of 24 patients with SCI who were then divided into two groups, BMD of the total proximal femur and trochanter of patients in the treatment group were increased significantly compared with the control group. [74] Both of the trials indicated that the increase

in BMD effects of PEMFs may relate to the features of the subjects. People with spinal cord injury are younger than osteoporosis patients, the osteoblasts and osteoclasts of patients with spinal cord injury may be more sensitive to the PEMFs stimulation than that of the old people.

Clinical examination and management of bone loss in paraplegia	
• history of the patient (co morbidities, neurologic complications, use of drugs which impair bone metabolism, alcohol, smoking and information about the level of injury, duration of paralysis, immobilization period, onset of rehabilitation, use of assistive devices and orthoses).	• pharmacological treatment with bisphosphonates p.os and i.v. that have been studied in patients with spinal cord injuries and had positive effects on bone parameters. • Use of calcium supplements (monitoring renal function) and vitamin D.
• anthropometric parameters (age, weight, body mass index, BMI)• clinical examination (level of injury according to American Spinal Injury Association Impairment Scale, AIS) and assessment of spasticity)	• Education on falls prevention • Counseling regarding osteoporosis and related factors and identification of fractures in regions of impaired sensation.
• imaging (bone densitometry by DXA at the hip and spine, and if possible, p QCT at the the tibia or femur)	• physical therapy including: a) range of motion exercises, b) loading of the skeleton to reduce bone loss, d) therapeutic standing-walking with orthoses, e) passive-active cycling
• measurement of bone turnover indices in the serum (parathyroid hormone, alkaline phosphatase, calcium, vitamin D, PINP molecule, osteocalcin) and urinary excretion of 24 hour (calcium, hydroxyproline, aminoterminal (NTx) and carboxylterminal (CTx) intermolecular cross-linking domain of bone type-1 collagen), which provide a good indicator of bone resorption.	• dietary interventions to improve dietary intake of calcium and nutrition indices.

Table 1. An algorithm for the screening and management of osteoporosis in subjects with spinal cord injury (should be read top to bottom starting with the left column); adapted from: Dionyssiotis Y. (84) (with permission).

3.4. Drugs

Calcitonin in varying doses and methods of administration has given variable results in paraplegia (preferred dosage regimen, treatment duration, and administration route for adequate efficacy in SCI patients' remains unclear). [75, 76] Likewise, the outcome using bisphosphonates has been variable. Etidronate produced long-term benefit in lower limb bone mineral density (BMD) in selected walking SCI patients; whereas tiludronate appeared effective in reducing bone resorption and preserving bone mass in a histomorphometric study in 20 paraplegic patients. [77, 78] Intravenous pamidronate has been shown to attenuate bone loss in SCI and normalize serum calcium in immobilization hypercalcemia. [79] Alendronate

(1000 times more potent than etidronate), in an open observational study, reversed BMD loss in men with established SCI increased both axial and trabecular bone density and has proven efficacy and safety in men treated for osteoporosis, prevents hypercalciuria and bone loss after bed rest and lower leg fracture. [80, 81] Six months after using zolendronic acid in the treatment group BMD showed differences in the response to treatment between the mixed trabecular/ cortical regions (narrow neck and intertrochanteric) and the purely cortical shaft. With respect to cross-sectional geometry, bone cross-sectional area and sectional modulus (indices of resistance to axial and bending loads, where higher values would indicate a positive effect of treatment) increased at the hip and buckling ratio (an index of the instability of thin-walled cross sections, where lower values would suggest that the treatment is improving stability) decreased consistent with improved bone outcomes; at 12 months, narrow-neck femur values declined and intertrochanteric and femoral shaft BMD was maintained vs. placebo group which showed a decrease in bone outcomes and an increase in buckling ratio at the hip at 6 and 12 months, while with respect to bone prevention 4 mg i.v. were effective and well-tolerated to prevent BMD loss at the total hip and trochanter for up to 12 months following SCI. [82, 83]

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Malnutrition in Paraplegia

Yannis Dionyssiotis

Additional information is available at the end of the chapter

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1. Introduction

Despite the advances in medical and nutritional science surveys show that 40-50% of patients admitted to hospitals are at risk of nutritional deficiency; one in three hospitalized patients are malnourished upon admission and up to 12% are severely malnourished [1, 2]. Malnutrition is a state in which a deficiency, excess or imbalance of energy, protein and other nutrients causes adverse effects on body form, function and clinical outcome [3, 4]. Studies report a variable prevalence of obesity from 40 to 66% in persons with SCI completing the spectrum of newly introduced concept in nutritional deficiency [5, 6, 7].

After the lesion paralysis and loss of function that usually occur and well documented hypercatabolic responses may lead to deleterious effects such as loss of lean body mass, obesity, increased susceptibility to infections, and reduced wound healing [5, 8, 9]. Unwanted weight gain should be prevented because induces the risk for diseases such as diabetes, coronary heart disease and dyslipidaimias in this population [8]. Mortality and pathogenesis of critically ill patients are affected by nutritional status. Body fat has been identified as a significant predictor of mortality. Moreover, some disorders such as carbohydrate intolerance, insulin resistance, lipid abnormalities, and heart disease occur prematurely and at a higher prevalence in disabled populations may be related to immobilization and skeletal muscle denervation [10]. According to the above the term malnutrition should include not only undernourishment but also obesity [11]. Therefore, the objective should be either the maintenance of optimal nutritional status of the patient, either to supplement the deficiencies in nutrients. Nutrition support therapy should be tailored to each patient. An optimal nutritional assessment and management of the disabled subject can minimize the complications associated with acute traumatic injury and long-term rehabilitation [12].

This chapter reviews methods of nutritional assessment and describes the physiopathological mechanisms of malnutrition, reviews specific nutritional studies, and the supplemental support which can be used in paraplegic subjects.

2. Nutritional assessment

For an initial assessment of nutritional status serial measurements to assess trends over time and then monitor the response to a dietary intervention may be useful. The proposed assessments should be interpreted collectively including the examination of possible factors that contribute to the nutritional status, such as age, sex, over-or under-hydration, interactions between drugs-food, metabolic stress, infection, and the existence of other diseases[13].

2.1. Diet history

During hospitalization adequate intake of nutrients is intercepted by many factors, and may be caused by anorexia, early satiety, immobility, depression. Moreover, gastrointestinal function is compromised: gastric dilatation and paralytic ileus occurs often, although the intestinal activity usually returns within the first week after injury.

2.2. Nutritional requirements

The provision of energy and nutritional requirements is a very important factor for patient management. Malnutrition, in this case undernourishment or over nutrition-obesity, can lead to muscle loss, atrophy of the lining of the intestine, immunochemical reduction, poor wound healing and fluid overload, hyperglycemia, high levels of urea nitrogen in blood, high triglycerides, elevated liver enzymes, respiratory exhaustion due to increased production of CO_2, and difficulty weaning from the oxygen, respectively. The assessment of nutritional requirements includes not only calculations but also the opinion of an expert clinician in order to assess the clinical and morphometric data before applying the equations that provide the energy and protein requirements [14].

There have been several methods for predicting energy expenditure (EE); the components and the methods for its determination and estimation, summarizing their main advantages and limitations have been recently reviewed [15]. However, because of various confusing factors such as infections and sepsis, hyper nutrition supportive nutritional diets, clinical procedures, postoperative medications, and changes in body weight such as sarcopenia, obesity, amputations and significant weight loss, the prediction equations can be complex and invalid [16].

A group of equations among these are Mifflin–St Jeor equation [17], the Harris-Benedict equation [18], the American College of Chest Physicians (ACCP) recommendation based on kcal/kg body weight [19], the Faisy equation [20], the Ireton-Jones equations [21, 22] and the Penn State equations [23, 24]. Because the Mifflin equation was designed for healthy people is not analyzed here.

The Harris-Benedict is calculated by sex with the following formula:

Men: Resting Metabolic Rate (RMR) (kcal/d)=67+Body Weight x 13.75+Height x 5 – Age x 6.8 [18, 24].

Women: RMR (kcal/d)=655+Body Weight x 9.6+Height x 1.85 – Age x 4.7 [25].

Ideal body weight is calculated by the Hamwi rule of thumb while metabolically active weight (MAW) is calculated as 25% of excess weight (actual weight − ideal weight) added to the ideal body weight [26]. The Ireton-Jones equations include one specifically for obese patients and one for general critical care populations:

Obesity: RMR (kcal/d)=Wt x 9+Gender x 606 – Age x 12+1844 [27].

Nonobese: RMR (kcal/d)=Wt x 5 – Age x 10+Gender x 281+Trauma x 292+1925 (for gender: male=1, female=0) [28].

To determine accurately the early energy expenditure after spinal cord injury, studies compared measurements of real resting energy expenditure (REE) with the Harris-Benedict equation (basic energy expenditure, BEE) [18]. During the first two weeks after the injury, the exact measurements of REE are similar to the estimated calorie needs, when used with BEE stressor/injury factor of 1.6. To avoid overestimation of calorie needs, the deletion of factor activity of 1.2 (rest in bed) is proposed. Kearns et al. reported that in 10 patients, the mean REE after acute injury was only 67% of BEE predicted by Harris-Benedict formula. They hypothesized that non-specific changes in neurogenic stimuli and reduced oxygen consumption by relaxing muscles contributed to their findings. Also, an interesting feature observed is that the REE was raised by 5% with the return of muscle tone [29]. Jeejeboy and Cerra proposed an alternative approach that uses body weight (kg) alone as a determining factor, and omits the variables of age, sex and height as used in HB equation. This type of assessment has proven to be accurate and efficient over time [30, 31]. Ireton-Jones and Owen et al. have developed specific formulas for the obese patient, which is common in SCI subjects. The predefined types may overestimate their needs due to increased fat mass in this population [21, 22, 32].

2.3. Assessment of subjects in the clinical setting

Patients admitted in the hospital should be examined for actual or potential occurrence of malnutrition because of an unintentional weight loss or gain. In the clinic this examination includes measurements of body weight depicting a loss of more than 10% of normal body weight within 6 months or loss of more than 5% of usual body weight within 1 month or 20% more or less than ideal body weight (IBW), calculation of body mass index (BMI) <18, depletion of visceral protein (serum albumin <3.5 g/dl, serum transferrin <200 mg/dl, serum cholesterol <160 mg/dl, serum pre – albumin <15 mg/ml, creatinine height index (CHI) <75% (measured by 24-hour creatinine excretion, which is typically associated with muscle mass of the patient as an indicator of malnutrition, especially in young men), and the presence of diet modifications (patient receives total parenteral nutrition (TPN) or enteral nutrition (EN), inadequate food intake due instructions for stopping any food by mouth (NPO), liquid diet, disorders of absorption, reduced swallowing capacity, increased metabolic needs, gastrointestinal disturbances (nausea, vomiting, diarrhea, constipa-

tion). Unintentional weight gain is an increase in body weight that occurs when a person takes in more calories than the body needs or uses [33, 34].

For able bodied persons the World Health Organization (WHO) advocates use of BMI as a population-level indicator of obesity which is not a direct measure of body fat, but a more accurate indicator of overweight and obesity than relying on weight alone. BMI is calculated using the equation weight (Kg)/height (m^2), which is a very practical and useful measure that allows the easy determination of categories of weight status. In able-bodied subjects overweight is defined as a BMI of 25–29.9 kg/m^2 and obesity as a BMI of ≥30.0 kg/m^2 and extreme obesity≥40 kg/m^2 (Table 1) [35, 36].

Classification	BMI (kg/m^2)	Obesity Category
Underweight	<18.5	-
Normal	18.5-24.9	-
Overweight	25.0-29.9	-
Obesity	30, 0-34, 9	I
Moderate obesity	35.0-39.9	II
Extreme obesity	> 40.0	III

Table 1. Classifications based on the weight for BMI and obesity category (published with permission from Dionyssiotis Y. [36])

In a chronic SCI population with paraplegia values of body mass index (BMI, kg/m^2) were not significant vs. controls, which is a finding in line with the literature [10, 37]. Nevertheless, Gupta et al demonstrated the usefulness of BMI as an indicator of obesity [38]. Whether the criteria of BMI may assess obesity in people with spinal cord injury the latest studies show the opposite [39]. The applicability of conventional BMI cut off values is into question [40, 41]. Another critical issue is that the relationship between BMI and disease is typically U-or J-shaped with those in the middle categories of BMI having the lowest risk compared to the lowest extreme and upper levels of BMI. It is under question if the cut-points for underweight, normal, overweight, and obese used in able-bodied populations can be applied to disabled subjects [42]. Not many studies investigated BMI in patients with MS. Nevertheless, BMI was found statistically less compared to age comparable controls [43].

Anthropometric standards such as the ideal body weight (IBW), the triceps skin fold thickness and the middle arm circumference which are common tools for assessment of nutrition may not be valid for disabled subjects due to water changes, atrophy of muscles because of immobility, increased body fat, and the inevitable weight loss beyond the normal. Patients' early weight loss is mainly due to loss of muscle rather than fat which bias the results of validity. In chronic paraplegics, the ideal weight has been estimated to be 4.5 to 6.5 kg below their respective controls finding which is in line with our recently published results [37]. Indeed, height and weight measurements are the key elements in nutritional assessment. The IBW is determined by the height. No matter which method of

calculation is used, the IBW should be adjusted for body type (frame sizes: small-IBW 10% reduction, middle size-no changes required, large size-IBW increased by 10%) and spinal cord injury (paraplegia-decrease IBW by 10-15%, tetraplegia-by 15-20%, respectively). The weight in admission is probably the most reliable measure of weight in determining the actual body weight (ABW) of the patient because is unreliable postoperatively or during an acute illness due to administration of fluids or due to edematous condition. As a chronic index, one can assume that the weight gain or loss is associated with an increase or decrease in lean body mass. To determine the weight which should be used on the nutritional calculations, first % IBW should be calculated through the equation: % IBW=actual body weight (actual body weight, ABW / ideal body weight (IBW) x 100. If the actual body weight (ABW) is less than IBW, use ABW, to define the nutritional requirements, if is greater than IBW, but less than 120%, it is necessary to determine nutritional needs using the adjusted relationship of body weight in the calculation needs: IBW+(ABW-IBW x 0.25). The nutritional status of patients can be categorized according to their ABW as a percentage of IBW as follows: over 200% of IBW (pathologic obesity), over 150% of IBW (obese), more than 120% IBW (overweight), 100% of IBW+/-10% (normal), 80-90% of IBW (mildly malnourished), 70-80% of IBW (moderately malnourished), less than 70% of IBW (severe nutritional deficiency–malnutrition), respectively [1].

3. Biochemical measurements

As with the visceral and somatic visceral proteins, non-dietary factors (i.e. blood loss, chronic infections, and fluid overload) should be considered as potential reasons for the reduction of serum concentrations [1]. Proteins are essential for tissue growth, maintenance and rebuilding their synthesis of hormones, enzymes, antibodies and cells transport molecules. In cases of protein excess protein is either metabolized for energy or stored as fat. The recommendations for protein intake in patients with spinal cord injury vary with respect to acute or chronic phase of the lesion and the presence of decubitus ulcers or not. Specific proteins (albumin, transferrin, and pre-albumin) are biochemical indicators used for assessing nutritional status [44].

The level of serum albumin is not a definitive measure of visceral protein status, but reflects the complex relationship between synthesis, degradation, and distribution. Given the long half-life of 21 days, serum albumin cannot be effectively used for monitoring the acute response to nutritional therapy. Therefore, albumin levels should be included in the initial profile for food control and monitoring purposes during hospitalization for measuring trends of visceral protein or as an indicator of chronic nutritional status. Beside this limitation there are many non-dietary factors that reduce the levels of albumin, regardless of nutritional status (inadequate composition: acute stress, hypoxia, impaired digestion, as in malabsorption, modified status as edematous fluid status and fluid overload, chronic loss of protein) (Table 2) [36].

Albumin (g/dl)	3.5-5	3-3.5	<3.5	<3.0	<2.5
nutritional status	normal	point that dietary intervention should be revised or adjusted	associated with poor outcome of surgery, rising costs of hospitalization and prolonged stay in ICU	severe malnutrition	increased morbidity and mortality

Table 2. Basic levels of albumin and nutritional status distribution (published with permission from Dionyssiotis Y. [36])

Due to the lower half-life (8-9 days) and the smaller size as a constituent body, transferrin is a better indicator of nutritional status of visceral protein from albumin. Normal levels of transferrin are between 200-400 mg/dl, and 150 mg/dl are considered nutritionally decision point or a point where nutritional support should be revised or adjusted. The transferrin levels are reduced in impaired synthesis as chronic infections, increased secretion, fluid overload, increased iron stores and increased in reduced iron stores as iron deficiency anemia and chronic blood loss, increased protein synthesis on estrogen therapy and oral contraception and dehydration. The serum concentration of transferrin is approximately 0.8 times the total iron binding capacity (TIBC). If direct measurement of transferrin is not possible due to the high cost and limited availability of equipment required, the level of transferrin can be easily calculated from TIBC, using the following formula: TIBC x 0.8-43=transferrin [45].

The third protein biochemical indicator is pre-albumin, which has very short half-life (2 days), making it an excellent nutritional index and due to this reason is increasingly used as an indicator of response to nutritional therapy. Reference values for pre-albumin are 16-35 mg/dl. A value of dietary intervention is 11 mg/dl because a value below this level means malnutrition. The failure of patients to increase pre-albumin above 11 mg/dl with dietary therapy is an indication that nutritional needs are not met. Concentrations should increase about 1 mg/dl per day or twice a week when the treatment is the appropriate. Non-dietary factors that reduce pre-albumin include stress, inflammation [46, 47, 48].

Physical measurements include protein nitrogen balance studies and measurement of creatinine / height index (CHI). Nitrogen balance studies measure the net change in total body protein. An assessment of nitrogen balance can be achieved by measurement of urinary urea (UUN) and compare it with the intake of nitrogen at the same time. The nitrogen balance is calculated as follows: N_2=balance intake N_2-N_2 elimination or=[protein (gr)]-(24 hour UUN+3) [6.25 gr nitrogen]. An "agent" of 3 is added to the equation for nitrogen losses in feces, skin, and the drainage of body fluids. When calculating the nitrogen balance a value of 0 meaning nitrogen balance (healthy adults), nitrogen balance> 0 (protein anabolism exceeds catabolism, usually consistent with pregnancy, growth, and recovery from disease or may indicate nutrient saturation, the goal in nutrition replenishment is a positive nitrogen balance of 4-6 grams per day and nitrogen balance <0 (the protein catabolism exceeds protein anabolism, occurs in situations of famine, increased catabolism due to trauma or surgery, and inadequate nutrition therapy), respectively. CHI measures the 24-hour creatinine excretion in urine and compares with an optimum value based on the ideal weight for height [49].

4. Malnutrition screening tools

Screening is important for the early detection of patients who are undernourished or at risk of developing malnutrition. Since January 2010, the Dutch Health Care Inspectorate (HCI) has defined under nutrition as a main care problem in rehabilitation centres, by establishing it as a Performance Indicator for Risk Steering Supervision. Dutch rehabilitation centres are now obligated to screen all rehabilitants for under nutrition on admission The Short Nutritional Assessment Questionnaire (SNAQ) is the recommended screening tool in this benchmark (Figure 1) [50]. However, various screening tools have been developed to detect a patient's nutritional status in many healthcare settings, but not in the rehabilitation setting. In the Netherlands, the SNAQ [51] and the Malnutrition Universal Screening Tool (MUST) are used for the hospital situation [52, 53]. The HCI advises the use of the SNAQ for under nutrition screening in rehabilitation centres [51]. Our results suggest the use of the SNAQ65+as a screening tool. This tool showed the best diagnostic accuracy of the quick and easy screening tools investigated (sensitivity 96%, specificity 77%) [52, 54].

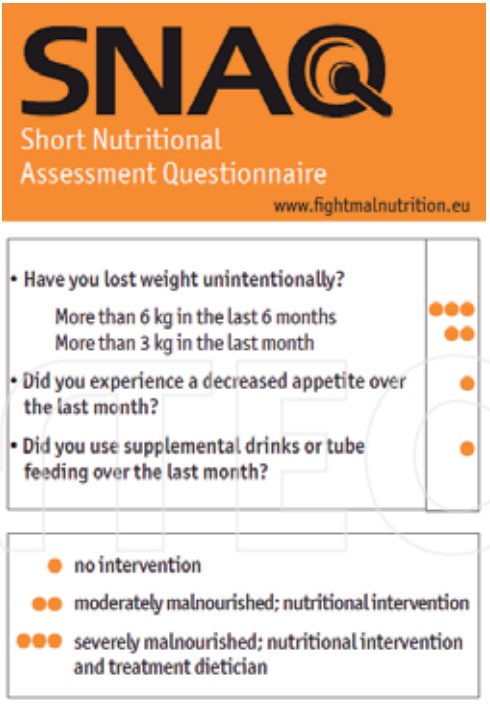

Figure 1. The Short Nutritional Assessment Questionnaire (SNAQ). Published with permission from: http://www.fight-malnutrition.eu/fight-malnutrition/screening-tools/

5. Monitoring

Healthcare professionals with relevant skills and training should review the indications, route, risks, benefits and goals of nutrition support at regular intervals. The time between reviews depends on the patient, care setting and duration of nutrition support. Intervals may increase as the patient is stabilised on nutrition support [55]. (NICE Clinical Guideline 32 Feb.2006 Nutrition Support in Adults: Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition, the whole guideline can be downloaded from: http://www.nice.org.uk/nicemedia/live/10978/29979/29979.pdf)

6. Physiopathological mechanisms of malnutrition

6.1. Malnutrition in the acute phase of paraplegia

Pathophysiological mechanisms of malnutrition in paraplegia are multifactorial. There is a dramatic increase in energy expenditure, endogenous protein catabolism and nitrogen excretion after lesion-injury. Extensive multiple organ trauma, soft tissue injuries and fractures, may further increase hyper catabolic reactions. Also, the body temperature and energy expenditure increases due to pulmonary infections or urinary tract infractions, and pancreatitis. The metabolic rate does not seem to be affected by the small reductions in thyroxin levels in plasma observed after the injury [56, 57].

Metabolic changes are also present with the elevated catabolic hormonal and cytokine responses including increased blood levels of counter regulatory hormones (e.g., cortisol, catecholamines, and glucagon), increased blood and tissue levels of proinflammatory cytokines (i.e., interleukin-1, interleukin-6, interleukin-8, and tumor necrosis factor α), and peripheral-tissue resistance to endogenous anabolic hormones (i.e., insulin and insulin-like growth factor 1) to be primarily responsible for the initial changes in metabolism [58-61].

Glucose intolerance, which cannot be readily apparent during the acute phase, but may be caused by complications and physiological processes of acute care such as the initial hyper metabolic-catabolic stress response, administration of steroids, the parenteral / enteral nutrition, and atrophy as a consequence of aponeurosis which results in gluconeogenesis [62]. Glucose and lipid metabolism disrupt in acute post-traumatic phase. Increased hepatic gluconeogenesis and regional response to insulin result in hyperglycemia. The metabolism of glucose in combination with acute nerve injury has been studied extensively, especially as related to ischemia. These studies suggest that hyperglycemia which follows immediately after head injury or spinal cord may worsen the outcome. High serum glucose levels increase the availability of substrate for anaerobic glycolysis, and thus the production of lactic acid, which may have the reverse effect on neurological recovery from injury. The prevention of hyperglycemia, particularly during the first 2 to 8 hours after injury, seems to be very critical for optimal recovery. After 2 to 8 hours after injury, elevated glucose levels may be beneficial, allowing the beginning of intestinal or parenteral feedings in a short time after the injury. It is also likely the serum triglyceride levels to be found elevated due to the accelerated lipogenesis,

decreased lipoprotein lipase activity, and impaired clearance of triglycerides [63]. Glucose is the preferred energy molecule for the central nervous system, red blood cells, the cellular tissue, etc. A minimum quantity of 100-150 gr glucose per day is required for these functions and prevents the consumption of endogenous protein. The normal rate at which the body metabolizes carbohydrates or glucose is approximately 2-4 mg/ Kg/min. In times of severe stress, glucose metabolism may be increased to 3-5 mg/Kg/min. In most patients, administration of more than 400-500 gr glucose per day, exceeding the body's ability to metabolize and stored as energy. Sources of glucose include not only the liquid diet and peritoneal fluid filtration. Excess glucose is converted into fat (lipogenesis) and leads to an increased ratio of VCO_2/VO_2 (or RQ) [64].

The provision of lipids as a source of increased calories can facilitate protein maintenance, reduce the risk of excessive carbohydrates and reduce the total volume of liquid. Lipids are required to account for 30% of total calories supplied. In the acute phase after injury, large amounts of fat, especially as linoleic or omega-6 fatty acids have an immunosuppressive effect by triggering the release of arachidonic acid. This leads to synthesis of prostaglandins and then compresses the delayed hypersensitivity cell-regulated, proliferation of lymphocytes. In the presence of sepsis, high levels of serum triglycerides (250 gr/ml) indicate limited tolerance and decreased need for intravenous fluid delivery. A minimum of 4% of total energy requirements is necessary for the essential fatty acids to avoid deficiencies [65]. Unfortunately, although the hormonal cataract through increases in glycogenolysis and gluconeogenesis, is enhancing lipolysis, which provides endogenous glucose, amino acids, and free fatty acids that are required for cellular and organ function and wound healing and certain plasma levels of substrates are increased (i.e., glutamine) they could be insufficient to meet metabolic needs due to limited availability for use by peripheral tissues (because of factors such as insulin resistance and inhibition of lipoprotein lipase) [60, 61].

Acute post-traumatic nitrogen requirements are much higher than in normal state. Another serious metabolic issue is negative nitrogen balance, due to excessive secretion of nitrogen because of protein use by the body to meet energy needs in the first week, with a peak at 3 weeks and can last for a period of 7 weeks. This imbalance will respond only slightly increased protein intake and may be non-modifiable as a process during the acute phase. The more severe the injury the greater the amount of nitrogen excreted. The accelerated catabolism of muscle mass results in a supply of amino acids for the acute-phase of protein synthesis, gluconeogenesis, and the healing of wounds. Moreover, administration of glucocorticosteroids after injury may increase the catabolism of protein. The losses of nitrogen in the urine, mainly due to muscle atrophy because of paralysis, are increasing with the severity of the injury. On the other side, Cooper and Hoen stated that the secretion of more than 25 gr/day of nitrogen in the urine during the first two weeks after the injury is insufficient prognostic indicator for functional recovery of paralyzed muscles. The nitrogen losses after an injury are always present and last at least 7 weeks. In cases of acute injury, despite the provision of sufficient quantities of calories and protein usually occurs a negative nitrogen balance (NB), which peaks during the third week after injury. The same phenomenon has been observed in cases of severe poisoning with botulinum toxin (botulism) which resulted in paralysis of muscles. Negative

nitrogen balance following injury, has been associated with further findings. During the first weeks after injury, many patients experience a transient positive nitrogen balance, possibly due to initial delays in the loss of nitrogen [66]. Four conscientious objectors were immobilized on pelvic corset and leg casts for 6 to 7 weeks in a metabolic chamber. All 4 subjects showed an increase in nitrogen excretion and negative nitrogen balance. However, it took 4 to 5 days to develop. In conclusion, acute immobilization of paralyzed patients contributes to increased excretion of nitrogen which starts about a week after the injury [67].

Deficiencies in zinc and vitamin C have been associated with poor wound healing. The provision of these micronutrients supplementation in patients with these deficits enhances the healing. Adequate quantities of salts and vitamins are usually provided in a balanced diet. The supplemental micro-nutrient dietary substances are necessary if we suspect shortcomings intake or increased requirements because of circumstances specific diseases. Zinc is often prescribed to improve stress ulcers, is known to be involved in structural integrity of collagen. However, zinc levels in serum is similar in patients taking supplements that contain sulfur (220 mg daily) and do not affect the healing process of ulcers sprawling over a period of 2-3 months. Opposite physiological effects, such as metabolism of copper, copper deficiency and anemia may be caused by long-term supplementation of large amounts of zinc [68]. The role of vitamin C in collagen synthesis is crucial. Although the supplementation with vitamin C did not accelerate the healing of decubitus ulcers in patients, dietary intake of vitamin C has not been associated with the development of decubitus ulcers. Moreover, given that the subclinical deficiencies are difficult to show up, the minimum recommended dietary intake is proposed to 60mg [69]. Excessive excretion of potassium and abnormal hyponatremia; hypercalcemia, due to immobilization, particularly in young men and hypercalciuria exceed the normal range in 4 weeks, with higher values at 16 weeks, which can persist for a long time. Hypercalcemia occurs with anorexia, abdominal cramps, nausea, vomiting, constipation, polydipsia, polyuria, dehydration and did not respond to diets which restrict the intake of calcium and need to be treated with medication, hydration, and mobilization [70].

Finally the effect of drugs such as analgesics and barbiturates is crucial. Drugs that are frequently administered to acute paraplegic patients may themselves increase skeletal-muscle breakdown (corticosteroids), decrease splanchnic blood flow (pressor agents), or increase urinary loss of electrolytes, minerals, and water-soluble vitamins (diuretics). Infection, operative trauma, and other stresses may increase energy expenditure and protein and micronutrient needs [71-74]. The average daily dietary needs are modified because of the altered physiology of each body system and psychological integrity of a patient susceptible to an injury, potentially at any age, which cannot exclude the possibility of a pre-existing disease causing nutritional problems [75].

Moreover, the frequent coexistence of injuries from other systems, such as brain injury, maxillofacial injuries, fractures, etc., disturbs the normal physiology further. Studies in malnourished patients stated that malnutrition before a spine stabilization surgery is leading to postoperative complications, hyperthermia, which increases the caloric needs of the patient, and denervation, leading to atrophy and paralysis, which supply amino acids for gluconeogenesis, which, in turn, supplies glucose to meet caloric needs [1].

Serum hemoglobin and hematocrit may reflect a general state of malnutrition. Anemia, defined by low hemoglobin levels (<14 mg/dl) and hematocrit (<36%) reduces the oxygen in the blood and impedes the wound healing. Anemia may be due to a preexisting condition or as the result of unbalanced production and distribution of blood cells as a result of reaction to stress, gastrointestinal bleeding or obvious bleeding due to other trauma [76]. Low levels of total serum protein (<6.4 mg/dl) and protein (<3.5 mg/dl), accelerate the development of edema, which causes a decrease in skin elasticity and prevent the transfer of oxygen and nutrients from the blood to the skin. Also, the swelling may increase local tissue pressure, causing loss of regional blood flow and tissue damage. The loss of protein and protein secretion in pressure ulcers increases the deficiencies in proteins. The paralytic ileus occurs as a result of disturbance of the autonomic and simultaneous or ischemia as a complication of hypokalemia, abdominal trauma or sepsis, generally persists for 72 hours-1 week and may restrict the movement of the diaphragm [77]. Parenteral nutrition is indicated if paralytic ileus persists for more than 3-5 days. Ulcers and bleeding, which occur as a result of paralytic vasodilatation with ischemia, steroids, nasogastric tube irritation, and other causes should be treated with oral or enteral feeding as soon as possible but may require parenteral nutrition [78].

6.2. Malnutrition in the chronic phase of paraplegia and during aging

During aging with paraplegia other complications are added in the physiopathological context of "malnourished paraplegics".

A neglected factor is muscle tonus: hypotonia (low muscle tone, floppiness) results in a lower resistance to muscle movement. The lower the resistance, the fewer calories burned during movement. Furthermore, hypertonia (high muscle tone, spasticity) is limiting muscle movement and reduces caloric needs. Lack of movement results in muscle atrophy and a lower lean body mass, which in turn reduces the number of calories burned even at rest [79].

In spinal cord injured subjects is mainly central or abdominal obesity leading to metabolic, cardiovascular issues etc. There is conflicting evidence about the contribution of visceral and subcutaneous adipose tissue to different metabolic disorders after SCI. Moreover subjects with longstanding disabilities (i.e. spinal cord injury) are at increased risk for cardiovascular disease and cardiopulmonary disease because of extensive fat intake and limiting activities. In generally, subjects with disabilities are prone to developing vitamin D deficiency. Earlier work by Bauman et al suggested that approximately 32% of veterans with spinal cord injury (SCI) were absolutely deficient in vitamin D (25 hydroxyvitamin D [25(OH)D]). Most subjects have a high incidence of vitamin D deficiency as defined by levels of 25(OH)D<20 ng/mL. The reasons might be due to a combination of low dietary vitamin D intake and avoiding sun exposure because of depression or sensitivity in drugs i.e. dantrolene [80]. The low intake of vitamin D, which is supplied by food either in vitamin D2 (ergocalciferol, activated ergosterol), found in yeast, or vitamin D3 (cholecalciferol), found in fish, can be bypassed through supplements [81].

Moreover, reduced mobility and immobilization for long period cause pressure ulcers of the skin and the wound but can be prevented by adequate intake of quantity of protein, vitamin E, zinc, and fluids to maintain skin integrity [82].

Pneumonia and paralysis of respiratory muscles through malnutrition may further weaken the respiratory muscles. On the other site excessive feeding may lead to increased oxidation of glucose and production of carbon dioxide to be eliminated and further stress on the respiratory system. The fluid overload or aggressive implementation of parenteral support can lead to pulmonary edema. The reduced hydration can lead to reduced drainage of secretions, atelectasis, and pneumonia. Abdominal distension due to unabsorbed food by mouth or enteral feeding or swallowing air during feeding can lead to compromise the functioning of the diaphragm and predisposes to hypoventilation or aspiration [83]. Neurogenic bowel requires the right amount of food, fiber and fluids in order to be successful retraining of the bowel, and prevent constipation, diarrhea, incontinence, and autonomic dysreflexia as a result of fecal impaction. Bowel function may be compromised by hyperosmolar feeding through a tube, lactose intolerance or pseudomembranous colitis, prolonged treatment with antibiotics, which can cause diarrhea and require parenteral nutritional support. For neurogenic bladder vitamin C and other supplements are necessary for the acidification of urine and prevention of infection of the urinary tract.

7. The nutritional support

The provision of a nutritional supplement is definitely not a frontline management technique for poor oral intake. Supplements when administered correctly to patients can easily optimize nutrition and should be an adjunctive to nutrition.

Per os feeding is recommended for patients who are weaned from tracheal tubes, which are awakened, may follow commands and have good swallowing and intestinal function. Patients with central nervous system (CNS) acute diseases are frequently in coma or have their swallowing reflexes impaired and need parenteral nutrition or enteral tube feeding [84, 85]. Enteral nutrition (EN) is recommended for patients who are tubed, not able to swallow or to receive adequate diet orally but have good bowel function.

Early nutrition support through the enteral route has been shown to blunt catabolism, reduce complications and reduce length of stay in a number of patient populations, including both surgical and non-surgical neuro patients [86, 87]. However, nutrition support must be initiated within the 48-to 72-hour period immediately following injury or surgical insult to achieve these benefits. Clinicians are often hesitant to feed critically ill neuro patients too soon. However, studies indicate patients with severe neurological deficits and clinically silent abdomens can tolerate low-rate jejunal feedings within 36 hours of injury with a gradual increase in feeding rate to meet initial caloric goals within two to four days [88, 89]. If jejunal feedings are initiated prior to induction of pentobarbital infusion, even patients in pentobarbital coma can be fed enterally [90].

Nasogastric or nasoenteric feeding tubes should not be used for periods longer than 4 weeks because of discomfort and the risk of nasal injury and sinusitis. Placement of a percutaneous endoscopic gastrostomy (PEG) tube should be considered for patients who continue to require enteral feeding beyond 4 weeks[90]. PeG is also indicated as firstline intervention in conditions

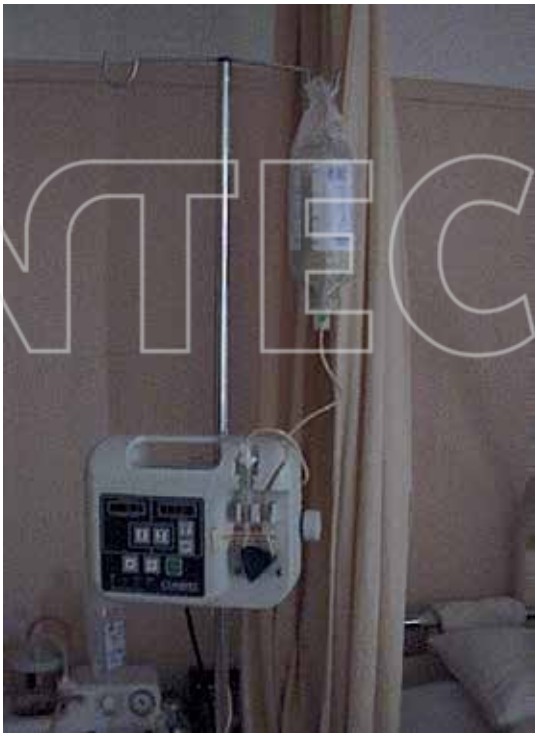

Figure 2. The enteral feeding pump type COMPAT (unpublished photo courtesy of Dionyssiotis Y). The system is a relatively simple, lightweight, easy to use for managing all types of enteral feeding. Have an audible and visual alarm that alerts you when each of the following conditions: empty container feeding, low battery, change the dose, or the existence of j free flow out of the system (waste). The memory of the pump retains infusion rate, volume delivered, dose limit even after turning it off. It is designed to provide precision dosing. Start enteral feeding schedule and progress.

where enteral feeding is expected to be required for longer than 2–4 weeks, for example in patients with acute stroke [91]. Although complications of PEG tube feeding are rare in stable patients, they become increasingly common in critically ill and debilitated patients. One of most feared complication of enteral feeding: aspiration hypoxia/ pneumonia. Clinically, gastric residual volume (GRV) measurement was frequently used as marker to predict aspiration & pneumonia. Elevated GRV: associated with comorbidities such as vasopressor use, sedation sepsis, vomiting. GRV: no significance between GRV> 200ml and GRV> 400ml, low sensitivity as a marker of aspiration [92].

With increasing frequency, nasogastric feeding tubes are replaced by PEG to provide semi-long-term enteral nutrition because of various advantages of a PEG in daily use [93-95]. In contrast to a nasogastric feeding tube, PEG does not interfere with the swallowing mechanism, which reduces the possibility of choking, especially when oral feeding is initiated during

neurological recovery. The cosmetic advantage of a PEG, which can be worn invisibly underneath the patients' clothes, may play a psychological role during recovery. PEG placement is associated with a mortality rate of 1-3 per cent, major complication rates of 3-9 per cent and minor complication rates of 5-45 per cent. The risk of aspiration, frequently associated with nasogastric feeding tubes, has not been eliminated with PEG placement [96-100].

Another interesting issue is early compared with late introduction of the feed. With data limited to ICU patients there was no overall difference in mortality rates with either EN or PN with no apparent difference in mortality rates across groups receiving EN or PN (RR 1.08; 95% CI 0.70 to 1.65). As suggested compared with PN, EN was associated with a significant reduction in infectious complications (RR 0.61; 95% CI 0.44 to 0.84; p=0.003). The early compared with late introduction of enteral feed only suggested that early EN was associated with a trend toward a reduction in mortality (RR 0.52; 95% CI 0.25 to 1.08; p=0.08) when compared with delayed nutrient intake and infection risk was not different [101]. The compilation of 11 high quality studies comparing enteral and parenteral nutrition revealed a significant effect in favor of parenteral nutrition [odds ratio (OR) 0.51, 95% confidence interval (CI) 0.27–0.97]. A subgroup analysis of trials comparing parenteral nutrition with early or late enteral feeding showed that there was no survival benefit in parenteral nutrition when enteral nutrition was provided early. The benefit of parenteral nutrition was confined to trials comparing it with late enteral nutrition. Therefore, this metaanalysis confirms at least a finding already reported in earlier metaanalyses: there is no increased mortality risk with parenteral nutrition! [102].

A major concern with EN is the discrepancy between prescribed and delivered amount of nutrient, the major causes of which are diarrhea, vomiting or gastric stasis. Furthermore, enteral nutrient delivery is gradually increased in critically ill patients in order to avoid the possibility of gastrointestinal intolerance, so that a few days are required to achieve the caloric target. Administering the total nutritional requirement of mechanically ventilated medical patients starting on day 1 was associated with greater infectious complications and prolonged length of hospital stay compared to patients in whom a gradual approach was implemented [103]. Despite the caloric deficiency, EN is still superior to PN so that non-energetic effects of EN, such as immune modulation or protection of the intestinal mucosal barrier, seem to be of greater value in the critically ill than the mere energetic supply. The issue of the better enteral access (gastric vs. post-pyloric route) is not yet settled. However, available evidence does not support the routine insertion of post-pyloric tubes as long as the gastric route is effective [104, 105, 106].

Aside from the potential problems associated with receiving in adequate or excessive nutrition or medication therapy, additional injury to the patient may result from using the gut that is at risk for bacterial or candidal translocation. Therefore, enteral nutrition should be started only if the potential benefits outweigh the risks [107, 108].

However, nutritional support is not without adverse effects and risks. Early EN may be associated with high gastric residuals, bacterial colonization of the stomach, and increased risk of aspiration pneumonia. PN has been associated with gut mucosal atrophy, overfeeding,

hyperglycemia, an increased risk of infectious complications and increased mortality rates in critically ill patients [104, 105].

8. Transition from parenteral to enteral feeding and vice versa

Malabsorption and maldigestion must be recognized early in the decision making process in the use of enteral nutrition. Weight loss, signs of macronutrient (i.e., decreased visceral protein status, hypoglycemia, and steatorrhea) and micronutrient (electrolytes, trace elements, and vitamins) abnormalities suggest that the intestine may not be optimally functioning [107].

The European Society for Clinical Nutrition and Metabolism guidelines recommends that: "All patients receiving less than their targeted enteral feeding after 2 days should be considered for supplementary parenteral nutrition" [108].

Despite considerable controversy in this field, physicians generally agree on two key aspects: firstly, the enteral route is preferable whenever possible, and secondly, if possible, enteral nutritional support should be started early (within 24–48 h after admission) [101, 108, 109].

The American Society for Parenteral and Enteral Nutrition (ASPEN) and Society of Critical Care Medicine (SCCM) guidelines recommend that parenteral nutrition be initiated after 1 week, unless the patient is severely malnourished. By contrast, the European Society of Enteral and Parenteral (ESPEN) guidelines recommend consideration of a combination of enteral and parenteral nutrition after only 2–3 days in the ICU if enteral nutrition alone is insufficient at that time [108, 110].

In the early phase of rehabilitation enteral feeding solutions with low osmolarity (<300 mOsm/l) to prevent hyperosmolar diarrhea (appeared in case of long time left unfeeded intestine, and low calorie <1Kcal/ml) are usually used (Table 3).

Products	Novartis Novasource start 500ml	Nutricia Pre-nutrison 500ml	Fresenius Intestamin 500ml	Abbott Osmolite HP
Energy Kcal/ml	0, 75	0, 5	0, 5	1
Protein g/100ml	5 27%	2 16%	8, 5 68%	5, 2 20, 8%
Gluamine g/100ml	1	N.A.	6	1, 4
Carbohydrates g/100ml	8 43%	6, 1 49%	17, 7 54%	16, 4 64, 9%
Fat g/100ml	2, 5 30%	1, 95 35%	0, 2 2%	1, 5 13, 3%
Fibers	0, 5	0	0	0
Osmolarity	250	140	N.A.	269

Table 3. Starters for enteral nutrition

The rate of early products' infusion is shown in the Table 4. Moreover, Table 5 depicts most used enteral products according to categories and their characteristics.

Day	Rate	Drops per minute (20 drops=1ml)	Total Volume
1	30ml/h	10	max 500ml
2	40ml/h	10	max 1000ml
3	60ml/h	20	max 1500ml
4	90ml/h	30	max 2000ml
5	100ml/h	30	max 2000ml

Table 4. Starting enteral nutrition rate

Categories	Products	Characteristics
Isotonic	Osmolite HN (Abbott)	1 kcal/ml
	Pediasure (Abbott)	
	Frebini (Fresenius)	
	Fresubin Original (Fresenius)	
	Isosource Standard (Novartis)	
	Nutrison Standard (Nutricia)	
	Nutrini Standard (Nutricia)	
	Tetrini Standard (Nutricia)	
Enriched with fibers	Jevity FOS (Abbott)	1 kcal/ml
	Fresubin Energy Fibre (Fresenius)	1, 5 kcal/ml
	Fresubin Original Fibre (Fresenius)	1 kcal/ml
	Novasource Forte (Novartis)	1, 5 kcal/ml
	Novasource Gl Control (Novartis)	1, 1 kcal/ml
	Cubison (Nutricia)	1 kcal/ml
	Nutrison Multifibre (Nutricia)	
	Stresson Multi Fibre (Nutricia)	1 kcal/ml
Hypercaloric	Ensure Plus (Abbott)	1, 5 kcal/ml
	Fresubin Energy (Fresenius)	
	Fresubin HP Energy (Fresenius)	

Categories	Products	Characteristics
	Novasource Forte (Novartis)	
	Nutrison Energy (Nutricia)	
	Nutridrink (Nutricia)	
Hyperprotein	Perative (Abbott)	1, 31 kcal/ml
	Fresubin HP Energy (Fresenius)	1, 5 kcal/ml
	Intestamin (Fresenius)	0.5 kcal/ml)
	Infatrini (Nutricia	1 kcal/ml

Table 5. Most used enteral solution products per company

The goal of rehabilitation is to return through a gradual transition from the feeding tube back in swallowing if possible. The steps for neurocognitive and neuromuscular patients are based in a clinical algorithm proposed by Buchholz [111].

The initial (preparatory) phase focuses on physiologic readiness for oral nutrition and incorporates medical and nutrition stability (normal swallowing function and nutrition values in normal range), and includes implementation of intermittent tube feeding, and swallowing assessment. The second (weaning) phase is described as a graduated increase in oral feeding, with corresponding decreases in tube feeding. In a patient able to consume more than 75% of his nutrition requirements consistently by mouth for 3 days, all tube feedings are discontinued. Subjects during weaning phase are being continuously evaluated for specific clinical parameters including weight, hydration, and swallowing ability, focusing on respiratory complications [111, 112].

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CAUSES AND TREATMENT OF BONE AND MUSCLE CONDITIONS

RESEARCH COLLECTION

Health conditions in which muscle function is impaired and bones are damaged can be highly debilitating. This makes study of their causes and potential therapeutic protocols highly important, and this book offers state of the art knowledge regarding aspects of such conditions. Osteoporosis, the degeneration of bone mass, is considered in several contributions to this book, with chapters on rehabilitation techniques, neurological osteoporosis and paraplegia-related osteoporosis. Body composition is another special concern, with two chapters on body composition's role in disabilities of the central nervous system and paraplegia. Finally, there is a chapter on the effects of malnutrition in paraplegia. Given the range of these studies, this book has much to offer health practitioners and patients alike.

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