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The weight bearing paraplegic arm

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INTRODUCTION

- Paraplegia causes a sudden immobilization and denervation of the skeletal muscles below the neurological level of injury (NLoI).*(1)*
- After paraplegia patients lose muscle mass and bone and gain fat mass especially in lower limbs.(*2)*
- Immobility leads to modifications in body composition.(*2,3)*

1.Spungen AM, Adkins RH, Stewart CA, Wang J, Pierson RN Jr, Waters RL,Bauman WA. 2003 Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol.95: 2398.2407.
2.Wilmet E, Ismail AA, Heilpom A, Welraeds D, Bergmann P. 1995 Longitudinal study of the bone mineral content and of soft tissue composition after spinal cord section. Paraplegia.33:674.677.
3.Uebelhart D, Demiaux-Domenech B, Roth M, Chantraine A. 1995 Bone metabolism in spinal cord injured individuals and in others who have prolonged immobilisation. A review. Paraplegia.33: 669.673.

- Clinical studies also indicated that neurological injuries are associated with the development of a rapid and severe bone loss that is not only due to a compromised biomechanical function but can have a central nervous system origin.*(4)*

4.Takeda S.2005 Central control of bone remodelling. Biochem Biophys Res Commun.328(3):697.9.

- On the other hand, paraplegia is associated with continued use of upper extremities.
- More than 90% of people with spinal cord injury (SCI) routinely use wheelchairs for mobility and/or activities of daily living (ADLs) (5).

5. Biering-Sorensen F, Hansen RB, Biering-Sorensen J. Mobility aids and transport possibilities 10–45 years after spinal cord injury. Spinal Cord. 2004;42(12):699–706.

OBJECTIVE

- **The purpose of this study was to investigate the changes of composition of paraplegic upper limb according to the neurological level of injury.**

MATERIAL AND METHODS

- This study was carried out in the 2nd Rehabilitation department of the National Rehabilitation Center "EIAA" in Athens, in cooperation with the Laboratory for Research of the Musculoskeletal system in the University of Athens, in KAT Hospital.

- The study included paraplegics in chronic phase (> 1.5 years) with complete paraplegia (AIS A)
- Paraplegics were volunteers recruited from the 2nd Rehabilitation department of National Rehabilitation Center “EIAA” in Athens (outpatients) and from the Greek Paraplegic Society after announcement for participation in a clinical research effort of the Laboratory for Research of the Musculoskeletal System of Athens University.
- The control group consisted of volunteers working in the laboratory and the hospital.

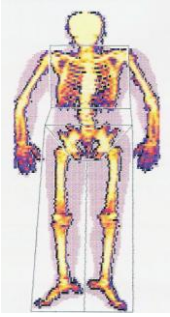
Paraplegics were divided according to the neurological level of injury

- **in group A (n = 16, high paraplegia: above thoracic (T) 7 neurological level of injury (NLoI)** and
- **group B (n = 15, low paraplegia, T8-T12 NLoI**
- compared with 33 healthy controls (group C) of similar anthropometric characteristics.

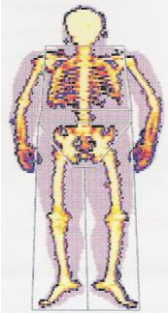
PARAPLEGIC PATIENTS	
INCLUSION CRITERIA	**EXCLUSION CRITERIA**
sex: all men	age < 25 years at examination
complete paraplegia (ASIA A)	pts with heterotopic ossifications
injury was result of traffic accident	pts with co-existing traumatic brain injury (TBI)
all underwent vertebral fixation procedures	pts whith chronic administration 1) of bone acting drugs
chronic paraplegia >1,5yr	or 2) drugs which promote the bone loss
all wheelchair bound not bedridden	coexisting diseases which impair bone tissue

DXA body composition measurements

- All were examined by whole body DXA (Norland XR 36, Norland Corp., USA) regarding the local (arm) bone density, bone mineral content, muscle and fat mass.



Total BMD (g/cm) : 0.985
Total BMC (g) : 3104
Total Lean Mass(g): 43992
Total Fat Mass (g): 18991
Total Fat % : 28.7



Total BMD (g/cm) : 1.160
Total BMC (g) : 3145
Total Lean Mass(g): 62716
Total Fat Mass (g): 25283
Total Fat % : 27.7

RESULTS

Anthropometrics and clinical data

Subjects Parameters	controls **n=*33***	High paraplegics **n=*16***	Low paraplegics **n=15**	**p-value** (N.S)
Age (yrs)	33,9±3,81	32,88±15,6	39,47 ±13,81	0,3
Weight (kg)	80 ± 6,5	72,88 ± 8,16	76,82 ± 8,33	0,08
Height (m)	1,79±0,05	1,74 ± 0,07	1,75 ± 0,04	0,09
BMI (kg/m^2)	24,91±2,06	24,11 ± 2,55	25,09 ± 2,5	0,4
Age at injury (yrs)	•	26,63 ±14,35	33,57 ± 12,3	0,118
Duration of Paralysis (yrs)	•	5,97± 5,9	5,65± 5,8	0,87

Table 4
Measured Parameters of the Arms in the Control and Paraplegic Groups

Whole body DXA/ parameters	Controls (n = 33), mean ± SD	High paraplegics (n = 16), mean ± SD	Low paraplegics (n = 15), mean ± SD	*p* Value
Arms				
BMD (g/cm^2)	0.76 ± 0.11	0.66 ± 0.10	0.76 ± 0.12	0.008
Lean mass (g)	6570 ± 1498	6150 ± 1676	6008 ± 1602	N.S.
Fat mass (g)	2025 ± 874	1951 ± 961	2657 ± 1839	N.S.

Journal of Clinical Densitometry: Assessment of Skeletal Health *Volume 11, 2008*

Dionyssiotis Y, Petropoulou K, Rapidi CA, Papagelopoulos P, Papaioannou N, Galanos A, Papadaki P, Lyritis GP. Body composition in paraplegic men. J Clin Densitom. 2008 Jul-Sep;11(3):437-43.

Dependent Variable	(I) GROUP	(J) GROUP	Sig.
ARBMD	High	Low	,028
		Control	,010

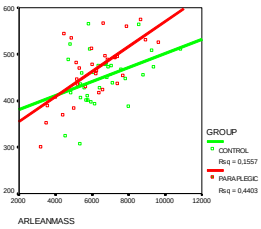
- Bone mineral density was found statistically significant between groups (p = 0.008) and pair-wise comparisons revealed statistically significant differences between high vs. low paraplegia group and controls (p = 0.028, p = 0.01, respectively).

Measured parameter BMC in upper limbs in the two paraplegic groups and controls.

WHOLE BODY DEXA	PARAMETERS	CONTROL GROUP n=33 mean value ± SD	PARAPLEGICS n=31 mean value ± SD	p-value
UPPER LIMBS	BMC, g	449.88 ±57.3	465.15 ± 65.71	N.S

WHOLE BODY DEXA	Parameters	Control Group n=33 mean value ± SD	High Paraplegics n=16 mean value ± SD	Low Paraplegics n=15 mean value ± SD	p-value
UPPER LIMBS	BMC, g	449.88 ± 57.3	454.86 ±68.10	476.13 ± 63.53	p = 0.391

Correlation ARM BMC-ARM LEAN MASS

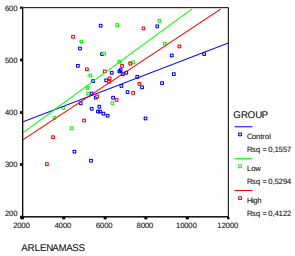


PARAPLEGIC		AR Lean MASS
ARBMC	Pearson Correlation	,664(**)
	Sig. (2-tailed)	,000
	N	31

CONTROL		AR Lean MASS
ARBMC	Pearson Correlation	,395(*)
	Sig. (2-tailed)	,023
	N	33

bone per unit of muscle mass
Controls 0.068 bone/muscle vs. paraplegics 0.07 bone/muscle (NS).

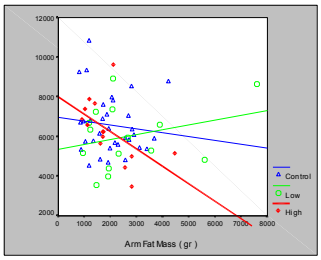
Correlation ARM BMC-ARM LEAN MASS
Neurological Level of Injury



- **Arm lean mass was positively related to arm BMC in SCI and controls;**
- however, in paraplegic groups there was more bone per unit of muscle mass.

Lean mass – fat mass

- In group of high paraplegia a negative correlation was found of lean muscle to fat mass (p = 0.009, r = -0.67).

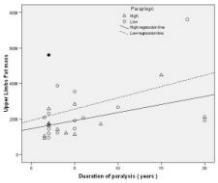


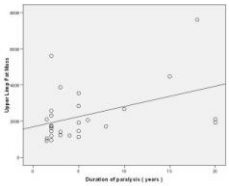
ARM LEAN MASS (HIGH/ LOW*100) = 102%
ARM FAT MASS (HIGH/ LOW*100) = 73.4%
meaning

Muscle mass was increased by 2% and fat mass decreased 26% in high paraplegics compared with low paraplegics.

Table 5
Correlations Between Duration of Paralysis and Measured Parameters in the Two Paraplegic Groups and in Total Paraplegics

Duration of paralysis	Correlations: High paraplegics	Low paraplegics	Total paraplegics
Arms' fat mass			
r	0.55	0.281	0.43
p	0.042	0.310	0.020





Correlations - DoP

Duration of Paralysis		High Paraplegia	Low Paraplegia	Total
AR-Bmd	Spearman's r	0,239	-0,435	-,018
	p-value	0,373	0,105	,923
AR -Fat Mass	Spearman's r	0,550	0,281	,429
	p-value	0,042	0,310	,020

DISCUSSION

Do we need to take in mind completeness and neurological level of lesion?

- In this study investigation regarding the NLoI unmasked BMD values significantly lower, LM values higher and FM values lower (but without significance) *in high paraplegics compared with low paraplegics and controls.*

- Spungen et al in a mixed paraplegic population (complete and incomplete paraplegics) found that the percentage of lean mass, but not absolute LM, in paraplegics' arms was significantly lower than controls suggesting that the higher amount of absolute fat mass in paraplegics were responsible for this result .

Spungen, Ann M., Rodney H. Adkins, Charles A. Stewart, Jack Wang, Richard N. Pierson, Jr., Robert L. Waters, and William A. Bauman. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol 95: 2398–2407, 2003.

- In line with this we found in those with paraplegia that lean mass in the arms was lower than controls.
- Among paraplegics higher lean mass values were found in high compared with low paraplegics (mean 6150 ±1676 vs. mean 6008 ± 1602, p=0.451,respectively)
- This could be explained by the higher amount of fat mass in the arms in those *with low paraplegia only* compared with controls.

<a concept which is first described by Spungen et al in a mixed paraplegic population (complete and incomplete paraplegics)>

Spungen, Ann M., Rodney H. Adkins, Charles A. Stewart, Jack Wang, Richard N. Pierson, Jr., Robert L. Waters, and William A. Bauman. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol 95: 2398–2407, 2003.

What happened in high paraplegics?

explained. Taking in mind that the arm is theoretically only a non weight bearing bone in paraplegics an explanation of this finding could be that high paraplegics are trying to overcome their handicap through an arm overuse (high mechanical forces) reducing regionally adiposity and inducing LM. In

Dionyssiotis Y, Petropoulou K, Rapidi CA, Papagelopoulos P, Papaioannou N, Galanos A, Papadaki P, Lyritis GP. Body composition in paraplegic men. J Clin Densitom. 2008 Jul-Sep;11(3):437-43.

- Another question arising from these results is whether the higher FM values *in low paraplegics' arms* are responsible for the higher values in BMD found in this group.

- There is evidence that larger body mass imposes a greater mechanical loading on bone, and that bone mass increases to accommodate the greater load.
- It has been proposed that increases in adipose tissue, with increasing BMI in postmenopausal women, results in increased estrogen production, osteoclast suppression, and a resultant increase in bone mass.

Zhao LJ, Liu YJ, Liu PY, Hamilton J, Recker RR, Deng HW. Relationship of obesity with osteoporosis. *J Clin Endocrinol Metab.* 2007 May; **92**:1640-6.

- Wilmet et al using a Hologic DEXA apparatus studying an age similar paraplegic population have not found any significant loss in arms' BMC in body composition.
- On the contrary, we found higher values of BMC in paraplegics' upper limbs compared with able-bodied population; although, these values were not statistical significant.

Wilmet E, Ismail AA, Heilporn A, Welraeds D, and Bergmann P. Longitudinal study of the bone mineral content and of soft tissue composition after spinal cord section. Paraplegia 33: 674–677, 1995.

What is happening below NLoI

- Bauman et al found significant correlation between FM and legs BMD in SCI subjects. *According to the authors this relation may suggest a possible influence of hormonal mechanisms.*
- ***It is not known yet if these results could be transferred to the "weight bearing" arm.***

Bauman WA, Spungen AM, Wang J, Pierson RN Jr, Schwartz E. Relationship of fat mass and serum estradiol with lower extremity bone in persons with chronic spinal cord injury. *Am J Physiol Endocrinol Metab*. 2006 Jun;**290**:E1098-103.

Correlations BMC, FM, LM

- Yamauchi et al found no correlation between percentage of fat and BMD (9).
- Bedogni et al concluded that BMC is associated more with lean tissue mass than with fat mass (12).

9.Yamauchi M, Sugimoto T, Yamaguchi T, Nakaoka D, Kanzawa M, Yano S, Ozuru R, Sugishita T, Chihara K (2001) Plasma leptin concentrations are associated with bone mineral density and the presence of vertebral fractures in postmenopausal women. Clin Endocrinol (Oxford) 55:341-347
12.Bedogni G, Pietrobelli A, Heymsfield SB (2000) Influence of body composition on bone content in elderly women. Ann NY Acad Sci 904:489-90

- Spungen et al have demonstrated a strong relationship between lean tissue and bone mineral content in the arms of SCI subjects, regardless of level of lesion.
- In the present study, we found significant correlations between lean mass and BMC in paraplegics and controls and negative correlation of BMC and FM in high paraplegics.

Spungen AM, Wang J, Pierson RN, Jr., Bauman WA. Soft tissue body composition differences in monozygotic twins discordant for spinal cord injury. *J Appl Physiol* 2000;**88**:1310-5.

BMD-DoP

- There was a significant inverse relationship between arm BMD (low paraplegia) and time since SCI (but not in high paraplegia)
- Although this finding cannot be entirely explained it has been proposed that the bone repartition may be influenced by a variety of factors, including SCI induced changes in regional blood circulation; total-body bone resorption, formation, and calcium metabolism unique to SCI; and increased force on the forearm during transfers to and from wheelchairs.

Clasey JL, Janowiak AL, Gater DR. Relationship between regional bone density measurements and the time since injury in adults with spinal cord injuries. Arch Phys Med Rehabil 2004;85:59-64.

- Therefore, factors as number of transfers, occupation, recreation participation, ADLs, and use of manual as opposed to automated wheelchairs, may have contributed to the fact that the inverse relationship between arm BMD and duration of paralysis *was weaker in high paraplegics (kept more bone over time).*

FM - DoP

- Arms' FM was correlated with the duration of paralysis in total paraplegic group, but this was a result because of the strong correlation of high paraplegics, meaning that these subjects tend to increase more rapidly FM over the years of paralysis.
- *The question here is why?*

The association of the duration of paralysis with parameters above *(and below)* the NLoI raises the question of the existence of an hormonal mechanism as an influential regulator in paraplegics' body composition.

- ***Leptin activates the sympathetic nervous system through a central administration.*** [2,3]

2. Dionyssiotis Y, Petropoulou K, Rapidi CA, Papagelopoulos P, Papaioannou N, Galanos A, Papadaki P, Lyritis GP. Body composition in paraplegic men J Clin Densitom. 2008 Jul-Sep;11(3):437-43.
3. Teasell RW, Arnold JM, Krassioukov A, Delaney GA. 2000 Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil 81:506-516.

- ***At a local level, bone marrow adipocytes produce leptin, which may enhance osteogenic activity and inhibit adipogenic activity.***

Odaba E, Ozata M, Turan M (2000) Plasma leptin concentrations in postmenopausal women with osteoporosis. Eur J Endocrinol 142:170-173

IBMS BoneKEy. 2009 September;6(9):311-322
http://www.bonekey-ibms.org/cgi/content/full/ibmske;6/9/311
doi: 10.1138/20090395

PERSPECTIVES

The Bone-Fat Mass Relationship: Laboratory Studies

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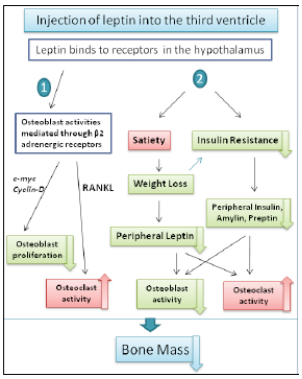
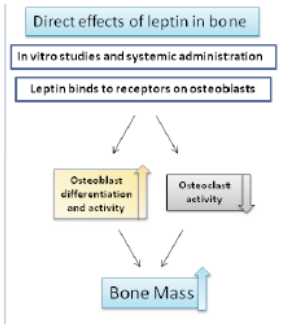
Department of Medicine, University of Auckland, Auckland, New Zealand



1) The direct effect of leptin via the sympathetic nervous system on β-adrenergic receptors expressed on osteoblasts.
2) An alternative mechanism that explains the reduction in bone mass, where leptin acts via the sympathetic nervous system to increase insulin sensitivity and to induce satiety.

Blockade of the sympathetic nervous system abrogates these effects
(see high paraplegia)



- studies of peripheral administration of leptin in intact or leptin-deficient animals result in increases in bone formation and skeletal mass and reduced bone fragility

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Intact Sympathetic Nervous System Is Required for Leptin Effects on Resting Metabolic Rate in People with Spinal Cord Injury

JUSTIN Y. JEON, ROBERT D. STEADWARD, GARRY D. WHEELER, GORDON BELL, LINDA McCARGAR, AND VICKI HARBER

The Steadward Center, Department of Physical Education and Recreation, and Faculty of Agriculture, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada T6G 2H9

- People with SCI suffer decentralization of the SNS after the injury.
- Complete SCI results in a loss of motor and sensory functions via afferent and efferent spinal pathways and also in an interruption of pathways from the brain to the peripheral SNS.
- This interruption leads to pathological changes in sympathetic innervation through the anatomic reorganization of pathways in the spinal cord.
- As a result, leptin's influence on the regulation of energy intake and energy expenditure in people with high lesion SCI may be impaired and may increase the risk of obesity.

- The observation of neuronal mediation of leptin antiosteogenic action is important in explaning BMD differences between the two groups.*(35)*
- Sympathetic regulation of bone does exist in humans and plays a clinically important role.*(36,37)*

35.Pogoda P, Priemel M, Rueger JM, Amling M. 2005 Bone remodeling: new aspects of a key process that controls skeletal maintenance and repair.Osteoporos Int..16Suppl 2:S18.24.
36.Schwarzman RJ .2000 New treatments for reflex sympathetic dystrophy. N Engl J Med.343 : 654.656
37.Levasseur R, Sabatier JP, Potrel-Burgot C, Lecoq B, Creveuil C, Marcelli C. 2003 Sympathetic nervous system as transmitter of mechanical loading in bone. Joint Bone Spine.70: 515.519.

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