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)

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)

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).

References:
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.
coexisting diseases which impair bone tissue
all wheelchair bound
not bedridden

or 2) drugs which promote the bone loss
pts with co-existing traumatic brain injury (TBI)

1) of bone acting drugs
pts with heterotopic ossifications

injury was result of traffic accident

all underwent vertebral fixation procedures

chronic paraplegia >1,5yr

• 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.

EXCLUSION CRITERIA

age < 25 years at examination
sex: all men
pts with co-existing traumatic brain injury (TBI)
pts with heterotopic ossifications

INCLUSION CRITERIA

SEXUAL PATIENTS

DXA body composition measurements

RESULTS

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

<table>
<thead>
<tr>
<th>Total BMD (g/cm )</th>
<th>Total BMC (g)</th>
<th>Total Lean Mass (g)</th>
<th>Total Fat Mass (g)</th>
<th>Total Fat %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.085</td>
<td>3104</td>
<td>43992</td>
<td>18991</td>
<td>28.7</td>
</tr>
<tr>
<td>1.160</td>
<td>3145</td>
<td>62716</td>
<td>25283</td>
<td>27.7</td>
</tr>
</tbody>
</table>
Anthropometrics and clinical data

<table>
<thead>
<tr>
<th>Subjects Parameters</th>
<th>controls n=33</th>
<th>High paraplegics n=16</th>
<th>Low paraplegics n=15</th>
<th>p-value (N.S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>33.9±3.81</td>
<td>32.88±15.6</td>
<td>39.47±13.81</td>
<td>0.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80 ± 6.5</td>
<td>72.88 ± 8.16</td>
<td>76.82 ± 8.33</td>
<td>0.08</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.79±0.05</td>
<td>1.74 ± 0.07</td>
<td>1.75 ± 0.04</td>
<td>0.09</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.91±2.06</td>
<td>24.11 ± 2.55</td>
<td>25.09 ± 2.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Age at injury (yrs)</td>
<td></td>
<td>26.63 ± 14.35</td>
<td>33.57 ± 12.3</td>
<td>0.118</td>
</tr>
<tr>
<td>Duration of Paralysis (yrs)</td>
<td>*</td>
<td>5.97± 5.9</td>
<td>5.65± 5.8</td>
<td>0.87</td>
</tr>
</tbody>
</table>

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).

Correlation ARM BMC-ARM LEAN MASS

<table>
<thead>
<tr>
<th>GROUP</th>
<th>AR Lean MASS</th>
<th>ARBMC Pearson Correlation</th>
<th>Sig. (2-tailed)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARAPLEGIC</td>
<td></td>
<td>0.644(*** )</td>
<td>0.000</td>
<td>31</td>
</tr>
<tr>
<td>CONTROL</td>
<td></td>
<td>0.395( * )</td>
<td>0.023</td>
<td>33</td>
</tr>
</tbody>
</table>

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

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

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.
Correlations - DoP

<table>
<thead>
<tr>
<th>Duration of Paralysis</th>
<th>High Paraplegia</th>
<th>Low Paraplegia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR-Bmd</td>
<td>Spearman’s r</td>
<td>0.239</td>
<td>-0.435</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.373</td>
<td>0.105</td>
</tr>
<tr>
<td>AR-Fat Mass</td>
<td>Spearman’s r</td>
<td>0.550</td>
<td>0.281</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.042</td>
<td>0.310</td>
</tr>
</tbody>
</table>

DISCUSSION

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

- In this study investigation regarding the NLol 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.

• 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)>

What happened in high paraplegics?

• 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.


• 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.


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.


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).

• 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.


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.

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.²³


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


PERSPECTIVES

The Bone-Fat Mass Relationship: Laboratory Studies

Jillian Cornish, Jessica L. Costa and Dorit Naot
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)

- 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 explaining BMD differences between the two groups. (35)
- Sympathetic regulation of bone does exist in humans and plays a clinically important role. (36, 37)

• 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

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

Justin V. Zhou, Robert D. Staudaher, Gary D. Wheeler, Gordon Bell, Linda McClellan, and Vicky Guazzelli

The Development Center, Department of Theriogenology and Reproduction, and Faculty of Agriculture, Food and Nutritional Sciences, University of Alberta, Edmonton, Alberta, Canada T6G 2R3

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