Soft tissue body composition differences in monozygotic twins discordant for spinal cord injury

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Spungen, Ann M., Jack Wang, Richard N. Pierson, J r., and William A. Bauman. Soft tissue body composition differences in monozygotic twins discordant for spinal cord injury. J Appl Physiol 88: 1310–1315, 2000.—To determine the effect of paralysis on body composition, eight pairs of male monozygotic twins, one twin in each pair with paraplegia, were studied by dual-energy X-ray absorptiometry. Significant loss of total body lean tissue mass was found in the paralyzed twins compared with their able-bodied co-twins: 47.5 ± 6.7 vs. 60.1 ± 7.8 (SD) kg (P < 0.005). Regionally, arm lean tissue mass was not different between the twin pairs, whereas trunk and leg lean tissue masses were significantly lower in the paralyzed twins: −3.0 ± 3.3 kg (P < 0.05) and −10.1 ± 4.0 kg (P < 0.0005), respectively. Bone mineral content of the total body and legs was significantly related to lean tissue mass in the able-bodied twins (R = 0.88 and 0.98, respectively) but not in the paralyzed twins. However, the intrapair difference scores for bone and lean tissue mass were significantly related (R = 0.80 and 0.81, respectively). The paralyzed twins had significantly more total body fat mass and percent fat per unit body mass index than the able-bodied twins: 4.8 kg (P < 0.05) and 7 ± 2% (P < 0.01). In the paralyzed twins, total body lean tissue was significantly lost (mostly from the trunk and legs), independent of age, at a rate of 3.9 ± 0.2 kg per 5-yr period of paralysis (R = 0.87, P < 0.005). Extreme disuse from paralysis appears to contribute to a parallel loss of bone with loss of lean tissue in the legs. The continuous lean tissue loss may represent a form of sarcopenia that is progressive and accelerated compared with that in ambulatory individuals.

AN INDIVIDUAL WITH SPINAL cord injury (SCI) and the resultant extreme disuse has a predisposition to medical consequences and secondary disabilities, such as lipid abnormalities (5, 8, 12), carbohydrate intolerance (5, 15), and cardiovascular disease (3, 4, 6). One hypothesis for these secondary disabilities of extreme disuse consists of the adverse changes in body composition (33, 38, 39), which may contribute to insulin resistance and associated disorders. Previous investigators, by using cross-sectional designs comparing age- and height-matched reference populations, have demonstrated lean tissue loss and/or fat tissue gain in individuals with SCI (13, 23, 24, 38). Because of wide individual variability in body composition and the absence of premorbid body composition measurements, a study employing a cross-sectional design is inherently limited in accurately determining the amount of lean tissue lost and fat tissue gained that is attributable exclusively to paralysis. Longitudinal studies are relatively expensive and pose enormous logistical problems, including performing measurements before the body composition changes have occurred, immediately after SCI, a time when the patient is often medically unstable or reluctant to participate in a research study. The task of recruiting subjects to perform these measurements intermittently over ensuing decades is problematic. Thus a creative solution to defining these changes in body composition that is independent of genetic variability and aging is a monozygotic twin model in which one twin has paralysis from traumatic SCI.

METHODS

Subjects. Eight pairs of healthy identical twins, a paralyzed and an able-bodied twin, were studied. The subjects were recruited throughout the United States. To control for known variability within individuals with SCI, a group similar for gender and level and completeness of injury was selected to participate in the study. All subjects were men with motor complete paraplegia, levels T6–L1. None of the paralyzed twins was able to bear weight or had voluntary movement below the level of lesion since the time of injury. The duration of injury was 3–26 yr. All paralyzed twins used their arms daily for wheelchair mobility and were able to transfer independently. The able-bodied and paralyzed twins were in good health with no present known medical problems. The subjects were provided verbal and written information about the study, and written consent was obtained. Institutional Review Board approvals from the Veterans Affairs Medical Center and the Mount Sinai Medical Center were obtained for the study.

Genetic testing for zygosity was performed in all pairs at six independent, highly polymorphic loci (Life codes, Stanford, CT). All eight pairs were found to be strongly consistent with monozygosity, with a probability of being nonidentical of 1 in 4,096.

Body composition studies. Height was measured in the standing position for the able-bodied twins and in the supine
position with the subject fully extended for the paralyzed twins. Weight was measured on a Weight-Tronix scale (Scale Electronics Development, New York, NY). Body mass index (BMI) was calculated as total body wt (kg) ÷ height (m²). The soft tissue compartments of fat and lean tissue mass were measured by dual-energy X-ray absorptiometry (DXA) on a total body scanner (model DPX, Lunar Radiation, Madison, WI) with the methods described by Wang et al. (40), Piersen et al. (31), Heymsfield et al. (26), and Mazess et al. (30). Calibration of DXA consisted of six graded mixtures of lean beef and fat, ranging from 3.7 to 85.6% fat, as measured by chemical analysis (31, 40). The subjects were asked to lie on a table, and whole body scanning was carried out with a congruent beam of stable dual-energy radiation (~1 mrem) at 40 and 70 keV; the radiation passed through the patient from below while the differential absorption was measured above. The ratio of absorption between the two X-rays of different energies was linearly related to the fat tissue mass in the soft tissue compartment. The procedure for scanning was ~30 min in duration and was well tolerated by all subjects studied. DXA provides a three-compartment partition of the body: bone mineral, fat mass, and fat-free mass. Lean tissue was calculated by the subtraction of bone mineral (g) from the fat-free mass (g). The precision and accuracy of DXA for soft tissue and bone have been reported to be ~99% with <1% error (29). Total body and regional percent fat were calculated as a percentage of soft tissue mass, with the skeleton and skull excluded. A previous detailed report has addressed the content (BMC), and lean and fat tissue measurements. Linear regression analyses were used to plot lean and fat tissue mass IPDs as a function of weight IPD. Effect size and power calculations were performed on the variables.

Statistical analyses. Values are means ± SD. Unpaired t-tests were performed to determine group differences, and paired t-tests were used to determine significant differences within the pairs. Intraclass difference (IPD) scores (paralyzed twin – able-bodied twin) were calculated within the twin pairs for body weight, total body and regional bone mineral content (BMC), and lean and fat tissue measurements. Linear regression analyses were used to plot lean and fat tissue mass IPDs as a function of weight IPD. Effect size and power calculations were performed on the variables.

Simple- and multiple-regression analyses were also used to determine the effect of age and duration of injury on lean and fat tissue mass. In the paralyzed twins, linear regression was used to determine the effect of the IPD scores for total body and regional lean tissue mass on age and duration of injury, the association between lean IPD and bone IPD for total body and regional areas, and the relationship between level of lesion and absolute lean tissue mass and lean IPD. Analysis of covariance was used to determine the relationship between fat mass and BMI in both sets of twins.

RESULTS
A relatively young group of twins was studied (40 ± 10, range 25–58 yr). The mean duration of injury for the twins with paralysis was 16 ± 9 (range 3–26) yr. Height was similar for both sets of twins. Weight and BMI were significantly lower in the twins with paralysis than in their able-bodied co-twins: 71.4 vs. 81.5 kg (P < 0.05) and 22.3 vs. 25.4 kg/m² (P < 0.05), respectively (Table 1).

Total body and regional lean tissue and BMC. The twins with paralysis had significantly less total body, leg, and trunk lean tissue than the able-bodied co-twins. Arm lean tissue mass was not significantly different between the twin groups (Fig. 1). The mean total body lean tissue loss in the twins with SCI was 12.6 ± 7.9 kg (Table 2). The majority of this lean tissue atrophy was found in the trunk and leg regions, which were significantly reduced in the twins with paralysis: −3.0 ± 3.3 kg (P < 0.05) and −10.1 ± 4.0 kg (P < 0.0005), respectively (Table 2). The power for total body and leg lean tissue differences between the twin groups was 0.91 and 0.99, respectively.

In the paralyzed twins, increasing duration of injury was significantly associated with total body lean tissue loss (R = 0.87, P < 0.005; Fig. 2). Multiple-regression analysis was performed to test the association of duration of injury with total body IPD lean tissue with control for age. Independent of age, duration of injury was significantly predictive of total body lean tissue loss (partial r = 0.51, P = 0.03). In the twins with paralysis, no relationships or trends were found for level of trunk musculature innervation (T6–L1) with paralysis, no relationships or trends were found for level of trunk musculature innervation (T6–L1) with total body or trunk lean tissue mass or IPD.

In the able-bodied twins, total body and leg BMC were highly correlated with total body and leg lean tissue mass, but no such relationship was found in the paralyzed twins (Fig. 3). However, in the paralyzed twins, the IPD scores for total body and leg BMC and total body and leg lean mass were significantly related (Fig. 4).

Total body and regional fat tissue. The percent fat in the legs was 17.5 ± 11.7% (P < 0.005) higher in the paralyzed than in the able-bodied twins (Fig. 1). Total

Table 1. Characteristics of the twins

<table>
<thead>
<tr>
<th>Twin Pair No.</th>
<th>LOL (Para)</th>
<th>DOI (Para)</th>
<th>Height, m</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T11–L2</td>
<td>22</td>
<td>1.85</td>
<td>76.0</td>
<td>22.2</td>
</tr>
<tr>
<td>2</td>
<td>T10–11</td>
<td>21</td>
<td>1.78</td>
<td>58.6</td>
<td>21.5</td>
</tr>
<tr>
<td>3</td>
<td>T9</td>
<td>25</td>
<td>1.83</td>
<td>66.0</td>
<td>20.4</td>
</tr>
<tr>
<td>4</td>
<td>T12–L1</td>
<td>24</td>
<td>1.83</td>
<td>77.0</td>
<td>23.0</td>
</tr>
<tr>
<td>5</td>
<td>T9</td>
<td>25</td>
<td>1.72</td>
<td>72.0</td>
<td>23.5</td>
</tr>
<tr>
<td>6</td>
<td>T11–12</td>
<td>22</td>
<td>1.73</td>
<td>68.6</td>
<td>22.9</td>
</tr>
<tr>
<td>7</td>
<td>T7–8</td>
<td>11</td>
<td>1.73</td>
<td>80.5</td>
<td>26.3</td>
</tr>
<tr>
<td>8</td>
<td>T5</td>
<td>25</td>
<td>1.73</td>
<td>72.7</td>
<td>21.7</td>
</tr>
</tbody>
</table>

Mean ± SD 16 ± 9 40 ± 10 1.79 ± 0.04 1.79 ± 0.05 71.4 ± 6.9* 81.5 ± 13.8 −10.1 ± 11.5 22.3 ± 2.3† 25.4 ± 3.4 −3.1 ± 3.2

Para, paralyzed twin with spinal cord injury; AB, able-bodied twin; LOL, level of spinal cord lesion; T, thoracic; L, lumbar; DOI, duration of injury; BMI, body mass index; IPD, intrapair difference score (paralyzed twin – able-bodied twin). *Pairing corrected by 10.220.33.3 on April 10, 2017 http://jap.physiology.org/ Downloaded from by 10.220.34.3 on April 10, 2017
body, arm, and trunk fat mass or percent fat was not significantly different between the twin pairs (Fig. 1).

A significant linear relationship was found between BMI and fat mass for both groups ($R = 0.75, P < 0.05$ for paralyzed twins and $R = 0.82, P < 0.01$ for able-bodied twins). No significant difference was noted between the slopes of these relationships. With control for BMI by multiple regression, fat mass and percent-age were significantly increased by an average of 4.8 ± 1.8 kg (partial $r = 0.59, P = 0.02$) and 7.2 ± 2.4% (partial $r = 0.60, P = 0.01$) per unit of BMI in subjects with paralysis compared with the co-twins (Fig. 5).

On average, total body weight was 10.1 ± 11.5 kg less in the paralyzed than in the able-bodied twins, predominantly from loss of leg lean tissue ($-2.10.1 ± 4.1$ kg). The soft tissue compartments in the leg changed in a direct linear relationship with total body weight (Fig. 6). Thus, as the IPD for weight increased, the IPD for lean and fat tissue also increased.

**DISCUSSION**

Total body, leg, and trunk lean tissue mass were significantly reduced in the paralyzed twins. Although limited by sample size, the linear loss of total body and regional lean tissue mass with increasing duration of injury independent of age may be an important finding that has not previously been appreciated; this association would not have been observed without the use of a monozygotic twin controlled design.

Sarcopenia, or loss of muscle mass, occurs with aging (16, 27, 34). A variety of causes of sarcopenia have been postulated, one of which is disuse atrophy due to the decreased level of activity associated with aging (14). Young et al. (41) studied the cross-sectional area by ultrasound of the quadriceps muscle group in the able-bodied population in persons in their 20s and 80s. Comparison of the two groups showed a 25% decrease...
in the size of the quadriceps in the elderly group. In another study by Rice and co-workers (33) using computerized tomography, leg muscle size was reduced by 28–36% in subjects 65 yr of age. Our subjects with paralysis appear to exhibit an exaggerated form of sarcopenia, which is strongly associated with duration of injury and trends with age. The twins with paralysis at a mean age of 40 yr had already lost 20% of their total body mass and 48% of their leg lean tissue mass. This is twice the amount of leg muscle loss and 40 yr earlier than has been previously described in the general population (16, 27, 34).

Several studies have shown that physical activity delays loss of muscle mass with increasing age (9, 18, 19, 28). Our twins with SCI had an abrupt change in level of activity coincident with paralysis. Thus the identical-twin model has provided the design necessary to address whether adverse changes in lean tissue mass as a result of paralysis reach a new plateau or continue to show an age effect. Our findings suggest that chronic inactivity is associated with accelerated and progressive sarcopenia.

A strong correlation between change in body weight and change in total body lean mass has been well established (20, 21). Forbes et al. (22) reported a significant linear relationship between intrapair variation for lean body mass with intrapair variation for weight in monozygotic and dizygotic twins. In our study, total body weight was ~10 kg less in the

![Fig. 3. Regression of leg bone mineral content (BMC) (A) and total body BMC (B) on leg and total body lean tissue in paralyzed (○) and able-bodied (■) twins. In leg and total body, able-bodied twins had highly significant relationships between BMC and lean tissue mass (R = 0.88, P < 0.005 and R = 0.98, P < 0.0001, respectively), but no such relationship was found in paralyzed twins.](http://jap.physiology.org/)

![Fig. 4. Regression of IPD scores for total body BMC (A) and leg BMC (B) on total body and leg lean tissue. For total body: BMC IPD vs. lean IPD, R = 0.80 and P < 0.02; for leg: BMC IPD vs. lean IPD, R = 0.81 and P < 0.01.](http://jap.physiology.org/)

![Fig. 5. Relationships of body mass index to total body fat mass in paralyzed and able-bodied twins. For paralyzed twins (n = 8), R = 0.75, P < 0.05, and slope coefficient = 3.193 ± 1.141 (SE). For able-bodied twins (n = 8), R = 0.82, P < 0.01, and slope coefficient = 2.461 ± 0.696. There is no significant difference between slopes of these lines. However, by use of multiple regression in subjects with spinal cord injury, fat mass was significantly increased by 4.8 kg per unit body mass index (partial r = 0.59, P = 0.02).](http://jap.physiology.org/)
In conclusion, in persons with paralysis from SCI, there is an accelerated form of sarcopenia, similar to that seen in the elderly during the sixth through the eighth decades of life. SCI appears to cause a chronic catabolic state, whereby total body lean tissue, albeit mostly from the legs in our subjects with lower SCI, is depleted at a rate of ~8 kg/decade, about twice the rate of matched controls. Loss of lean tissue is linearly related to loss of BMC. Without the use of an identical-twin model discordant for paralysis, the progression and severity of lean tissue loss throughout the chronic phase of immobilization could not have been identified with this degree of accuracy. In individuals with chronic immobilizing conditions, further studies with identical twins may identify other potential body composition changes, as well as hormonal and metabolic alterations, that may be associated with these body composition changes.

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REFERENCES


