FRACTURE RISK IN PATIENTS WITH MUSCULAR DYSTROPHY AND SPINAL MUSCULAR ATROPHY

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We aimed at studying fracture risk in patients with Duchenne’s muscular dystrophy (DMD), Becker’s muscular dystrophy (BEMD), and spinal muscular atrophy type II and III (SMA II and III). A self-administered questionnaire was mailed to 293 patients with DMD, BEMD, SMA II or SMA III of which 229 returned the questionnaire. Each respondent was compared with an age- and gender-matched control subject. The mean age was 23.9 ± 15.9 years for the patients and 23.3 ± 16.5 years for the controls. There were significantly more fractures among patients than controls after the diagnosis was made (RR = 1.9), but not before. The patients had more fractures of the femurs, lower legs, and upper arms than the controls. Low energy fractures were more frequent in patients than controls (9% vs 0%). Many fractures in the femurs (40%), lower legs (35%), and feet and toes (44%) led to a permanent loss of function. Loss of ambulation was the major risk factor for fractures. In conclusion, fracture risk is increased in neuromuscular disease.

Key words: fracture, muscular dystrophy, spinal muscular atrophy, Duchenne’s muscular dystrophy, Becker’s muscular dystrophy.

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INTRODUCTION

Immobilization leads to loss of mineral from the skeleton (1–5), and a low bone mineral increases the risk of fractures (6). Neuromuscular disease, such as muscular dystrophy or spinal muscular atrophy (7, 8), spinal cord injury following traumas (6) or myelomeningocele (9) may lead to immobilization and thus loss of bone mineral. In spinal muscular atrophy and spinal cord injury, the nervous system is primarily affected, and the muscles are affected secondarily. In these primary nerve lesions, the pattern of muscle affection may modulate the occurrence of fractures (6) and bone mineral loss (2). In rat models of tibial fractures, severing of the sciatic nerve to the fractured leg may have positive systemic effects on other parts of the skeleton suggesting that the nervous system may be involved in bone formation other than locally through the effect on the muscles (10). Furthermore, electrical stimulation of a severed sciatic nerve may preserve bone mineral in an otherwise immobilized rat leg suggesting that the mechanical load of the muscles may compensate for the immobilization (11). In spinal cord injury, patients with cervical lesions and paralysis have a lower bone mineral in the femoral neck than patients with lumbar lesions and spastic paresis (2). This may be the result of the tone of the spastic muscles being able to maintain some external load on the bones and thus conserve bone mineral. On the other hand patients with lumbar lesions tend to have more fractures than patients with cervical lesions (6). This discrepancy between bone mineral and fracture occurrence may be the result of a higher level of physical activity and thus risk of falling in patients with lumbar lesions and stresses the necessity of not solely relying on measured bone mineral in predicting fracture risk among immobilized patients. The neuromuscular diseases include Duchenne’s type muscular dystrophy (DMD), Becker’s muscular dystrophy (BEMD), and spinal muscular atrophy (SMA). The primary muscle diseases without impairment of the locomotor system are DMD and the milder form BEMD. Among neuromuscular diseases of the nervous system leading to secondary muscular atrophy are spinal muscular atrophy type II (SMA II) and the milder form spinal muscular atrophy type III (SMA III) (12, 13). Muscular dystrophy and spinal muscular atrophy thus presents an excellent model for studying potential differences in skeletal biomechanical reaction to primary nervous system disease and primary muscle disease with principally intact innervation when stratifying for the level of physical impairment.

In a previous study, Granata et al. (14) reported that 16.5% of 145 patients DMD had had previous fractures while 9.3% of 93 patients with SMA I, II or III had had previous fractures. The fractures were particularly fractures of the femurs and humeral bones. Likewise, Hatano et al. (15) found that 12.8% of 148 patients with DMD had had previous fractures, especially femur and humerus fractures. Many of the fractures in patients with neuromuscular diseases are due to falls in general and falls from wheelchairs in particular (16)—falls that do often result in femur fractures (16, 17). The previous reports have mainly studied patients with DMD (15–19), and only one study has presented a larger group of SMA patients (14). Most of the studies have presented case series (16–19). None of the studies have compared patients with the different types of neuromuscular diseases or have compared fracture incidence to control groups from the background population. Apart from the loss of bone
mineral, it may also be expected that the patients with neuromuscular diseases have a somewhat lower level of physical activity than the background population, and thus perhaps are less prone to fracture producing traumas.

We chose to perform a study on fracture occurrence in a cohort of patients with muscular dystrophy and spinal atrophy to assess the frequency, the distribution, the nature, and the clinical consequences of fractures. This with special reference to the difference between patients with primary muscle disease and patients with muscular atrophy secondary to nervous system impairment.

MATERIAL AND METHODS

A self-administered questionnaire was mailed to 293 patients with muscular dystrophy and spinal muscular atrophy who were living in Denmark. After 6 weeks the questionnaire was re-issued to non-respondents. The study was approved by the Regional Ethics Committee (Aarhus County no. 1998/4347). The patients were compared with responses from identical questionnaires from an age- and gender-matched control group, randomly drawn from an issue of the questionnaire to a random sample of subjects from the background population. This control group consisted of 2634 responses to 4600 previously issued questionnaires (response rate 57.3%). The fracture rate among the controls was close to that seen in the general Danish population, and repeated issues of the questionnaire yielded similar responses. The questionnaire had been validated in both adults and children, and had been used with success in previous studies (6, 20). The main concerns concerning fracture occurrence were: “have you ever sustained a fracture to a bone?”, and in case of fractures: “how old were you, when you sustained the fracture?”, “what bone in the skeleton fractured?”, etc. All patients were diagnosed at specialized units of neurology, and the diagnoses were based on clinical criteria, blood samples (creatine kinase CK), muscle biopsy, family history, and in some cases genetic testing according to international guidelines (13) (Table I).

The degree of physical impairment was assessed using the Vignos scale (21, 22) (Table II) based on the patients’ reports in the questionnaires. The study had a power of 90% to detect a doubling of crude fracture incidence among 228 patients and 228 controls with a mean observation period after diagnosis of 15 years. Variables covered by the questionnaire are shown in Tables I and II. In case of fractures the participants were asked—in their own words—to describe which bone(s) had fractured, what had caused each individual fracture (e.g. a fall, an automobile accident etc.), whether or not he or she had undergone surgery for each fracture, whether or not he or she had been treated with plaster of Paris for each fracture, and whether each individual fracture had been treated on an inpatient or outpatient basis. If the patient was a...

<table>
<thead>
<tr>
<th>Group</th>
<th>DMD</th>
<th>BEMD</th>
<th>SMA II</th>
<th>SMA III</th>
<th>P*</th>
<th>All patients</th>
<th>Normal controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/females</td>
<td>90/–</td>
<td>40/–</td>
<td>29/23</td>
<td>21/16</td>
<td>–</td>
<td>189/39</td>
<td>189/39</td>
</tr>
<tr>
<td>Age (years)</td>
<td>16.3 ± 8.1</td>
<td>31.3 ± 16.6</td>
<td>23.0 ± 15.3</td>
<td>37.5 ± 19.3</td>
<td>&lt;0.001</td>
<td>23.9 ± 15.9</td>
<td>23.3 ± 16.5</td>
</tr>
<tr>
<td>Age at final diagnosis</td>
<td>3.5 ± 1.9</td>
<td>8.1 ± 7.8</td>
<td>1.4 ± 1.8</td>
<td>13.0 ± 16.5</td>
<td>&lt;0.001</td>
<td>5.3 ± 8.4</td>
<td>–</td>
</tr>
<tr>
<td>Time since diagnosis</td>
<td>12.8 ± 7.8</td>
<td>23.4 ± 15.4</td>
<td>21.6 ± 14.6</td>
<td>23.9 ± 15.9</td>
<td>&lt;0.001</td>
<td>18.5 ± 13.5</td>
<td>–</td>
</tr>
<tr>
<td>Use of wheelchair (%)</td>
<td>70</td>
<td>50</td>
<td>90</td>
<td>29</td>
<td>&lt;0.001</td>
<td>65</td>
<td>0</td>
</tr>
<tr>
<td>Response (%)</td>
<td>73</td>
<td>85</td>
<td>87</td>
<td>73</td>
<td>0.087</td>
<td>78</td>
<td>–</td>
</tr>
<tr>
<td>RR (95% CI) before diagnosis</td>
<td>2.0 (1.4–2.8)</td>
<td>1.5 (0.96–2.4)</td>
<td>2.6 (1.9–3.5)</td>
<td>1.1 (0.6–1.9)</td>
<td>0.030</td>
<td>1.9 (1.5–2.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>RR (95% CI) after diagnosis</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

DMD: Duchenne’s muscular dystrophy, BEMD: Becker’s muscular dystrophy, SMA II/III: spinal muscular atrophy type II or III

* Comparison of patient groups.

b Age at which a final definite diagnosis was made, several patients had had symptoms for a period before the final diagnosis was made.

c Based on the Vignos Scale.

d Some patients were too young to use wheelchairs.

e Calculated in a Cox regression (forward likelihood ratio method) with time until first fracture as dependent variable, and diagnosis type (all four types entered) as independent variable.

Table II. The Vignos scale (21)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Function level</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Walks and climbs stairs without assistance</td>
<td>11 (5%)</td>
</tr>
<tr>
<td>2</td>
<td>Walks and climbs stairs with aid of railing</td>
<td>44 (20%)</td>
</tr>
<tr>
<td>3</td>
<td>Walks and climbs stairs slowly with aid of railing (&gt;25 seconds for eight standard steps)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>4</td>
<td>Walks unassisted and rises from chair but cannot climb stairs</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>5</td>
<td>Walks unassisted but cannot rise from chair or climb stairs</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>6</td>
<td>Walks only with assistance or walks independently with long leg braces</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>7</td>
<td>Walks in long leg braces but requires assistance for balance</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>8</td>
<td>Stands in long leg braces but unable to walk even with assistance</td>
<td>143 (65%)</td>
</tr>
<tr>
<td>9</td>
<td>Is in wheelchair</td>
<td></td>
</tr>
</tbody>
</table>
minor (<18 years) the parents were asked to fill in the questionnaire. A separate analysis of those responding in the first and second round of the questionnaires did not change the results concerning age and gender distribution, or fracture rates significantly.

Based on the participants’ accounts of the fractures, the energy (force) associated with each fracture was categorized in a blinded design by one of the investigators (PV) into: (1) low-energy fracture (i.e. a fracture occurring after minor or no trauma); (2) medium-energy fracture (i.e. a fracture occurring after a fall at the same level, dropping medium weight objects onto/squeezing fingers or toes etc.); and (3) high-energy trauma (i.e. a fracture occurring after a fall from one level to another, car accidents, etc.). The blinded intra-observer Kappa coefficient for this classification was 0.87. A comparison of forearm bone mineral density (BMD) in a consecutive series of 23 patients with forearm fractures showed significantly higher BMD in the non-fractured forearm in those with high (n = 8, mean BMD 0.482 ± 0.076 g/cm²) than in those with medium energy traumas (n = 15, mean BMD 0.380 ± 0.072 g/cm², 2p < 0.01). This indicates that the classification is a valid indicator of bone biomechanical competence. The location of the fractures was categorized in a blinded design by one of the investigators (PV) based on the descriptions made by the patients or their parents into the categories shown in Table III. This classification had an intra-observer Kappa coefficient of 0.90. The fracture rates in the control group were comparable with those from the Danish population in general when comparing with tables from the Danish Board of Health (23). The validity of fracture reports was evaluated in an independent sample. Among these subjects 10 of 163 fractures could not be verified as being fractures (6.1%, 95% CI: 3–11%) upon review of files from hospitals, general practitioners, and X-ray departments. The fractures that could not be verified, were three rib fractures, two toe fractures, and a fracture of the knee cap, of the orbital margin, the upper arm, a finger and the coccygeal bone. No fractures were detected among subjects not reporting fractures.

If more than one fracture occurred at the same time the largest bone that fractured was counted as the fractured bone. Incidence rates were calculated as number of fractures per 10000 observation-years (i.e. multiple fractures at the same time point counted as one fracture episode).

Incidence rates were compared by relative risks (RR) and statistical comparisons were made using Mantel-Haenszel type \( \chi^2 \) statistics. Numbers were compared by \( \chi^2 \) for contingency tables, Fisher’s exact test or Mann-Whitney statistics when appropriate. Mantel-Haenszel statistics were used to compare fracture occurrence in groups. All comparisons were age- and gender-adjusted. Multiple comparisons were performed by Cox proportional hazard method using SPSS for Windows 6.1.3. In the Cox analysis, patients with and without fractures were compared using as time intervals the time from diagnosis until the first fracture date or time until current date if no fractures had occurred. Patients with BEMD and DMD were grouped together as primary muscle disease and SMA II and SMA III grouped together as spinal muscular atrophy to separate between primarily muscle disease and muscular atrophy secondary to primarily neurogenic disease in the Cox analysis.

### RESULTS

Table I gives baseline characteristics of the respondents. A total of 229 patients (78%) returned the questionnaire, one questionnaire could not be analysed due to missing general information, and a further 13 questionnaires could not be analysed due to missing information on fracture occurrence. In none of the patient groups did the age among respondents differ from that of the non-respondents. A total of 228 age- and gender-matched control subjects were used for comparison.

The gender distribution among the SMA II and III respondents was the same as the entire group of SMA II and III patients who were contacted. The mean time since diagnosis was 18.5 years among the patients. Table II shows the best level of function (the Vignos scale).

Before the diagnosis was made, the risk of fractures was not increased among the patients compared to the control group (Table I). After the diagnosis was made, there was a significant increase in fracture risk in all patient groups compared with the control group (Table I).

However, as can be seen from Table I, there was a close association between the RR and the proportion of users of wheelchairs in each diagnosis group, e.g. among patients with SMA II 90% used wheelchairs and the RR of fracture was 2.6, while only 29% of SMA III patients used wheelchair and their RR was 1.1. Adjustment for physical impairment was done using a Cox regression with age at diagnosis, muscular dystrophy vs. spinal muscular atrophy, and total loss of ambulation (and thus dependency on wheelchair, Vignos grade 9) vs ability to walk or stand as independent variables and time.

**Table III. Fracture risk in patients compared with normal controls stratified by skeletal site**

<table>
<thead>
<tr>
<th>Site</th>
<th>DMD + BEMD RR (95% CI)</th>
<th>SMA II + III RR (95% CI)</th>
<th>All RR (95% CI)</th>
<th>Permanent loss of function following the fracture n yes/no, and (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull and jaws</td>
<td>0.0 (–)</td>
<td>2.7 (0.2–39.1)</td>
<td>1.3 (0.1–21.1)</td>
<td>Q/1 (0%)</td>
</tr>
<tr>
<td>Spine</td>
<td>0.0 (–)</td>
<td>1.4 (0.1–15.0)</td>
<td>0.7 (0.1–7.2)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.5 (0.2–1.1)</td>
<td>0.1 (0.0–0.3)*</td>
<td>0.3 (0.1–0.6)*</td>
<td>1/7 (13%)</td>
</tr>
<tr>
<td>Upper arm</td>
<td>3.1 (1.0–9.6)*</td>
<td>2.7 (0.8–9.0)</td>
<td>2.9 (1.1–8.0)*</td>
<td>2/8 (20%)</td>
</tr>
<tr>
<td>Hands and fingers</td>
<td>0.2 (0.1–0.7)*</td>
<td>0.0 (–)*</td>
<td>0.1 (0.0–0.3)*</td>
<td>1/1 (50%)</td>
</tr>
<tr>
<td>Femur</td>
<td>27.3 (10.5–70.8)*</td>
<td>15.1 (4.9–46.6)*</td>
<td>21.4 (7.9–57.7)*</td>
<td>12/18 (40%)*</td>
</tr>
<tr>
<td>Lower leg</td>
<td>8.2 (4.0–16.7)*</td>
<td>5.5 (2.4–12.3)*</td>
<td>6.9 (3.4–13.8)*</td>
<td>12/22 (35%)</td>
</tr>
<tr>
<td>Feet and toes</td>
<td>1.7 (0.6–4.8)</td>
<td>0.9 (0.2–3.4)</td>
<td>1.3 (0.5–3.4)</td>
<td>4/5 (44%)</td>
</tr>
<tr>
<td>Clavicles</td>
<td>1.9 (0.6–5.8)</td>
<td>0.8 (0.2–3.8)</td>
<td>1.3 (0.5–3.8)</td>
<td>0/7 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>0.0 (–)</td>
<td>2.7 (0.2–39.1)</td>
<td>1.3 (0.3–21.1)</td>
<td>Q/1 (0%)</td>
</tr>
<tr>
<td>Overall</td>
<td>1.8 (1.3–2.5)*</td>
<td>1.1 (0.7–1.6)</td>
<td>1.5 (1.1–1.9)*</td>
<td>32/71 (31%)</td>
</tr>
</tbody>
</table>

\* \( p < 0.05 \), Mantel-Haenszel \( \chi^2 \) test.

A permanent function loss refers to a self-reported permanent loss of any function, e.g. the ability to walk.

DMD: Duchenne’s muscular dystrophy, BEMD: Becker’s muscular dystrophy, SMA II/III: spinal muscular atrophy type II or III.

RR: relative risk compared with normal controls adjusted for age and sex.
until first fracture after diagnosis as dependent variable. This Cox analysis showed that use of wheelchair as best level of function was associated with an increased fracture risk ($RR = 4.2$, $95\%$ CI: 1.7–10.5) while patients with spinal muscular atrophy had borderline significantly fewer fractures than patients with primary muscle disease ($RR = 0.55$, $95\%$ CI: 0.31–0.98). Age at diagnosis was not associated with fracture risk ($p = 0.94$) neither in muscular dystrophy nor in spinal muscular atrophy. If the Vignos scale (use of wheelchair as best level of function vs ability to walk or stand at any time during the day) was replaced by use of wheelchair at any time during the day vs. no use of wheelchair at all, there was no difference between those with muscular dystrophy and those with spinal muscular atrophy ($p = 0.075$) in the Cox analysis. However, use of wheelchair was still significantly associated with fracture risk ($RR = 3.4$, $95\%$ CI: 1.1–10.8). Age at diagnosis was not associated with fracture risk ($p = 0.76$).

The patients had an increased risk of fractures to the lower legs—in particular the femurs (Table III). A large percentage of the fractures—especially the abundant fractures of the femurs, lower legs, and feet and toes were followed by a permanent loss of function (e.g. ability to walk)—Table III. The loss of function after fractures in the lower extremities was more pronounced in patients with DMD and BEMD than in SMA II and III (50% vs 19% of fractures of femurs, lower legs, or feet and toes led to permanent function loss, $2p = 0.01$).

There was a significantly increased frequency of low energy fractures: 10 (9.2%) fractures in the patients resulted from minor or no trauma versus none (0%) in the control subjects ($p < 0.01$). Among the patients 68 (62.4%) of all fractures were medium energy fractures versus 53 (53.5%) in the controls. For the high-energy fractures, 31 (28.4%) of fractures in the patients were high-energy fractures against 46 (46.5%) in the controls.

No single risk factor other than those mentioned could be associated with fracture risk among the patients. Participation in sports activities was not associated with an increased fracture risk ($RR = 1.1$, $95\%$ CI: 0.7–1.6). Use of corticosteroids was also not associated with an increased fracture risk ($RR = 1.2$, $95\%$ CI: 0.7–2.2), but only 22 of the patients (10% vs 6% of controls, $p = 0.09$) had ever used corticosteroids, and most of the patients (63% vs 25% of controls, $2p = 0.09$) had used them for less than one year.

Fig. 1 shows the RR of fractures in patients compared to controls before and after diagnosis. There was an increase in crude fracture risk in patients more than five years after diagnosis.

**DISCUSSION**

Among the patients there was an increased fracture risk in the femurs, and the lower legs similar to the observations in patients with spinal cord lesions (6). The fracture risk was especially prominent in the femurs (in particular in the femoral shaft) which is a part of the skeleton with predominantly cortical bone. The fractures had a significant impact on the patient level of activities, approximately 35–40% of fractures of the femurs or lower legs resulted in self-reported permanent loss of function e.g. the ability to walk. Even small fractures of the feet and toes often led to a permanent loss of function, especially among patients with DMD and BEMD. The fractures may thus have a major impact on overall quality of life and perhaps also on survival. Fracture prevention is thus an important feature (30% of all patients in this study had sustained at least one fracture after they had been diagnosed). The higher loss of function following fractures in DMD and BEMD in contrast to SMA II and III may be a natural consequence of the fact that DMD and BEMD patients have had a better initial ambulatory function at the time of fracture. A loss of or difficulties in walking can in the case of DMD or BEMD be perceived as a consequence of the fracture. Among patients with an ambulatory function, even a shorter period of immobilization (e.g. following a fracture) may lead to a permanent loss of ambulation due to deterioration in muscle function. In contrast, SMA II and III are more stable conditions with little tendency towards progression, and most patients are wheelchair users after childhood. Thus a fracture may not contribute to further loss of function, since ambulation may already be absent in most patients at the time of fracture.

The decreased risk of finger and forearm fractures was probably the result of the impaired general functional level of the patients.

Since the fracture risk was highest in patients with DMD and BEMD, this group may benefit the most from fracture prevention especially as fractures seemed to result in pronounced deterioration of function in these patients. Fracture prevention may thus involve multidisciplinary measures, primarily through maintenance of external load on the lower extremities for as long as possible through stimulation of the standing and/or walking function. This may be implemented e.g. through the use of long leg braces in patients who have lost the ability to walk. In patients with spinal cord injury it has been shown that use of standing devices helped maintain bone mineral in the lower extremities (24) through the external load. Besides external loading some studies have shown beneficial effects of bisphosphonates on bone mineral in patients immobilised due to spinal cord injury (25–27), and this approach may be useful in selected patients. Use of calcium...
supplements should be considered carefully as immobilized patients may have an increased excretion of calcium in the urine (3) and thus an increased risk of kidney and urinary tract calcifications.

The patients with DMD and BEMD had an increased fracture risk in the upper arms, but no increased fracture risk in the forearms. This in contrast to the patients with spinal cord lesions who have a decreased risk of forearm fractures and no increase in the risk of upper arm fractures (6). However, the patients with muscular dystrophy and spinal muscular atrophy had a generalized loss of muscular tone thus also in the upper extremities and the shoulder girdle muscles. The patients with cervical spinal cord lesions have some normal muscular function and tone left in the shoulder girdle (28) while patients with lesions below the cervical spine had full normal function of the upper extremities and probably a higher daily load on these than most of the normal controls due to the use of manual wheelchairs. It thus seems that external load to the bone is essential not just due to mechanical loading, but also from the muscular tone (both resting and during activity) that acts on the upper extremities (especially the humerus).

The main predictor of fractures was use of wheelchair which is a proxy variable for the type of disease, degree of immobilization, degree of reduced physical activity (loss of ambulation), and the degree of reduced muscular tone. It is possible, that the small difference between patients with primary muscle disease (DMD and BEMD) and spinal muscular atrophy (SMA II and III) was due to more subtle differences in the degree of muscle impairment not identified by the functional classification used. Other studies have also shown that fracture risk is increased in patients with physical impairment irrespective of the cause of the impairment (9, 29). In patients with spinal cord injury the time interval from the injury until an increased fracture risk can be detected is about three years (6). In the present study, an increased fracture risk presented more than 5 years after diagnosis. This discrepancy may be the result of a more gradual loss of motor function, especially in DMD and BEMD, than in spinal cord injury, where the loss of motor function is of sudden onset.

The age of our study group was much younger than that usually seen in patients with osteoporosis, and our study group was still in a phase of life with a growing skeleton in contrast to older patients who are in a phase of life with a loss of bone. Despite their younger age, the patients displayed a similar fracture pattern as seen in much older patients with osteoporosis following immobilization after spinal cord injury (6). Previous studies on bone mineral in patients with neuromuscular disorders have reported decreased bone mineral compared with matched control groups (7, 8). We did not measure BMD in our patients, but the higher proportion of low energy fractures suggests a lower BMD in the patients. However, it should be noted that in small children in the age groups comparable with our patients, BMD may pose an uncertain measure, and controversy exists as to the appropriate measurement sites and the appropriate values to measure. As the skeleton is in a growing phase, BMD may tend to increase simply as a consequence of the enlargement of the skeleton, and some prefer measurements of bone mineral content (BMC) over BMD. Furthermore, epiphyses may pose a problem for regional scans, and whole body scans have been recommended, although the interpretation of these is uncertain with respect to normal range, some preferring to use the child as its own reference over time (30). Furthermore, children with chronic diseases are often underweight, and this may tend to give a false low BMD upon measurement with bone mineral scanning (30).

The limitations of the study are mainly linked to the accuracy of the fracture reports, the patients perhaps being more likely to respond and to report fractures than the controls. However, the fracture reports did in general seem valid in accordance with findings from other studies (31).

The absence of an effect of corticosteroid use on fracture risk may be due to the low number of users, and the short duration of use.

In conclusion it seems that the physical impairment following muscular dystrophy and spinal muscular atrophy leads to a significant increase in the risk of fractures, particularly of the lower extremities, and that these fractures frequently leads to a deterioration of function level, especially in DMD and BEMD. No major differences between primarily muscle and primarily nerve disease was present.

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REFERENCES