Musculoskeletal abnormalities in juvenile idiopathic arthritis—a 4-year longitudinal study

J. Roth, M. Linge¹, N. Tzaribachev¹, R. Schweizer¹ and J. Kuemmerle-Deschner¹

Objectives. Bone density in juvenile idiopathic arthritis (JIA) is largely normal whereas geometric parameters of bone are abnormal. The most prominent changes are a reduction in muscle cross sectional area (CSA) and muscle force. The aim of this study was to assess the evolution of these changes throughout the course of the disease.

Methods. Twenty-five JIA patients were assessed by peripheral quantitative computed tomography longitudinally with a median of 48 months between measurements. At the non-dominant forearm, parameters of bone density and geometry as well as muscle CSA were recorded. The strength–strain index (SSI) as an indicator of bone strength was determined.

Results. Muscle CSA improved from a median Z-score of −1.94 to −1.10 at follow-up. Cortical thickness increased from −1.55 to −0.97 whereas marrow area remained enlarged at 0.96 vs 1.05. Cortical density remained normal at 0.34 vs 0.69 and trabecular density improved from −0.75 to −0.36. The SSI increased from −0.79 to −0.38.

Conclusions. JIA patients show some improvement in muscle CSA and an increase in cortical thickness. The marrow area remains enlarged but by increasing the cortical thickness, area and diameter, bone strength increases. These geometric adaptations, for the first time shown in this study, nevertheless represent a disturbance in skeletal development. In addition to efficient disease control, training modalities to improve muscle strength and subsequent bone development have to be included in therapeutic approaches.

KEY WORDS: Juvenile idiopathic arthritis, Osteoporosis, Musculoskeletal system, Bone, Muscle.

Introduction

Bone mass in juvenile idiopathic arthritis (JIA) is reduced. The main reasons are thought to be the disease activity itself, medication, reduced physical activity and unbalanced nutrition [1, 2]. Only recently a detailed analysis was possible using peripheral quantitative computed tomography (pQCT) [3, 4]. Both studies showed that the most prominent changes are abnormalities in bone geometry and a reduction in muscle cross-sectional area (CSA) and muscle force, challenging the traditional concept of osteoporosis in JIA as a primary problem of bone density. They rather suggest that bone loss in JIA mostly occurs secondary to a loss of muscle. Interestingly, all of the possible aetiological factors for a decrease in bone mass named above may—apart from a direct interference with bone metabolism—well act indirectly on bone via a decrease in muscle mass (glucocorticoid-induced, nutrition-induced or inactivity-induced sarcopenia, cytokines acting on muscle). The abnormalities in bone geometry are of concern as both the amount and the geometric distribution of bone mass determine bone strength and the fracture threshold [5, 6].

The aim of the present study was to assess the evolution of these changes longitudinally in order to estimate the risk of persistent changes and identify possible pathogenesis-oriented therapeutic interventions.

pQCT was used as it is the only technique currently available in clinical practice that will allow for direct measurements of volumetric bone density, the separate analysis of trabecular and cortical bone and the determination of parameters of bone geometry like cortical thickness and area [7]. Using the geometric variables measured, the strength–strain index (SSI) can be calculated, which represents an excellent indicator of bone strength and fracture threshold [7–9]. Compared with other CT-measurements, pQCT offers the advantage of a very low radiation dose of <2 μSv.

Patients and methods

Patients

Twenty-five patients were assessed by pQCT. Thirteen were suffering from the oligoarticular and 12 from the polyarticular form of the disease. Active arthritis was present in all patients initially and in 64% of patients at the time of the second measurement. No patients with delayed puberty were included in the study. Written informed consent was obtained from parents and patients >18-ys-old, and assent from patients < 18-ys-old according to the declaration of Helsinki. The study protocol had been approved by the ethic committee of the University of Tuebingen.

Study design

Two pQCT measurements were taken longitudinally with a median interval of 48 months (range 43–67 months). Height and weight were measured at the same visit. Height was measured in a standing position to the nearest 1 mm using a wall-mounted stadiometer (System Dr. Keller 1, Luengenmesstechnik GmbH, Limbach, Germany). Weight was determined to the nearest 0.1 kg using an electronic scale (Seca 753 E; Vogel and Hanke, Hamburg, Germany) with the children clothed in underwear. The joint assessment and determination of pubertal development was also done at the same visit by the treating physician. The stage of sexual development was determined in all study participants by physical examination using the grading system by Tanner for breast development in girls and genital status in boys [10]. Criteria for delayed puberty were failure to reach stage 2 at an age >12 yrs in girls and >14 yrs in boys. According to these criteria, none of the study subjects suffered from delayed puberty. The medication of the patients was recorded and the childhood health assessment questionnaire (CHAQ) was used in

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Peripheral quantitative computed tomography

PQCT measurements were performed at the non-dominant arm using an XCT-2000 scanner (Stratec, Pforzheim, Germany) equipped with a low energy (38 keV) X-ray tube. The effective radiation dose is <0.2 μSv for the measurements of this study. Measurements were taken at two sites. The first one at a distance of 4% of the forearm length either from the most distal portion of the growth plate when it was still open or from the ulnar border of the radius, when the growth plate was no longer visible (as described in [12]). The second measurement was taken at a distance of 65% of the forearm length proximal to the ulnar styloid process. At each site a 2-mm-thick single tomographic slice was sampled at a voxel size of 0.4 mm. The speed of the translational scan movement was set at 15 mm/sec. Image processing and the calculation of numerical values were performed using the manufacturer’s software version 5.40. The threshold for cortical bone was set at 710 mg/cm². For trabecular bone, the threshold was set at 240–280 mg/cm² and voxels with an absorptiometric density between 20 and 60 mg/cm² and peripheral to cortical bone were interpreted as muscle. All parameters measured were compared with reference data that had been obtained from a comparable German population comprising 371 healthy Caucasian children and adolescents aged 6–23 yrs [12–14]. The measurement sites, measurement parameters and devices were identical with those used for the reference data. These reference data were available in two sets: one related to age and one related to height. In order to exclude a possible influence of growth retardation in our patients, which might give false low results especially for geometrical parameters, patient data were compared with both age- and height-matched references.

The following parameters were analysed: at the 4% site trabecular density expressed as mg/cm³ was measured. At the 65% site cortical density in mg/cm³ and the geometrical parameters bone CSA (cortical CSA including the marrow area), cortical area (bone CSA minus marrow area), marrow area (bone CSA minus cortical area), cortical thickness in millimeters and muscle CSA were measured. The polar SSI was calculated on the basis of the polar moment of inertia and the section modulus and the cortical bone density by the following formula:

\[
SSI = \sum \left( d^2 \ast A \ast \frac{vBMD_{vox}}{vBMD_{max}} \right) / d_{\text{max}}
\]

\( A \) is the CSA of a voxel (0.4 π 0.4 mm = 0.16 mm² in our case), \( d \) is the distance of the voxel from the centre of gravity, \( vBMD_{vox} \) is the volumetric bone mineral density in the voxel (g/cm³), \( d_{\text{max}} \) is the maximum distance of any of the voxels of the cortical cross section from the centre of gravity and \( vBMD_{max} \) is the maximum mineral density of human bone set at 1200 mg/cm³.

Statistical analysis

Patient data were compared with age-, height- and sex-matched reference data. Results are given as a Z-score using the formula [(patient result) – (age/height- and sex-specific mean of the reference population)]/(standard deviation (SD) in the reference population). 95% confidence intervals were calculated for both patient data and reference data and if there was no overlap between both, differences were considered to be significant. The significance of differences between patient groups and between longitudinal measurements in the same patient group was calculated using the Mann-Whitney U-test with an \( \alpha = 0.05 \).

Results

General data of the study population

The general data of the study population are shown in Table 1. No significant differences as compared with the reference values were found for height, weight and BMI in the oligoarticular and polyarticular subgroup, although some patients were clearly growth retarded or obese. The number of patients in remission at follow-up was much higher in the oligoarticular group. Patients in remission in both subgroups had neither inflamed joints nor elevated C-reactive protein levels or ESR-rates at follow-up (data not shown). The oligoarticular group contained younger patients as expected from the epidemiological age distribution of JIA subgroups. The younger age is also reflected by a higher percentage of pre- and peripubertal patients.

Results of pQCT measurements

In Table 2 the results of the pQCT measurements for geometrical properties of bone and muscle at the diaphysis (muscle CSA, bone CSA, cortical area, cortical thickness and marrow area), density (trabecular and cortical) and the strength index (SSI) are shown for all patients together initially and at follow-up.

As growth retardation might lead to false low results especially for geometrical parameters, patient results were compared with reference data from corresponding age groups (A) as well as corresponding body height groups (H) in Table 2. In Tables 3 and 4, the same parameters are shown only in a height-matched reference analysis and according to subgroups (Table 3) or remission (Table 4).

Cortical bone density was not affected. Trabecular density was reduced initially (Table 2). The analysis according to subgroups showed, that polyarticular patients had a significantly reduced trabecular density whereas the oligoarticular patients were normal. Geometrical parameters were strongly affected and in each subgroup muscle CSA was clearly reduced initially. Bone CSA was increased in the oligoarticular as well as marrow area in both subgroups, whereas cortical area was reduced as well as cortical thickness. In the course of the disease, muscle CSA improved significantly in the oligoarticular group together with a strong improvement of the geometrical parameters of bone,
Table 2. pQCT results initially and at follow-up for all patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age-matched (old)</th>
<th>Age-matched (new)</th>
<th>Height-matched (old)</th>
<th>Height-matched (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle CSA</td>
<td>−2.31 (−5.99, −0.14)*</td>
<td>−1.87 (−4.82, 0.63)*</td>
<td>−1.94 (−4.68, 0.39)*</td>
<td>−1.10 (−4.81, 1.58)*</td>
</tr>
<tr>
<td>Bone CSA</td>
<td>−0.03 (−1.82, 2.03)</td>
<td>0.25 (−1.45, 3.35)</td>
<td>0.10 (−1.52, 3.88)</td>
<td>0.57 (−1.45, 3.90)*</td>
</tr>
<tr>
<td>Cortical area</td>
<td>−1.31 (−4.44, 0.19)*</td>
<td>−1.19 (−2.75, 0.62)*</td>
<td>−1.17 (−2.53, 2.59)*</td>
<td>−0.48 (−2.40, 2.59)*</td>
</tr>
<tr>
<td>Cortical thickness</td>
<td>−1.68 (−4.73, −0.10)*</td>
<td>1.24 (−3.93, 0.75)*</td>
<td>−1.55 (−4.49, −0.10)*</td>
<td>−0.97 (−2.93, 1.57)*</td>
</tr>
<tr>
<td>Marrow area</td>
<td>0.93 (−0.10, 3.14)*</td>
<td>0.96 (−0.58, 5.18)*</td>
<td>0.96 (−0.10, 4.37)*</td>
<td>1.05 (−0.52, 5.18)*</td>
</tr>
<tr>
<td>Density</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical density</td>
<td>0.33 (−1.56, 1.05)</td>
<td>0.05 (−4.06, 1.97)</td>
<td>0.34 (−1.05, 1.45)</td>
<td>0.69 (−2.86, 2.96)*</td>
</tr>
<tr>
<td>Trabecular density</td>
<td>−0.60 (−2.76, 0.62)*</td>
<td>−0.18 (−4.31, 1.58)</td>
<td>−0.75 (−2.31, 0.86)*</td>
<td>−0.28 (−3.85, 2.68)*</td>
</tr>
<tr>
<td>SSI</td>
<td>−1.44 (−2.74, 0.37)*</td>
<td>−0.87 (−2.33, 0.93)*</td>
<td>−0.79 (−1.31, 1.57)*</td>
<td>−0.13 (−2.33, 1.80)*</td>
</tr>
</tbody>
</table>

Data for parameters of bone geometry, bone density and bone strength are shown for all patients together initially (old) and at follow-up (new) and are expressed as medians of Z-scores compared with either age-matched or height-matched reference groups. The range of individual patients’ values is given in brackets. *Indicates significant values (P < 0.05) as compared with the reference population.

Table 3. pQCT results according to subgroups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oligo-JIA (n = 13)</th>
<th>Poly-JIA (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Height (old)</td>
<td>Height (new)</td>
</tr>
<tr>
<td>Geometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle CSA</td>
<td>−1.58 (−3.01, 0.39)</td>
<td>−0.55 (−2.13, 1.58)*</td>
</tr>
<tr>
<td>Bone CSA</td>
<td>0.30 (−0.66, 1.21)</td>
<td>0.56 (−0.82, 3.18)</td>
</tr>
<tr>
<td>Cortical area</td>
<td>−1.02 (−2.53, 0.19)</td>
<td>−0.34 (−1.58, 2.59)*</td>
</tr>
<tr>
<td>Cortical thickness</td>
<td>−1.39 (−4.49, −0.10)</td>
<td>−0.88 (−2.36, 1.57)</td>
</tr>
<tr>
<td>Marrow area</td>
<td>1.31 (−0.10, 4.37)</td>
<td>0.35 (−0.52, 4.67)</td>
</tr>
<tr>
<td>Density</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical density</td>
<td>0.42 (−0.89, 1.45)</td>
<td>1.17 (−1.37, 2.82)</td>
</tr>
<tr>
<td>Trabecular density</td>
<td>−0.15 (−2.06, 0.86)</td>
<td>−0.09 (−1.79, 2.68)</td>
</tr>
<tr>
<td>SSI</td>
<td>−0.75 (−2.11, 1.57)</td>
<td>0.14 (−1.80, 1.80)*</td>
</tr>
</tbody>
</table>

Data for parameters of bone geometry, bone density and bone strength are shown for both subgroups of patients initially (old) and at follow-up (new) and are expressed as medians of Z-scores compared with height-matched reference groups. The range of individual patients’ values is given in brackets. *Indicates significant values (P < 0.05) when follow-up measurements were compared with the initial measurement using the Mann–Whitney U-test for dependent variables. #Indicates significant values (P < 0.05) when results for oligoarticular patients were compared with results of polyarticular patients using the Mann–Whitney U-test for independent variables.

Table 4. pQCT results according to remission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>JIA (n = 8) in remission</th>
<th>JIA (n = 17) not in remission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Follow-up</td>
</tr>
<tr>
<td>Geometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle CSA</td>
<td>−1.66 (−4.09, −0.14)</td>
<td>−0.80 (−2.13, 0.16)</td>
</tr>
<tr>
<td>Bone CSA</td>
<td>0.25 (−0.66, 1.09)</td>
<td>0.08 (−0.82, 3.18)</td>
</tr>
<tr>
<td>Cortical area</td>
<td>−1.27 (−2.53, 0.19)</td>
<td>−0.52 (−1.58, 0.82)</td>
</tr>
<tr>
<td>Cortical thickness</td>
<td>−1.75 (−2.74, −0.21)</td>
<td>−0.66 (−1.80, 0.02)</td>
</tr>
<tr>
<td>Marrow area</td>
<td>1.47 (0.69, 2.20)</td>
<td>0.30 (−0.30, 3.81)*</td>
</tr>
<tr>
<td>Density</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical density</td>
<td>−0.21 (−0.59, 0.52)</td>
<td>0.95 (−1.37, 2.96)</td>
</tr>
<tr>
<td>Trabecular density</td>
<td>−0.15 (−2.17, 0.25)</td>
<td>−0.78 (−2.49, 0.35)</td>
</tr>
<tr>
<td>SSI</td>
<td>−0.77 (−2.36, 0.16)</td>
<td>−0.34 (−1.80, 0.72)</td>
</tr>
</tbody>
</table>

Data for parameters of bone geometry, bone density and bone strength are shown initially and at follow-up for patients in remission (n = 8, left) and patients not in remission (n = 17, right). Data are expressed as medians of Z-scores compared with height-matched (H) reference groups. The range of individual patients’ values is given in brackets. *Indicates significant values (P < 0.05) when patient groups are compared using the Mann–Whitney U-test.

although the latter did not reach significance for all parameters, probably due to the relatively small sample size. In contrast, muscle CSA remained abnormal as did geometric parameters of bone in the polyarticular group. The only significant difference between the two groups was muscle CSA at follow-up (Table 3).

These data indicate, that the musculoskeletal interaction is intact in JIA and with a normalization of muscle CSA, the geometric parameters of bone will also improve. The functional muscle bone unit is further illustrated by the strong correlation between cortical area and muscle cross sectional area which was even stronger at follow-up than initially (Fig. 1).

A schematic graphical illustration of a normal diaphyseal bone as compared with the geometric distribution of bone mass initially (black) and at follow-up (grey) according to subgroups is given in Fig. 2.

Comparison of patients with and without remission

In Table 4, a comparison between patients with and without remission is shown at follow-up. Remission was defined according to [15]. Bone geometry remains abnormal in both groups, but especially in children without remission. The aforementioned adaptations with a periosteal expansion leading to an increase in bone strength can be observed especially in the group without remission. The only significant difference was an increase in marrow area which was much more pronounced in the non-remission group.
Nevertheless showed clearly abnormal bone parameters which
was 0.61 initially with R < 0.001 and 0.69 at follow-up with P < 0.001.

In the group of polyarticular patients, the percentage on any significant influence of these agents on the measurement
median age was rather high reducing the bias mentioned.
We did not include any patients with delayed puberty and the underestimation of the patients' reduction in bone mass or size.
could therefore be influenced by the pubertal stages and lead to an
growth spurt. Comparison of patient data with reference data
comparison with younger subjects, especially around puberty.
A problem with height-matched reference groups might be the
analysis of muscle CSA and geometrical parameters of bone.
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especially in polyarticular JIA and also occur in patients who
normal. Abnormalities of the musculoskeletal system persist
incidence of low or very low total body bone mass. Compared to
study with dual energy X-ray absorptiometry measurements (DXA) [18]. In this study, children with early JIA had a higher
inflammatory arthritides. It is quite tempting to speculate that the skeleton thus compensates in part the
decrease in cortical thickness and increase of marrow area in order to improve the mechanical properties of bone even though the basic parameters still remain abnormal (Fig. 2).
The only other prospective study published so far was a 2-yr study with
Bone strength is not primarily a function of bone mass but bone size. It has been illustrated [7] that the same cortical area
distributed with a larger diameter results in a strong increase of the moment of inertia which is inversely related to the shear stress in bone created by torque. The section modulus, a closely related parameter that indicates the resistance of bone to bending, is also increased. On the other hand, the material properties also play a role in determining strength. In bone they are largely determined by the volumetric bone mineral density [17]. The SSI, calculated on the basis of the pQCT measurements, elegantly includes both the material and geometrical properties. To our knowledge this is the first study to show an increase of bone strength induced by periosteal expansion in inflammatory arthritides. It is quite
premature to conclude from this study that the skeleton thus compensates in part the decrease in cortical thickness and increase of marrow area in order to improve the mechanical properties of bone even though the basic parameters still remain abnormal (Fig. 2).
The only other prospective study published so far was a 2-yr study with
dual energy X-ray absorptiometry measurements (DXA) [18]. In this study, children with early JIA had a higher
incidence of low or very low total body bone mass. Compared to
JIA patients, healthy children had significantly greater gains in total body and distal radius bone mineral content and total body lean mass. The latter correlated with a reduction in weight-bearing activities in JIA patients. Polyarticular patients were more affected than oligoarticular patients. Although DXA cannot differentiate bone density from bone geometry, and therefore precludes a detailed analysis of the mechanisms leading to alterations of bone mass, the results of this study are in accordance with our results showing a clear reduction in muscle mass with a secondary disturbance in bone development.
The improvement of bone following an increase in muscle mass and force strongly supports the role of weight bearing exercise as an important part of the treatment of JIA in addition to fast and efficient disease control. These exercises might also be important for patients in remission as their muscle CSA and bone geometry might remain abnormal. An interesting and at the same time worrying observation is that pre-pubertal children seem to respond to physical training better than peri- or post-pubertal children [19]. This might add to the better improvement of bone geometry in the oligoarticular group in our study. These patients not only had a better disease course with a much higher percentage of patients in remission but also were younger. Their skeletal system might therefore be more responsive to the increase seen in muscle mass. This also underlines the need for early training interventions if possible at a younger age. On the other hand, older patients should also improve with increased loading from an increased muscle mass. Physical training studies in adults with rheumatoid arthritis have shown [20] that muscle force can be increased, this effect is sustained and results in a positive effect on the disease course. The gain in bone mass was relatively low

Discussion
These longitudinal data confirm that the main problem in children suffering from JIA is a secondary bone loss due to a reduction in muscle mass and force. Cortical bone density is normal. Abnormalities of the musculoskeletal system persist especially in polyarticular JIA and also occur in patients who achieve remission.
In most of the analyses shown in this report, we preferred height-matched reference groups as growth retardation is common in these patients and will interfere especially with the analysis of muscle CSA and geometrical parameters of bone. A problem with height-matched reference groups might be the comparison with younger subjects, especially around puberty. Muscle and bone development is very fast during the pubertal growth spurt. Comparison of patient data with reference data could therefore be influenced by the pubertal stages and lead to an underestimation of the patients’ reduction in bone mass or size. We did not include any patients with delayed puberty and the median age was rather high reducing the bias mentioned. In addition, the results of our patients were clearly abnormal, reducing the risk of an underestimation of the results.
The number of patients on glucocorticoids was low precluding any significant influence of these agents on the measurement results. In the group of polyarticular patients, the percentage on TNF-α blockers was high. These agents have been implicated with favourable effects on bone, as they might restore the balance between osteoprotegerin and RANK ligand that can be altered by TNF-α [16]. The results for the polyarticular patients in our study nevertheless showed clearly abnormal bone parameters which might indicate a bias towards very therapy resistant patients in our study.
The coincidence of an increase in muscle CSA and the improvement of parameters of bone geometry especially in oligoarticular patients suggests that the muscle bone unit is functional in JIA. The decrease in trabecular density which especially occurs next to inflamed joints (as had been shown in [3]) nevertheless suggests an additional negative interaction of inflammatory cytokines with bone metabolism. Patients in the more severely affected polyarticular group were not able to improve muscle mass and force as much as the oligoarticular patients probably due to ongoing disease activity. The rate of patients in remission was much higher in the oligoarticular group. Although bone remains abnormal in the polyarticular group, a periosteal expansion can be observed by enlarging the CSA above normal values together with an increase in cortical area. This finally translates into an increase of bone strength as reflected by the increase of SSI.

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The improvement of bone following an increase in muscle mass and force strongly supports the role of weight bearing exercise as an important part of the treatment of JIA in addition to fast and efficient disease control. These exercises might also be important for patients in remission as their muscle CSA and bone geometry might remain abnormal. An interesting and at the same time worrying observation is that pre-pubertal children seem to respond to physical training better than peri- or post-pubertal children [19]. This might add to the better improvement of bone geometry in the oligoarticular group in our study. These patients not only had a better disease course with a much higher percentage of patients in remission but also were younger. Their skeletal system might therefore be more responsive to the increase seen in muscle mass. This also underlines the need for early training interventions if possible at a younger age. On the other hand, older patients should also improve with increased loading from an increased muscle mass. Physical training studies in adults with rheumatoid arthritis have shown [20] that muscle force can be increased, this effect is sustained and results in a positive effect on the disease course. The gain in bone mass was relatively low
although it has to be noted that patients in the control group were also aggressively treated with DMARDs leading to rapid remission. Further studies have shown favourable effects of weight bearing exercise on inflammation and cytokine levels [21]. Studies in children with JIA have shown a strong correlation between weight-bearing physical activity and bone mass determined by DXA [22]. Intervention studies have shown that weight-bearing exercise is feasible in most patients and leads to an increase in muscular function [23, 24]. These studies have nevertheless been limited so far and larger well-controlled studies will have to differentiate between aerobic and anaerobic exercise and also measure muscle force, muscle power and parameters of bone geometry to proof the tolerability and the effectiveness of such interventions in children with JIA.

Apart from sustained remission, the musculoskeletal system is a very important marker for the long-term outcome of JIA. Outcome studies [25, 26] have shown a very high incidence of skeletal abnormalities in adults that have been suffering from JIA. The persistence of alterations over a 4-yr-period shown in this study even with new therapeutic approaches (TNF-α blockers) further stress this point. Initially, nutritional deficits, inactivity, inflammation and medication all interfere with both muscle mass/force and bone metabolism and also interact with each other (e.g. glucocorticoids reducing inflammation but interfering with bone and muscle metabolism). In those patients achieving remission, inflammation and medication are probably less important. It is therefore even more worrying that in some of these patients an abnormal musculoskeletal system persists. This indicates that their muscular function has not regained pre-disease levels. Regular assessments and possible interventions of the musculoskeletal system will have to be considered especially for polyarticular patients.

### Rheumatology key messages

- Alterations of muscle and bone geometry persist especially in polyarticular JIA.
- Bone strength increases due to a compensatory periosteal expansion.
- Musculoskeletal monitoring and interventions are mandatory in JIA.

The authors have declared no conflicts of interest.

### References