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Bone strength is related to muscle volume in ambulant individuals with bilateral spastic cerebral palsy

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ABSTRACT

Objective: The aim of this study is to investigate how bone strength in the distal femur and proximal tibia are related to local muscle volume in ambulant individuals with bilateral spastic cerebral palsy (CP).
Methods: Twenty-seven participants with CP (mean age: 14.6 ± 2.9 years; Gross Motor Function Classification System (GMFCS) levels I-III) and twenty-two typically developing (TD) peers (mean age: 16.7 ± 3.3 years) took part in this study. Periosteal and medullary diameter in the distal femur and cortical bone cross-sectional area (CSA) and thickness (CT) in the distal femur and proximal tibia were measured along with nine lower limb muscle volumes using MRI. Additionally, the polar section modulus (Zp) and buckling ratio (BR) were calculated to estimate bone bending strength and compressional bone stability respectively in the distal femur. The relationships of all measured parameters with muscle volume, height, age, body mass, gender, and subject group were investigated using a generalized linear model (GZLM).
Results: In the distal femur, Zp was significantly positively related to thigh muscle volume ($p = 0.007$), and height ($p = 0.026$) but not significantly related to subject group ($p = 0.076$) or body mass ($p = 0.098$). BR was not significantly different between groups and was not related to any of the variables tested. Cortical bone CSA was significantly lower in the CP group at both the distal femur ($p = 0.002$) and proximal tibia ($p = 0.009$). It was also positively associated with thigh muscle volume ($p < 0.001$) at the distal femur, and with subject height ($p = 0.005$) at the proximal tibia.
Conclusions: Bending and compressional strength of the femur, estimated from Zp and cortical bone CSA respectively, is associated with reduced thigh muscle volume. Increasing muscle volume by strength training may have a positive effect on bone mechanics in individuals with CP.

Introduction

There is a high prevalence of fractures in individuals with cerebral palsy (CP) [1–5], with lower limb fractures most prevalent [2,3], commonly occurring in the distal femur and proximal tibia [3]. In ambulant children with CP, high-energy fractures are the most common type, with fractures sustained through significant trauma. In typically developing (TD) children and adolescents, factors associated with bone fractures are bone mineral density (BMD), bone geometry, and bone size [6,7]. Poor nutrition, lack of weight-bearing physical activity, obesity and high exposure to trauma may also influence fracture risks in the general paediatric population [6].

Although dual-energy X-ray absorption (DXA) is the most common method for measuring BMD in CP, the technique suffers from systematic errors that depend on skeletal site and body size [8]. Since individuals with CP often have a smaller body size than their TD peers [9], an apparent low BMD score may be measured when assessed by DXA. Gold standard assessments using peripheral quantitative computed tomography, pQCT, suggest that children with CP do not have a deficit in BMD, but in fact have reduced cortical bone thickness (CT) [10]. Bone geometry can also be assessed using MRI [11], which has shown reduced cortical bone thickness at the mid-femur of children with quadriplegic CP [12].

Bone strength is related to BMD; however, it is determined predominantly by bone geometry. The ability of a bone to resist bending and torsional forces (estimated using the polar section modulus, Zp) is inversely proportional to bone length to the third power and directly related to bone diameter to the third power [13]. The stability of a bone to compressional forces can be estimated by the buckling ratio (BR),

Abbreviations: Zp, Polar section modulus; BR, Buckling ratio; CP, Cerebral palsy; CSA, Cross-sectional area; CT, Cortical thickness; GMFCS, Gross Motor Function Classification System; DXA, Dual-energy X-ray absorptiometry; BMD, Bone mineral density; pQCT, Peripheral quantitative computed tomography; TD, Typically developing.

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which is a ratio of the bone radius to cortical bone thickness. In TD children, before and after puberty, bone strength and geometry are determined primarily by bone length and muscle CSA, modulated by physical activity and dietary calcium [14].

In adults, bone mass decreases with age: bending strength is maintained by a gradual increase in bone diameter by periosteal addition of bone, and endosteal resorption leading to a wider bone and a relatively thinner cortex. This maintains bending strength but reduces the ability of the bone to remain stable in the presence of larger compressive loads. In non-ambulant children with CP, femoral bone bending and torsional strength, estimated from geometric measures, is lower than their typically developing peers [12]. Bone geometry in ambulant young adults with CP has not been assessed.

Mechanical forces are a significant factor affecting bone strength and development. Longitudinal growth increases the length of lever arms and bending moments leading to greater forces experienced by the bone [15], with bending and torsional forces being the predominant loading factors in the long bone diaphysis [16,17]. Muscle weakness [18] and reduced muscle volume [19–26] in individuals with CP is well documented. Therefore, in individuals with CP, the reduced bone strength and increased fracture rate may be due to the reduced mechanical loading applied to the bones by the local musculature.

In this study we investigate bone strength at the most common fracture sites in CP: the distal femur and proximal tibia [3]. Cortical bone cross-sectional area (CSA) and cortical bone thickness (CT) in the distal femur and proximal tibia, femoral cross-sectional geometry, and the volume of nine major muscles of the lower limbs were measured in adolescent and young adults with bilateral spastic CP and their TD peers. Bone strength in the distal femur was estimated through calculation of Zp and BR. We hypothesised that cortical bone CSA, CT, BR and Zp are significantly related to the local muscle volume, independently of diagnosis and body mass.

Materials & methods

Participants

The local research ethics committee granted ethical approval for this study. Individuals aged 10–24 years, with a diagnosis of bilateral spastic CP, Gross Motor Function Classification System (GMFCS) levels I–III, who met the safety requirements of MRI were included in this study. Patients who had undergone surgery, serial casting or botulinum toxin injections to the lower limbs within the previous year were excluded from the study. None of the subjects had had previous osteotomies of the long bones. This was a convenience sample of individuals attending our hospital department, with consecutive patients that met the inclusion criteria invited to participate in the study. 27 participants with bilateral spastic CP were recruited to the study (mean age: 14.6 years; age range: 10.2–23.1 years, GMFCS level I: $n = 5$, level II: $n = 17$, level III: $n = 5$, 19 male, 8 female) from clinics in our university hospital. 25 TD subjects were included in this study (mean age: 16.7 years; age range: 10.6–23.2 years, 17 male, 5 female). The TD subjects had no previous surgery to their lower limbs and had no known neurological or musculoskeletal condition. Z-scores for height-to-age and BMI-to-age were calculated based on the World Health Organization (WHO) growth reference data [27]. For individuals 20 years of age and older, the age-19 height and BMI *z*-score reference have been used in order to have a consistent metric of relative height and BMI for all subjects.

Data collection and analysis

MRI images of both lower limbs of all subjects were acquired with contiguous transverse slices from above the iliac crest to below the calcaneum. All subjects lay supine on the scanner bed with their feet resting against a wooden footplate giving an approximate plantarflexion angle of 25°.

MRI data was collected on 1.5 T and 3.0 T Phillips Achieva systems (Philips Medical Systems, Best, The Netherlands). On the 1.5 T MRI system, seven CP and nine TD subjects were scanned using a T1 weighted turbo spin echo sequence (TE/TR = 18/1104.4 ms, number of averages = 2, echo train length = 3, 1.8 × 1.8 mm in-plane voxel size) with a quadrature body coil. Slices were collected contiguously with a slice thickness of 2 mm over the hip, knee and ankle joints and every 4 mm over the remainder of the lower limb. Image acquisition took approximately 20 min for each subject. On the 3.0 T MRI system, twelve CP and ten TD subjects were scanned using a three point Dixon sequence (TE/TR = 4.6/13 ms, echo time shift = 1.53 ms (120° echo phase shift), 20° flip angle, 0.9 × 0.9 mm in-plane voxel size, number of averages = 2, 5 mm slice thickness) with a quadrature body coil. Each scan took approximately 30 min. On the 3.0 T MRI system, data was collected from eight CP and six TD subjects using a three point Dixon sequence (TE/TR = 2.11/5.2 ms, echo time shift = 0.76 ms (120° echo phase shift), 10° flip angle, 1.2 × 1.2 mm in-plane voxel size, number of averages = 2, 5 mm slice thickness) with a quadrature body coil. Image acquisition took approximately 15 min for each subject.

The proximal and distal endpoints of the femur and tibia were identified in the MRI images and bone length was calculated as the distance between the end points for each bone. The distal femur and proximal tibia were defined as 70% and 30% along the length of the bone from the proximal ends respectively. Cortical CSA was measured at the distal femur and proximal tibia by drawing regions of interest around the inner and outer cortical bone boundaries. Periosteal (T) and medullary diameter (M) were measured in the anterior–posterior direction at the distal femur and medio-laterally in the proximal tibia. CT was calculated using Eq. (1). In the distal femur, assuming a cylindrical bone shape with a circular cross-section, the polar moment of inertia (J) is calculated using Eq. (2) [28]. The polar section modulus (Zp), which is a measure of torsional and bending strength, is calculated using Eq. (3) [29]. Stability to compressional force was estimated by using the buckling ratio (BR), which is a ratio of the bone radius (r) to CT given by Eq. (4).

$$\text{Cortical thickness } (CT) = \frac{(T-M)}{2} \quad (1)$$

$$\text{Polar moment of inertia } (J) = \frac{\pi}{32}\left(T^4-M^4\right) \quad (2)$$

$$\text{Polar section modulus } (Zp) = \frac{J}{(T/2)} \quad (3)$$

$$\text{Buckling ratio } (Br) = \frac{r}{CT} \quad (4)$$

Where T = Periosteal diameter; M = Medullary diameter; r = Bone radius

The proximal and distal endpoints of each muscle belly were identified and regions of interest around the muscle cross-sections were manually outlined on every image slice with the exception of T1 weighted scans with 2 mm slice thickness where regions were drawn on every other slice (effective slice thickness = 4 mm). The total volume was calculated within the software as the sum of the outlined cross sectional areas multiplied by slice thickness. The volumes of the medial gastrocnemius (MG), lateral gastrocnemius (LG), soleus (SOL), tibialis anterior (TA), rectus femoris (RF), vastus intermedius and lateralis composite (VI + VL), semimembranosus (SM), semitendinosus (ST), and gluteus maximus (GMax) were measured. Sections of the boundary between