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Muscle Function, Dynamic Loading, and Femoral Neck Structure in Pediatric Females

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Abstract

Purpose—Muscle forces influence development of bone mass and structure, but dynamic loading via impact exercise is considered particularly osteogenic. We hypothesized that indices of local muscle function AND physical activity exposure would predict femoral neck structure in pre-menarcheal females.

Methods—We tested this hypothesis in 76 healthy, pre-menarcheal girls (46 gymnasts, 30 non-gymnasts). Height, weight, Tanner breast stage (TB) and prior year non-aquatic, organized physical activity (PAL) were recorded semi-annually. Hologic DXA scans (whole body, left femoral neck (FN)) yielded total body non-bone lean mass and bone outcomes, including narrow neck (NN) hip structural analysis data. Dynamometers assessed non-dominant hand grip (GR) and left hip flexion/extension indices. Parsimonious regression models tested the following as predictors of bone outcomes: local muscle function, PAL, gymnast status and lean mass, accounting for Tanner breast stage and height, as appropriate.

Results—Hip flexion indices were significantly correlated with indices of femoral neck mass, density, structure and strength ($p<0.05$). However, entry of PAL, gymnast status and lean mass into regression models supplanted local muscle function explanatory value. In contrast, for many variables, the significant association of gymnast status persisted after accounting for physical maturity, body size/lean mass and PAL. For all skeletal indices except FNArea, NNwidth, NN endosteal diameter and NN buckling ratio, gymnast status was more strongly associated with bone outcomes than PAL.

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Conclusion—Greater activity doses and exposure to extreme dynamic loading provide independent benefits to femoral neck structure during growth. Furthermore, weight-bearing activity and high-impact exercise exposure appear superior to local muscle force measures for prediction of femoral neck structure.

Keywords

HSA; pre-menarche; Biodex; DXA; physical activity

INTRODUCTION

Evidence suggests that mechanical loading via physical activity during growth may be a potent strategy for maximizing peak bone mass, improving bone strength and reducing lifetime fracture risk (2, 7, 11, 12, 17, 26, 27). Many investigators consider muscular forces to be paramount in exercise-related bone stimulation and subsequent advantages in skeletal strength. The mechanostat theory postulates a direct cause-and-effect relationship between muscular forces and bone structure under normal conditions (22, 23, 28, 29). Since muscular force is strongly positively correlated with muscle mass and cross-sectional area (CSA), these anatomic parameters have been used as proxies for muscle force (22, 25, 29, 37). In turn, positive associations between these muscle force proxies and bone outcomes are often cited to support the concept that increasing muscle mass (and therefore force generation capacity) provides the stimulus to increase bone mass and strength (22, 28, 29).

Judex and Rubin describe two muscle-mediated osteogenic pathways: 1) muscle generates osteogenic forces during resistance to external stimuli, and 2) external stimuli produce muscle hypertrophy, secondarily augmenting muscular osteogenic potential via capacity to generate greater muscular force (15). In addition, in the context of weight-bearing and impact exercise, muscle hypertrophy may yield greater body mass to be borne, increasing the “mass” component of external mechanical forces.

Impact exercise may be viewed as a special type of dynamic mechanical loading, as it generates rapid application of skeletal loads via three main routes: 1) concentric muscular contractions (propulsion), 2) eccentric muscular contractions (load dampening) and 3) “direct” loading at contact and articular surfaces (during both take-off and landing). Judex and Rubin have described “direct” osteogenic forces as “reactionary forces produced by the skeleton with a substrate (e.g. ground reaction forces)” and as “mechanical force (acceleration) traveling from the interface… to a given anatomical site” (15). In the case of the femur, “direct” skeletal loading is applied at both distal and proximal articular surfaces, elevating osteoarthritis risk in athletes exposed to high impact loads and high training volumes (14). In numerous animal models, “direct” loading has yielded osteogenesis, isolated from muscular forces (13, 24, 33, 35), demonstrating that skeletal adaptation to mechanical force may be stimulated without muscle mediation.

In human subjects, artistic gymnastics maneuvers have been shown to generate extreme ground reaction forces (4), which are often imposed at high training volumes. Thus, gymnastics may be considered an extreme form of dynamic loading that is likely to exaggerate both “direct” and muscle-mediated loading. In a recent study, we evaluated associations between extreme dynamic loading, muscle CSA and radius skeletal structure using the human model of gymnastic loading in a group of post-menarcheal girls (9). In that analysis, prior gymnastic exposure was a significant predictor of upper extremity indices of bone mass, geometry and strength, independent of local indices of muscle mass and cross-sectional area (9). These results suggest that exposure to “direct” forces applied via gymnastic loading may provide a stimulus for skeletal adaptation independent from muscular force.

We hypothesized that *both* increased exposure to dynamic loading *and* capacity to generate local muscular forces would be significant, independent predictors of bone mass, structure and theoretical strength at the proximal femur in young girls. To test this hypothesis, we evaluated physical activity dose and indices of muscular function as predictors of femoral neck (FN) structure in a group of pre-menarcheal gymnasts and non-gymnasts, accounting for physical maturity and body size/lean mass. If exposure to extreme dynamic loading (gymnastics) predicts femoral neck structure, independent of local muscular forces, these results would support the concept that bone adaptation is not modulated by muscular forces alone.

METHODS

In accordance with the Declaration of Helsinki, and after approval of study protocols by the Institutional Review Board of SUNY Upstate Medical University, eighty girls provided informed assent with parental consent to participate in a longitudinal study of bone growth in relation to physical activity. Subjects were healthy girls, age 8 to 15 years, free of bone disease. Non-gymnasts were recruited from the local community, representing heterogeneous physical activity participation. Gymnasts were recruited from gymnastics training centers in upstate New York. To account for even minimal or sporadic exposure to gymnastic loading, subjects with at least 1 h/wk annual mean gymnastic exposure for the year prior to the index DXA scan were categorized as gymnasts (GYM); those with <1 h/wk were classified as non-gymnasts (NON). In this manner, gymnastic status was used as a marker for exposure to extreme dynamic loading, while general physical activity level was used to sum and quantify all forms of mechanical loading via organized physical activity (as described below). Post-menarcheal girls were excluded from the current analyses.

Age was calculated to the nearest tenth of a year, subtracting birthdate from date of DXA. Height (m) was measured using a stadiometer; weight (kg) was measured in light clothing with an electronic scale (Detecto, Webb City, MO). With parental assistance, subjects used annotated line drawings to determine self-assessed Tanner breast stage; menarche status was also recorded. Organized physical activity participation for the preceding year was reported by subjects with assistance from their parent(s); prior comparisons between gymnasts’ training records and coaches logs indicated reliable reporting, $r > 0.97$ ($p < 0.001$) (10). These data were used to generate physical activity level (PAL) scores, defined as mean hours per week (h/wk) participation in organized, non-aquatic physical activity, including gymnastics.

Indices of muscular function were measured using dynamometers. Maximum non-dominant hand grip strength was assessed from 3 trials (GR, kg; Takei). Indices of left hip flexion and extension function were measured on a Biodex System 3 isokinetic dynamometer (Biodex, Shirley, NY), by the same 2 investigators (CS, KK). The Biodex was calibrated before each testing session, per manufacturer recommendations (3). Attachments were chosen based on hip width and femur length to ensure proper alignment and secure positioning on the thigh support; pediatric hip attachments were used for children with narrow thighs and/or short femurs.

Hip flexion and extension testing occurred in a supine position, with the seat-back fully reclined and the attachment shaft aligned with the axis of rotation, per the Biodex operation manual (3). To minimize upper body movement, two cross-chest shoulder straps were used, and subjects were instructed to cross their arms across their chest. The velocity of the hip flexion and extension testing was set at 60 degrees per second, in the isokinetic concentric/concentric mode. Prior to testing, each subject was given both verbal and visual instructions and performed 3 sub-maximal repetitions for familiarization with the protocol. After 1 minute of rest, each subject was instructed to perform 3 maximal repetitions with instructions to move the dynamometer lever arm “as hard and as fast as possible”; after 1 minute of rest the maximal protocol was repeated to yield 2 sets of maximal data. The coefficient of variation (CV) was evaluated to ensure that for at least 1 set, all 3 repetitions differed by no more than 15%. In the event that the CV exceeded 15% for both sets, the subject was given a 5-minute rest prior to repeating the test; during this rest, instructions were reviewed and the axis of rotation and proper stabilization were checked. The data with the lowest CV (15% or lower) were included in the present analyses. All dynamic torque data were filtered, windowed, and gravity-corrected. Biodex outcomes included indices of hip flexion and extension function as follows: peak torque (Nm), peak torque for body weight (%), maximum total work (J), total work (J), and average power (W). For Biodex variables, total group mean % CVs were 12.6% (hip flexion) and 10% (hip extension); by gymnastic exposure sub-group, mean CVs were: GYM hip flexion 11.0% and hip extension 8.7%; NON hip flexion 14.1% and hip extension 11.9%.

DXA scans were performed for the whole body and left proximal femur by one of two certified DXA technicians and analyzed by a single, trained investigator (JND) (Hologic Discovery A, software v.12.7.3.2:3). Whole body DXA scans yielded total body non-bone lean mass (tbFFM, kg) and left leg non-bone lean mass (legFFM, kg). Left proximal femur DXA scans yielded femoral neck (FN) and femoral narrow neck (NN) bone outcomes. For simplicity, both femoral neck and narrow neck outcomes are referred to in the text as “femoral neck” outcomes, with individual variables labeled as FN or NN, as appropriate. Dependent variables included femoral neck projected Area (FNArea, cm), bone mineral content (FNBMC, g) and areal bone mineral density (FNaBMD, g/cm^2), as well as hip structural analysis output (HSA) for femoral narrow neck bone geometry and theoretical strength. For the femoral narrow neck, HSA yields total bone tissue cross-sectional area (NNbCSA, cm^2); cross-sectional moment of inertia (NNCSMI, cm^4); NN periosteal width (NNwidth, cm); endosteal diameter (NNED, cm); cortical thickness, (NNCT, cm); section modulus (NNZ, cm^3) and buckling ratio (NNBR). Buckling ratio is a composite variable, derived as maximum distance from the bending plane centroid (a function of periosteal width) divided by cortical thickness (16). Accordingly, it is important to note that NNBR results demonstrate patterns that contrast with most of the other FN outcomes, as low NNBR values indicate lower fracture risk (greater bone strength) and high values indicate higher fracture risk (lower bone strength).

Coefficients of variation in our laboratory were calculated using duplicate scans of middle aged females. For the total body scans, 29 scan pairs yielded CVs for lean mass and left leg lean mass of 0.5% and 1.1%. For the femoral neck, 32 scan pairs yielded CVs <3.5% for all variables except NN buckling ratio (4.1%), NN section modulus (7.2%) and NN cross-sectional moment of inertia (9.3%). Aside from NNZ and NNCSMI, these CVs are lower than or within 0.6% of those reported by other research groups using FN and HSA data (16, 20).

Data were evaluated for normality of distribution. Most continuous variables were natural log (ln) normal and therefore were transformed prior to analysis; PAL scores were less normally distributed in natural log form so they were analyzed without transformation. Preliminary analyses included the calculation of descriptive statistics for the total sample and with stratification by gymnastics exposure status (GYM/NON), including assessment of possible gym status differences using analysis of variance (ANOVA). Correlations were performed to assess linear relationships and collinearity among independent variables (lnage, lnheight, lntbFFM, lnlegFFM, lnGR, Biodex variables (ln), PAL) and dependent variables (lnFNBMC, lnFNaBMD, lnNNbCSA, lnNNCT, lnNNCSMI, lnNNZ, lnNNBR).

Regression models were developed based on the results of the correlations. Specifically, for local muscular strength predictors, the variable with the highest correlation coefficient was entered; this was Hip Flexion Peak Torque (HFPT) for all variables except NNBR, for which Hip Flexion Maximum Total Work (HFMTW) was entered. Age and weight were not entered due to inferior explanatory value and strong collinearity with height and lean mass (age $r > 0.75$, 0.73; weight $r = 0.87$, 0.96, respectively). Moreover, height and lean mass were most appropriate for hypothesis testing. In order to account for the effects of physical maturity and body size, Tanner Breast stage and height were entered before evaluating the statistical effects of the following, in succession: 1) local muscular strength index, 2) organized physical activity exposure over the prior year and 3) exposure to extreme dynamic loading (gymnast status: GYM or NON). Finally, the full model was reevaluated, substituting total body lean mass (tbFFM) for height; substantial collinearity precluded simultaneous inclusion of height and tbFFM in the final model (variance inflation factors > 7). We used this final model to evaluate whether skeletal muscle mass encapsulated the effects of local muscle strength, activity dose, and exposure to extreme dynamic loading. Adjusted model r^2, unstandardized beta coefficients, 95% confidence intervals and significance levels are reported in tabular form. Significance was defined as alpha < 0.05.

This pilot analysis of muscle-bone relationships uses data from a longitudinal study of bone accrual in relation to gymnastic loading exposure. Sample size was originally determined to detect significant femoral neck aBMD differences for GYM versus NON with >80% power after at least 5 years of study (required cell sizes, n=17). GYM were oversampled to allow for potential training cessation; all subjects were oversampled to allow for 5-year subject attrition. Although no literature was available to power analyses concerning hip flexion indices versus hip structural analysis outcomes in GYM and NON, our sample (NON n= 30, GYM n= 46) nearly doubles that of a study that detected significant femoral neck aBMD differences between adult NON (n=22) and GYM (n=18)(32).

RESULTS

Subjects

Of 84 subjects originally recruited, 4 girls were excluded from analysis due to post-menarcheal status, and 4 girls were excluded due to incomplete data, yielding 76 pre-menarcheal girls with complete data for all bone and muscle parameters at the time of analysis (46 GYM, 30 NON). Subject characteristics are presented in Table 1 (TOTAL, NON, GYM). No significant differences were detected by ANOVA for any variable reported, except that GYM means were greater than NON means for FNaBMD, annual mean PAL and gymnastic training hours ($p<0.05$); group mean percent body fat was higher for NON than GYM ($p < 0.05$). Tanner breast stage distributions did not differ by activity group (χ^2 $p > 0.05$); overall 59% of subjects reported Tanner breast stage as TI, 32% reported TII, and 9% reported TIII (NON: 57% TI, 37% TII, 7% TIII; GYM: 61% TI, 28% TII, 11% TIII).

Correlations

Pearson correlation coefficients for independent variables versus femoral neck bone outcomes are presented in Table 2 for all subjects. Height, lean mass (tbFFM) and left leg lean mass (legFFM) demonstrated moderate to high correlations with the majority of bone outcomes, $p < 0.05$ ($r > 0.57$ for all but NNED and NNBR, legFFM specifics not shown). For all bone outcomes except NNED, correlations with lean mass were stronger than correlations with height. Lean mass and leg lean mass were highly, positively correlated ($r = 0.99$, $p<0.001$). Because total body lean mass correlations were slightly higher than those for leg lean mass for all bone outcomes except NNBR ($r = -0.276$ and -0.283, respectively), total body lean mass was chosen as the lean mass variable for regression model entry. Both non-dominant arm grip strength and hip flexion peak torque (HFPT) showed moderate to high, significant correlations with most bone outcomes; the exception was HFPT with NNED and NNBR. For NN endosteal diameter, the strongest hip strength correlate was Hip Flexion Maximum Total Work (HFMTW, $r = -0.23$, $p = 0.04$). In all cases, Hip Extension Peak Torque exhibited weaker correlations with bone outcomes (not shown). Grip strength correlated more strongly with all bone outcomes than any of the local hip muscle function indices. For the group as a whole, PAL showed moderate, significant correlations with FNBMC, FNaBMD, NN bone tissue cross-sectional area (NNbCSA), NN cortical thickness and NN buckling ratio.

Regression models (Tables 3a and 3b)

In the simplest height-based models, height was a significant predictor of all bone outcomes except cortical thickness (NNCT) and buckling ratio (NNBR). Tanner breast stage was significantly associated with FNBMC, FNaBMD, narrow neck bone tissue cross-sectional area (NNbCSA), NNCT and NNBR. Height was the strongest predictor of all bone outcomes except FNaBMD, NNCT and NNBR, for which Tanner breast stage was the most potent predictor. After accounting for the effects of physical maturity and body size, hip flexion index was significantly positively correlated with only two bone outcomes: FNBMC and narrow neck section modulus (NNZ), although there were trends for greater bone strength indices with stronger hip flexion for FNaBMD, NNCT, NNBR and NNCSMI ($0.06 \le p < 0.15$).

With entry of mean organized physical activity level for the year prior (PAL) into the regression models, hip flexion indices were no longer significant predictors of bone outcomes ($p > 0.08$). In contrast, height retained its significant associations with all bone outcomes except NNBR. Tanner breast stage associations remained statistically significant for FNBMC, FNaBMD, NNbCSA, NNCT and NNBR. PAL was significantly associated with all bone outcomes except FNArea and NNCSMI. Greater mean PAL was associated with greater FNBMC, FNaBMD, NNbCSA, NNCT and NNZ, but narrower bone width (NNwidth), smaller endosteal diameter (NNED) and lower buckling risk (NNBR), $p < 0.05$. For FNaBMD, NNCT and NNBR, both PAL and Tanner breast stage were stronger independent predictors than height.

When entered into models after Tanner breast stage, height, hip flexion index and PAL, gymnast status exhibited significant associations with all bone outcomes except FNArea, NNwidth and NN endosteal diameter, with a strong trend for lower NN buckling ratio in GYM ($p = 0.07$). After entry of GYM status, Tanner breast stage remained a significant predictor of FNBMC, FNaBMD, NNbCSA, NNCT and NNBR. The addition of GYM status to the models further reduced associations between hip flexion indices and all bone outcomes ($p > 0.10$). In these models, height explained the greatest proportion of variance for all bone outcomes except NN cortical thickness and buckling ratio. For NNCT, Tanner breast stage was the dominant predictor. For NNBR, PAL was the dominant predictor, with significant associations also observed for Tanner breast stage and GYM status.

Finally, total body non-bone lean mass-based models were built, entering Tanner breast stage, tbFFM, hip flexion index, PAL and GYM status; height was purposefully excluded due to collinearity with tbFFM. Lean mass exhibited significant positive associations with all bone outcomes except NNBR. After entry of tbFFM, Tanner breast stage was no longer associated with any variables ($p > 0.08$) other than NNCT and NNBR. Again, after entry of Tanner breast stage, tbFFM, PAL and GYM, no significant associations were observed between hip flexion indices and bone outcomes. Interestingly, physical activity exposure associations remained significant for NN width, NNED and NNBR (greater activity: narrower bone geometry, lower buckling risk, $p < 0.05$), although the positive relationship between PAL and NNCT was reduced to a strong trend ($p = 0.06$). GYM status remained a significant predictor of FNBMC, FNaBMD, NNbCSA, NNCT, NNZ and NNBR, whereas the previously significant association between GYM status and NNCSMI was weakened ($p = 0.11$). Lean mass explained the greatest proportion of variance for all bone outcomes, with the exception of NNBR, for which PAL was the strongest predictor, followed by Tanner breast stage and GYM status (tbFFM, $p > 0.70$).

To evaluate local versus distant muscle functional indices as predictors of femoral neck skeletal properties, we applied the same model structures, simultaneously entering grip strength and hip flexion index, for head to head comparisons. In these analyses, HFPT was not a significant predictor of FNArea in any of the model forms, whereas grip strength retained predictive value for FNArea in all models ($p \leq 0.05$). For FNBMC, both grip strength and HFPT were significant predictors before entry of PAL, but with entry of PAL, both variables lost explanatory value ($p = 0.14, 0.10$); GYM entry restored some explanatory value to grip strength ($p = 0.10$). Of all the other variables and models, only NNZ (section modulus) was predicted by HFPT ($p < 0.05$), but subsequent model building eroded its significance ($p \geq 0.10$); grip strength was not a significant predictor of NNZ in any of the regression models.

DISCUSSION

As hypothesized, in this cohort of pre-menarcheal girls, dose of prior year, weight-bearing physical activity (PAL) and exposure to extreme dynamic loading (GYM status) were robust predictors of indices of femoral neck structure. For many bone outcomes, the significant statistical effect of gymnast status persisted even after accounting for the effects of physical maturity, body size/lean mass and activity. For all skeletal indices, except FN area, NN width, NN endosteal diameter and NN buckling ratio, GYM status was more strongly associated with dependent variables than PAL. These findings suggest that extreme dynamic loading may be more osteogenic than other weight-bearing activities, consistent with our previous reports of significant associations between gymnastic loading and femoral neck skeletal indices (8). Nonetheless, PAL was a significant predictor of many femoral neck skeletal indices, providing evidence of the osteogenic nature of a variety of non-aquatic loading modalities, many of which included a lower extremity dynamic loading component, including both high and odd impacts (e.g. soccer, lacrosse, basketball). Our subjects’ varied activity profiles did not allow for activity-specific analysis, other than for gymnastics.

For variables that represent periosteal and endosteal dimensions (FNArea, NNwidth, NNED), associations between PAL and bone geometry were negative. Although GYM status was not a significant predictor for these variables, these PAL associations likely represent an inverse association between periosteal/endosteal dimensions and mechanical loading dose (PAL includes training hours for gymnastics and other activities). These findings corroborate our results from a more diverse cohort (Tanner breast I-V, pre- and post-menarche), in which dynamic loading dose (gymnastics) was inversely associated with both periosteal and endosteal dimensions, reflecting compact structure with a thicker, stronger cortical ring (8).

Contradicting our initial hypotheses, local indices of muscular strength and power were not robust, significant predictors of femoral neck structure. Even before accounting for the effects of total body lean mass, for all bone variables, associations with local muscle force were weaker than those for prior year weight-bearing activity dose and exposure to extreme dynamic loading (as represented by Hip Flexion Peak Torque or Maximum Total Work, PAL and GYM status, respectively). Furthermore, for all bone outcomes, ipsilateral leg (local) lean mass was not a stronger predictor than total body lean mass. Overall, these observations suggest an osteogenic role for mechanical loading via total body weight-bearing activity and via impact exercise, *separate from and in addition to* the action of local muscular forces and tissue factors. In these pre-menarcheal girls, local muscle forces do not appear to be tightly coupled with femoral neck bone mass or geometry, at least not as indicated by Biodex hip flexion/extension indices. In fact, with the possible exception of narrow neck section modulus, remote muscle strength (non-dominant grip) was, if anything, a stronger predictor of femoral neck outcomes than local muscle strength/power. It is possible that assessments of other hip muscular function, including hip abduction/adduction torques, may have yielded stronger or additional independent statistical effects to explain femoral neck structure; future research should investigate these possibilities.

We were surprised by the superiority of grip strength over local muscle functional indices as a correlate/predictor of most femoral neck bone outcomes. We had expected regional bone parameters to reflect regional loading and therefore regional muscle strength. It is possible that our ability to accurately measure grip strength was superior to our ability to measure hip strength (hand held dynamometer vs. Biodex), particularly in these young girls of small body-size. However, other investigators have noted the potency of grip strength as an indicator of muscle strength at other sites (38), as well as the superiority of grip strength versus local muscle strength assessments for predicting skeletal variability in both athletes and non-athletes (19, 30, 31). Thus, it seems unlikely that our findings should be attributed solely to methodological challenges. It is more likely that grip strength reflects overall maturity and body size to a greater extent than hip muscle functional indices, an assertion supported by a strong positive correlation between grip strength and tbFFM in this cohort ($r = 0.82$, $p < 0.001$) and other reports of strong correlations between grip strength and indices of body size (38). Alternatively, it is possible that this finding is attributable to other unknown confounding factors.

As an indicator of physical maturity and estrogen exposure, self-assessed Tanner breast stage was a significant predictor of many femoral neck bone outcomes. Even after accounting for the effects of height, local muscular function, physical activity dose and exposure to extreme dynamic loading, Tanner breast stage explained additional variance for several outcomes, including bone mass, density and cortical thickness (FNBMC, FNaBMD, bCSA, NNCT, NNBR). In contrast, Tanner breast stage did not exhibit significant associations with indices of bone size and bone size-related strength (Area, width, NNED, CSMI, Z). As would be expected based on the relationship between physical maturity and lean mass, Tanner breast stage statistical effects were weaker in the lean mass-based model. Nonetheless, overall, our results support the concept of a strong positive relationship between estrogen exposure and dense, cortically robust bone structure (8, 18, 21, 34).

Wetzsteon and colleagues evaluated ankle dorsiflexion peak torque as a predictor of 38% tibia pQCT indices (37). Main models for subjects < 21 yrs old included age, tibia length, Tanner stage, race, sex, muscle CSA (pQCT, 66% site), peak torque and body weight. In main models, peak torque demonstrated independent associations with polar section modulus (Zp), periosteal circumference and cortical area. Addition of PAL and moderate/high activity to the main models did not eclipse peak torque predictive value. In these compound models, PAL and moderate/high activity demonstrated independent predictive value for periosteal circumference ($p < 0.05$), and PAL was an independent predictor of Zp ($p < 0.05$). The persistence of peak torque predictive value, despite entry of activity variables into the model, differs from our results. This difference may be due to the fact that our cohort included gymnasts, whose exposure to dynamic loading activity is likely very different than that of Wetzsteon's subjects; thus, our subjects' more varied activity profiles may have yielded stronger associations between activity and bone outcomes. Alternatively, our contrasting results may reflect disparities in muscle forces at the hip versus the tibia. Notably, in both studies, total physical activity (or PAL) was an independent predictor of bone section modulus in models that include local muscle peak torque.

Daly and colleagues evaluated maximum vertical jump height (VJH) and right knee extension and flexion peak torques as predictors of FNBMC, FNwidth, FNCSA and FNZ in 103 pre-pubertal girls (5). PAL was low and uniform; 33% of subjects reported no organized activity (mean 1.0 h/wk, sd 1.4). Accordingly, correlations between local muscle peak torques and FN outcomes were most similar to those of our NON subgroup (Daly $r = +0.28$ to $+0.65$; our NON $r = +0.37$ to $+0.66$, mean PAL 3.8 h/wk). Similar to our results using total body lean mass, bone outcomes correlated more strongly with legFFM than with peak torques; legFFM was significantly, positively correlated with both peak torques. Despite limited activity variation, PAL was positively correlated with FN CSA and Z ($p < 0.05$). In contrast, VJH was not correlated with legFFM, peak torques or any bone outcomes. In separate regression models entering femur/leg length, legFFM, VJH and PAL: legFFM predicted FN BMC, width, CSA and Z; jump height was not predictive; PAL predicted FN CSA and Z. In models entering femur/leg length, knee extension peak torque (KEPT) and PAL: KEPT predicted FN BMC, width, CSA, Z; PAL predicted Z. After adjusting for both femur/leg length AND legFFM: KEPT predicted FN BMC, CSA, Z; PAL predicted CSA and Z. Daly and colleagues concluded that legFFM may be used as a surrogate of local muscular peak force, despite the persistent statistical effect of local muscle peak torque. In our cohort, total lean mass, PAL and GYM status encapsulated and eclipsed the statistical effect of local muscle function. This distinction may be attributed to greater overall variation in our cohort, with greater resultant explanatory value for maturity, PAL, and exposure to extreme dynamic loading, contrasted with the homogeneous Daly cohort.

Anliker and colleagues evaluated gains in muscular force and pQCT-assessed bone mass following a 9-month, randomized, controlled jumping intervention in 8–12 year old children (n=22 intervention, n=23 control) (1). The investigators hypothesized that muscle force improvement would be strongly positively correlated with skeletal improvement. Pre- and post-intervention, they identified a strong positive correlation between maximum voluntary ground reaction force (multiple one-legged hop, Fm1LH) and 14% tibia volumetric BMC ($r^2=0.51$–0.88). However, they detected no intervention-related differences for change in Fm1LH or BMC. Critically, absolute changes in Fm1LH were not related to absolute changes in BMC, implying lack of tight coupling and/or different time courses for adaptation. Similar to our results, body size was a stronger correlate with bone indices than muscle function, whether evaluated in terms of raw values or changes. In our study, assessment of GYM and PAL provided specific indices of extreme dynamic loading exposure and non-aquatic weight-bearing activity, adding to model predictive power.

Although Anliker et al. did not quantify PAL, subjects were separated into intervention (jumpers) and control groups (1); the observed lack of group differences suggests that the intervention was insufficient to yield an effect, or that background (non-intervention) loading confounded the study.

Weeks and colleagues performed an 8-month randomized, controlled jumping intervention in 53 pubertal girls (age: mean 13.7, sd 0.5 years, 74% post-menarche) (36). Restricting the discussion to females and femoral neck outcomes, significant FNBMC improvements were reported in jumpers (14%) versus controls (5%), although significant differences were not detected for rate of change in FNArea, bone mineral apparent density or CSMI. Interestingly, vertical jump height improvements were not significant. The fact that jumpers improved FNBMC, but not jump height, suggests that bone gains were a function of exposure to dynamic loading via impact exercise, not a result of increased muscle forces. Regression results supported this idea, attributing significant FNBMC gains in the intervention group to total body lean mass gains, whereas physical activity level and vertical jump height were not significant predictors. On the whole, the results of the study by Weeks et al. support the view that dynamic loading via impact exercise stimulates FNBMC accrual, independent of muscular function (36).

LIMITATIONS

Hip structural analysis variables can exhibit greater coefficients of variation than most other DXA outcomes, as they are particularly influenced by positional variation (16). In our laboratory, the CVs for NNCSMI and NNZ were particularly high (assessed in middle-aged women); for these variables, underlying positional variation may have hampered detection of muscle function associations.

Similarly, isokinetic strength testing can exhibit high coefficients of variation in pediatric subjects, especially if pediatric modifications, warm-up, familiarization, rest periods, and verbal feedback are not included (6). Thus, we specifically designed our Biodex protocols to optimize testing conditions, incorporating these key elements to maximize reliability and validity of results (minimize CV, maximize accuracy). In the current analysis, CVs were 12.6% and 10.0%, within the acceptable range for large muscle groups (≤15%) per manufacturer recommendations (3). Nonetheless, this variability may have affected our capacity to detect significant associations between hip muscle function indices and bone outcomes.

For practical reasons, we limited our analyses of local muscular function to hip flexion peak torque or maximum total work. It is possible that an index of hip abduction/adduction or a more complex measure of hip function would have been a stronger predictor of local bone mass, structure and strength indices. On this basis, our conclusions regarding the osteogenic role of capacity for force generation are limited to isometric hip flexion at the recommended pediatric angular velocity of 60 degrees per second.

Finally, HSA variables were developed and validated for estimation of skeletal parameters in adults. Accordingly, it may be problematic that HSA estimates NNbCSA based on a uniform, adult tissue vBMD standard, since tissue mineralization varies by age and loading status. These issues should be less problematic when comparing subjects of similar age and maturity and accounting for differences statistically. Nonetheless, it is possible that HSA underestimates loading-related bCSA advantages, with concomitant underestimation of loading-related advantages in bone geometry and strength (including endosteal diameter decrements) (8). Although HSA bone strength indices are of limited clinical relevance for healthy pediatric subjects, HSA provides safe, inexpensive assessments of femoral neck structure for pediatric longitudinal studies. Importantly, HSA allows evaluation of pediatric skeletal structure as the foundation for the adult skeleton.

CONCLUSIONS

At the femoral neck of pre-menarcheal girls, skeletal indices are a function of physical maturity and body size (total body lean mass) and/or reported physical activity (PAL). Body size (tbFFM) and grip strength, an index of remote muscle function, are superior to indices of local muscle strength as predictors/correlates of femoral neck skeletal parameters. The observed relationship between local muscle flexion strength/power and femoral neck structure is encapsulated and/or eclipsed by physical maturity, body size and physical activity exposure. The observed associations with activity dose (PAL) provide evidence that non-aquatic exercise is osteogenic during growth. In addition, GYM status statistical effects suggest the independent benefit of greater activity doses and extreme dynamic loading modalities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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