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Original Article

Pre-menarcheal physical activity predicts post-menarcheal lean mass and core strength, but not fat mass

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Abstract

Objectives: Youth exercise is associated with improved body composition, but details regarding timing and persistence are limited. We examined pre- and circum-menarcheal organized physical activity exposure (PA) as a factor in development of early post-menarcheal lean mass, fat mass and muscle strength. **Methods:** Participants in a longitudinal study of musculoskeletal growth using dual energy X-ray absorptiometry (DXA) were included based on: 1) Whole body DXA scans: 0.5-1.5 years *pre-menarche*, 0.5-1.5 years *post-menarche*; 2) PA records for ≥6 months preceding the first DXA (PREPA) and for the inter-DXA interval (CIRCUMPA). Dominant arm grip strength and sit-ups tests coincided with DXA scans; PA, height and maturity were recorded semi-annually. Regressions correlated PA with lean mass/fat mass/strength, accounting for maturity, body size, and baseline values. **Results:** Seventy girls [baseline: 11.8 yrs (sd 1.0), follow-up: 13.9 years (sd 1.0)] demonstrated circum-menarcheal gains of 25-29% for lean and fat mass and 33% for grip strength. PREPA correlated with pre- and post-menarcheal lean mass, sit-ups and pre-menarcheal fat mass ($p<0.05$), but not grip strength. CIRCUMPA correlated with only post-menarcheal sub-head lean mass ($p=0.03$). **Conclusions:** Lean mass and core strength at 1-year post-menarche were more strongly predicted by pre-menarcheal organized PA than by recent circum-menarcheal PA.

Keywords: Lean Mass, Strength, Menarche, Adolescence, Physical Activity

Introduction

The public health benefits of regular physical activity during youth are well accepted. Higher levels of physical activity have been associated with greater percent fat-free mass, lower percent fat mass, smaller waist circumferences, greater muscular strength and lower BMI for age in cross-sectional[1-12] analyses. In adolescent girls, three separate longitudinal studies have identified positive associations between physical activity and lean mass[13-15]. Each of these 6-7 year prospective studies evaluated girls from childhood/early adolescence to young adulthood, identifying a positive association between lean mass and varying amounts of leisure-time[14-15] and habitual[13] physical activity. In addition, one of these studies provided evidence that bone, lean and fat mass track from pre-puberty to young adulthood[14]. However, none of these studies attributed the relationship between physical activity and body composition to a specific maturity phase (early, mid or late puberty), and none included an evaluation of muscular strength development. Identification of the most sensitive maturity phase for exercise-based improvement of body composition and muscle strength would inform maturity-based targeting of broadly applicable exercise protocols. Theoretically, development of a strong early adult foundation should facilitate lifestyle-based maintenance of healthy muscle mass and function throughout adulthood, reducing fracture risk in senescence.

The purpose of the current analysis was to evaluate associations between physical activity participation and development of lean mass, fat mass and strength in adolescent girls, specifically focusing on maturation over a two-year circum-menarcheal window (from ~1 year pre-menarche through ~1 year post-menarche). We focused our analyses on the circum-menarcheal phase, be-

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cause a large proportion of total adult muscle and fat tissue mass is accrued during this period of accelerated growth and endocrine system maturation. We hypothesized that the influence of environmental factors such as physical activity participation may be amplified during this period. This concept is highly clinically relevant due to the possibility that circum-menarcheal development may have long-term consequences on adult body composition and physical function (e.g. tracking from adolescence into adulthood). Specifically, we hypothesized that circum-menarcheal physical activity participation would be positively associated with lean mass and strength development and negatively associated with fat mass development. To this end, we analyzed a subset of our longitudinal musculoskeletal growth data, prospectively collected in a cohort of young girls over the past 15 years. We evaluated repeated measures of lean mass, fat mass and strength in these adolescent girls within a circum-menarcheal window, accounting for maturity and stature, in order to isolate the explanatory value of physical activity participation for development of post-menarcheal body composition and muscle strength.

Methods

Study design, and participants

Study protocol was approved by the Institutional Review Board at SUNY Upstate Medical University (5332F) and conducted in accordance with the Declaration of Helsinki. At enrollment, study participants provided written, informed assent, and parents/guardians provided written, informed consent for their participation in study protocols.

For the present analysis, we evaluated the influence of organized physical activity exposure on repeated measures of lean mass, fat mass and strength, obtained ~1 year pre-menarche and ~1 year post-menarche. Participants included in the current analysis are a subset from an ongoing longitudinal study of musculoskeletal growth in relation to activity-specific loading exposure (1997-present), recruited from local gymnastics clubs, local grade schools and girl scout troops. Subjects were enrolled, over time, at age 7-11 years, in a series of three cohorts: Cohort 1 (n=90, 18-month pilot study, 1997), Cohort 2 (n=41, 3-year longitudinal study, 2001) and Cohort 3 (n=80, ongoing longitudinal study, 2008). The original study was designed to evaluate the role of impact loading in musculoskeletal growth, comparing girls who participated in gymnastics training vs. those who did not participate in gymnastics. Therefore, at enrollment, girls who did not participate in gymnastics were matched by group means for chronologic age, size, and physical maturity to those who did participate in gymnastics. Because subjects from Cohorts 1 & 2 were not originally enrolled for extended longitudinal observation, considerable sample attrition occurred after the original study periods ended at 18 months (Cohort 1) and 3 years (Cohort 2).

Subjects underwent annual whole body and regional DXA scans (forearm, hip, lumbar spine), as well as semi-annual recording of organized physical activity (PA) and physical maturity. Statural height and muscle strength outcomes were assessed annually, coincident with DXA scans. Medical history and medication use were recorded at baseline and at semi-annual follow-up sessions; subjects with medical illnesses or medication known to affect musculoskeletal growth were excluded from the analyses.

Physical maturity assessment

Subjects were pre-menarcheal at enrollment. Maturity status was quantified by semi-annual query until menarche was attained; menarche date was recorded to the day in most cases. In a few cases, the precise date was not recalled, and the 15th day of the menarche month was recorded. Gynecologic age (GA) was calculated as years pre-menarche (GA= negative number) or post-menarche (GA= positive number) by calculating the difference between DXA and menarche dates (to the nearest tenth of a year). Menarche is defined as GA= 0. In addition, Tanner stage was assessed using line drawings, supplemented by limited written descriptions, to represent each of the five stages. Participants reported Tanner breast and pubic stage at each six-month assessment, by circling the appropriate drawing to match their development. Tanner stage data are not used in the main analyses but are used to evaluate analytical bias and are reported to further define the study cohort.

Height and strength assessments

Height was measured semi-annually, without shoes, using wall-mounted rulers and a right angle (1997-2008) or a stadiometer (2008-present). Dominant hand grip strength was assessed annually via dynamometer (Takei, Japan); three trials were made and the best effort was recorded. Core strength and endurance were assessed annually as number of sit-ups performed in 60 seconds with good form (arms crossed, elbows to knees with feet secured).

Physical activity (PA) quantification

Organized activity participation (hours per week, h/wk) was quantified using semi-annual investigator queries, documenting training for sports and other organized PA (e.g. dance), as well as periods of illness/injury/vacation ≥1 week and associated activity modifications. PA means (h/wk) were calculated across the complete inter-scan interval (CIRCUMPA) and for the 6-12 month interval directly preceding DXA1 (PREPA). Non-organized activity and the vigorousness of individual PA bouts were not quantified. For a subset of this cohort (gymnasts), records were compared to coach daily training logs, demonstrating excellent correlation ($r>0.97$, $p<0.001$)[24].

Densitometry

Postero-anterior whole body DXA scans were performed per study protocol by one of two certified DXA technologists. A Hologic QDR4500W DXA scanner was used for the initial ten years of the study (1998-2008); baseline and follow-up scans were acquired on this scanner for 36 subjects included in the current analysis (enrolled 1998-2003). A cross-calibrated Discovery A scanner, in use for this study since November 2008, was used to acquire baseline and follow-up scans for the other 34 subjects included in the current analysis (enrolled during or after November 2008). All scans were re-analyzed by a single investi-

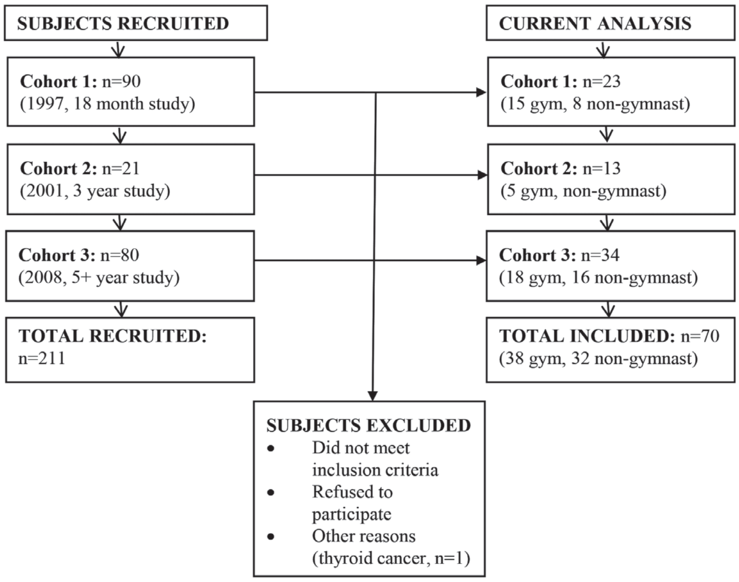

Figure 1. CONSORT diagram, demonstrating the derivation of subjects for the current analysis from the total cohort.

gator (JD) using Apex software (Hologic Discovery A, software v.12.7.3, Waltham, MA, USA). Care was taken to ensure that all soft-tissue was contained within the analysis box and that individual limb regions (arm, leg) were drawn consistently and in accordance with standard practice. Outcomes include non-bone fat free mass (lean mass) for sub-head, the sum of arm lean mass (left and right limbs), the sum of leg lean mass (left and right limbs) and sub-head fat mass. Sub-head measures were used as outcomes, rather than whole-body, in accordance with recommendations by the International Society for Clinical Densitometry regarding pediatric densitometric analyses.

DXA coefficients of variation (CVs) were calculated using duplicate scans (Discovery A) of 29 middle-aged females. To evaluate differences between DXA scanner results observed in young subjects, scans were also repeated on the two scanners in 132 subjects aged 8 to 24 years, from the same longitudinal study. For all regions of interest, lean mass was subtly underestimated on the QDR vs. the Discovery A (Wilcoxon Signed Rank, $p<0.05$), but fat mass assessments did not differ between machines. Coefficients of Variation (rmseCVs) for inter-scanner comparisons were similar to those for middle-aged adult scans repeated on the Discovery A only (inter-scanner vs. Discovery: sub-head lean mass 2.3% vs. 3.6%; leg lean mass 2.4% vs. 1.4%; sub-head fat mass 3.3% vs. 1.5%) except for arm lean mass, which demonstrated greater inter-scanner disparities (7.9% vs. 2.9%). For individual subjects, use of the same scanner for baseline and follow-up scans minimized the potential influence of these subtle inter-scanner differences in our analyses.

Inclusion criteria

Subjects were included in the present analysis based on the following criteria: 1) achievement of menarche; 2) DXA scans and complete accompanying data for a time-point falling between GA of -0.5 and -1.5 years (pre-menarche baseline scan= DXA1, ~GA-1) and a time-point falling between GA of +0.5 and +1.5 years (post-menarcheal= DXA2, ~GA1); 3) semi-annual PA records available for the inter-DXA interval and for at least 6 months preceding DXA1. Subjects who did not meet inclusion criteria were excluded from this analysis; one additional subject was excluded due to thyroid cancer. This yielded a TOTAL n= 70 for the current analysis (see Figure 1).

Statistical analysis

A 2-tailed alpha level of 0.05 was used for all analyses. Preliminary analyses included the calculation of frequencies for categorical variables and correlation coefficients across both independent and dependent variables. We used paired t-tests to evaluate descriptive statistics for unadjusted subject characteristics and lean mass/strength outcomes for the two scan dates (DXA1, DXA2), comparing differences across time in mean values. Examination of Q-Q plots indicated only subtle deviations from normality; therefore data were treated as normally distributed for ease of interpretation. Regression models were constructed, as detailed below, to evaluate associations between PA and lean mass/fat mass/strength outcomes. We reported adjusted model r^2, beta coefficients with 95% confidence intervals and significance levels for the regression coefficients. For adjusted relationships between bone outcomes and predictors of interest, individual variable significance and semi-partial correlation coefficients (SPCC) were evaluated; SPCC were squared to yield independent % variance explained by PA for each outcome.

Regression models: For the first set of analyses, we evaluated cross-sectional associations between pre-menarcheal PA and pre-menarcheal lean mass/fat mass/strength outcomes,

Variables	Pre-menarche baseline	Post-menarche follow-up
Age at Menarche (yrs)	13.0 (1.0)	
Chronologic Age (yrs)	11.8 (1.0)	13.9 (1.0)*
Gynecologic Age (yrs)	-1.1 (0.3)	0.9 (0.3)*
Standing height (cm)	149.0 (7.8)	160.0 (6.7)*
Weight (kg)	42.2 (8.1)	53.3 (8.1)*
Body Mass Index (kg/m^2)	18.9 (2.8)	20.8 (2.6)*
Arm Lean Mass (kg)	3.1 (0.59)	3.9 (0.68)*
Leg Lean Mass (kg)	10.4 (1.8)	13.4 (1.8)*
Sub-head Lean Mass (kg)	27.8 (4.4)	35.8 (4.5)*
Sub-head Fat Mass	9.4 (4.8)	11.7 (4.5)*
Sub-head %Fat	23.6 (7.5)	23.3 (5.4)
Dominant Arm Grip (kg)	19.8 (3.8)	26.3 (4.7)*
Sit-ups (#)	44.7 (11.2)	46.0 (9.1)
PA (h/wk)	7.7 (5.5)	8.3 (5.0)
Tanner Breast: n (%)	I-2, II-50, III-15, IV-3, V-0	I-0, II-3, III-31, IV-30, V-6
Tanner Pubic: n (%)	I-20, II-33, III-13, IV-4, V-0	I-0, II-5, III-26, IV-31, V-8

Mean (sd), n=70
PA = reported, organized physical activity exposure (h/wk)
** = significant difference from baseline value, paired t-test, p<0.01*

Table 1. Subject characteristics, mean (standard deviation).

evaluating the explanatory value of prePA after accounting for baseline gynecologic age (dxa1 GA) and baseline standing height (prePA-preOutcome analyses). For the second set of analyses, we evaluated possible associations between pre-menarcheal PA and post-menarcheal lean mass/fat mass/strength outcomes after accounting for post-menarcheal gynecological age (dxa2 GA) and post-menarcheal height (dxa2 height) (prePA-postOutcome analyses). In the third set of analyses, we evaluated associations between circum-menarcheal PA (circumPA) exposure and post-menarcheal outcomes (circumPA-postOutcome analyses). In these regression models, covariates included post-menarcheal gynecologic age (dxa2 GA), body size (change in height across the inter-DXA interval), and baseline pre-menarcheal lean mass/fat mass/strength status (dxa1). Inclusion of baseline status accounted for unmeasured factors in early childhood growth (e.g. genetics, diet and previous activity exposure). All girls were included in each set of analyses.

Results

Seventy girls, aged 11.8 years (sd 1.0) at baseline and 13.9 years (sd 1.0) at follow-up, were included in these analyses. However, five girls did not provide data for sit-ups, and one girl did not provide baseline grip strength data. Comparisons of baseline data for included subjects (n=70) versus excluded study enrollees (n=141) from the same cohorts detected no systematic differences for Tanner breast or pubic stage, race, ethnicity, age, height, mass, BMI, percent body fat, sub-head BMC or sub-head lean mass (both chi square and t-test p values >0.65).

The measurement interval (dxa1 to dxa2) spanned 24.3 months (sd 1.0, range 22.0-26.9). Subjects matured from gynecologic age -1.1 (sd 0.3) years at baseline to 0.9 (sd 0.3) years at follow-up and demonstrated mean gains of 11.0 (sd 3.4) cm in stature and 11.1 (sd 4.2) kg in weight. Subject characteristics and significance of differences from baseline to follow-up are presented in Table 1. All follow-up measures were greater than baseline measures (p<0.01), except for sit-ups and PA. Mean gains were 25-29% for lean and fat mass and 33% for dominant arm grip strength. PA participation was quite high at both timepoints. Tracking in PA level was indicated by Pearson correlation (r=0.82, p<0.05) and paired t-tests (no significant difference between prePA and circumPA). The majority of girls reported more than 5 h/wk of organized PA, not including physical education classes (57% and 69% of girls at baseline and follow-up, respectively). As these activity levels are greater than the national norm (37%), results in our cohort may not be generalizable to the entire population[20].

prePA-preOutcome analyses: Regression models for baseline lean mass/fat mass/ strength outcomes included baseline GA, height and prePA; these models predicted 39-65% of variation in pre-menarcheal lean mass (p<0.001) and strength (p<0.001) outcomes, but only 13% of variation in fat mass (p=0.006) (Table 2a). Standing height predicted all outcomes (p<0.03) except sit-ups; prePA predicted all pre-menarcheal outcomes (p<0.04), except grip strength. Significant variance was explained by prePA (positive association) for pre-menarcheal lean mass (3-10%), pre-menarcheal fat mass (6%), and pre-menarcheal sit-up performance (34%) (p<0.05) (Table 3).

prePA-postOutcome analyses: Regression models assessing prePA and follow-up, post-menarcheal lean mass/fat mass/ strength outcomes included follow-up height, follow-up gynecologic age and prePA; these models accounted for 13-36% of variation in follow-up outcomes (p≤0.006) (Table 2b). prePA was a

OUTCOME	TOTAL MODEL ADJUSTED R^2	BASELINE GYN AGE	BASELINE STANDING HEIGHT	prePA
Grip Strength	**0.40**[c]	0.25 (-2.36, 2.86)	**0.31**[c] (0.21, 0.40)	0.10 (-0.04, 0.23)
Arm Lean Mass	**0.49**[c]	0.03 (-0.34, 0.40)	**0.05**[c] (0.03, 0.06)	**0.04**[c] (0.02, 0.05)
Leg Lean Mass	**0.57**[c]	0.71 (-0.31, 1.72)	**0.16**[c] (0.13, 0.20)	**0.06**[a] (0.003, 0.11)
Sub-head Lean Mass	**0.65**[c]	2.12 (-0.15, 4.39)	**0.42**[c] (0.34, 0.50)	**0.20**[c] (0.09, 0.32)
Sit ups	**0.39**[c]	-6.41 (-14.16, 1.35)	0.20 (-0.08, 0.48)	**1.20**[c] (0.80, 1.60)
Sub-head Fat Mass	**0.13**[b]	2.38 (-1.48, 6.23)	**0.16**[a] (0.02, 0.30)	**-0.22**[a] (-0.42, -0.02)

Unstandardized betas, 95% confidence intervals (parentheses) and significance levels of betas are depicted for each variable. PA= organized physical activity exposure (h/wk); prePA= PA 6-12 months prior to baseline assessment; circumPA= PA between baseline and follow-up assessments. ***[a]=p<0.05; [b]= p≤ 0.01; [c]= p≤0.001.***

Table 2a. Regression results: assessment of BASELINE physical activity as a predictor of BASELINE, pre-menarcheal lean mass and strength, reporting total model ADJUSTED R^2, beta coefficients (95% confidence intervals).

OUTCOME	TOTAL MODEL ADJUSTED R^2	FOLLOW-UP GYN AGE	FOLLOW-UP STANDING HEIGHT	prePA
Grip Strength	**0.27**[c]	2.10 (-1.30, 5.5)	**0.37**[c] (0.22, 0.52)	0.16 (-0.02, 0.34)
Arm Lean Mass	**0.13**[b]	0.02 (-0.50, 0.54)	**0.02**[a] (0.003, 0.05)	**0.04**[b] (0.02, 0.07)
Leg Lean Mass	**0.29**[c]	-0.05 (-1.32, 1.22)	**0.15**[c] (0.09, 0.20)	**0.07**[a] (0.002, 0.14)
Sub-head Lean Mass	**0.36**[c]	1.11 (-1.86, 4.08)	**0.38**[c] (0.25, 0.50)	**0.24**[b] (0.09, 0.40)
Sit ups	**0.25**[c]	-2.84 (-9.72, 4.04)	0.06 (-0.23, 0.35)	**0.86**[c] (0.50, 1.22)
Sub-head Fat Mass	**0.18**[c]	**3.49**[a] (0.12, 6.86)	**0.25**[c] (0.10, 0.40)	-0.11 (-0.29, 0.07)

See legend of Table 2a.

Table 2b. Regression results: assessment of BASELINE physical activity as a predictor of FOLLOW-UP, post-menarcheal lean mass and strength, reporting total model ADJUSTED R^2, beta coefficients (95% confidence intervals).

significant positive predictor of all post-menarcheal outcomes ($p<0.001$ to $p<0.05$), except grip strength and fat mass, explaining 4-12% of variance in post-menarcheal regional and sub-head lean mass ($p<0.05$), and 27% of variance in post-menarcheal sit-ups ($p<0.001$) (squared SPCC, Table 3). Follow-up, post-menarcheal height was a significant predictor of all post-menarcheal outcomes except sit-ups; follow-up GA only explained significant variance in post-menarcheal fat mass.

circumPA-postOutcome analyses: Regression models evaluating associations between circumPA and follow-up, post-menarcheal lean mass/fat mass/strength outcomes included baseline status for the outcome, follow-up GA, change in height and circumPA. As expected, through incorporation of baseline status, these models predicted a large proportion of variance (58-82%) in all post-menarcheal outcomes ($p<0.001$) (Table 2c). Baseline status was a significant positive predictor for all follow-up outcomes ($p<0.001$); change in height was a significant predictor for all lean mass and grip strength outcomes ($p<0.015$), but not for fat mass or sit-ups. In contrast to strong prePA explanatory value for most pre-menarcheal outcomes (baseline), circumPA was not a significant predictor of follow-up, post-menarcheal outcomes for any variable, except sub-head lean mass ($p=0.032$). Squared

OUTCOME	TOTAL MODEL ADJUSTED R²	BASELINE VARIABLE	FOLLOW-UP GYN AGE	CHANGE IN STANDING HEIGHT	circumPA
Grip Strength	**0.60[c]**	**1.06[c]**	1.37	**0.31[a]**	-0.03
		(0.84, 1.27)	(-1.52, 4.26)	(0.05, 0.57)	(-0.19, 0.12)
Arm Lean Mass	**0.76[c]**	**1.07c**	0.17	**0.06[c]**	0.02[d]
		(0.91, 1.24)	(-0.14, 0.48)	(0.03, 0.09)	(0.001, 0.03)
Leg Lean Mass	**0.76[c]**	**0.95[c]**	-0.31	**0.16[c]**	0.04[e]
		(0.82, 1.09)	(-1.14, 0.53)	(0.09, 0.24)	(-0.006, 0.08)
Sub-head Lean Mass	**0.82[c]**	**1.01[c]**	0.12	**0.47[c]**	**0.11[a]**
		(0.89, 1.14)	(-1.65, 1.89)	(0.31, 0.64)	(0.01, 0.20)
Sit ups	**0.66[c]**	**0.66c**	2.84	0.34	0.18
		(0.51, 0.81)	(-2.32, 8.00)	(-0.10, 0.78)	(-0.15, 0.50)
Sub-head Fat Mass	**0.58[c]**	**0.70[c]**	0.76	-0.15	-0.04
		(0.55, 0.85)	(-1.98, 3.49)	(-0.37, 0.07)	(-0.19, 0.10)

See legend of Table 2a.
p=0.06[d], p=0.09[e]

Table 2c. Regression results: assessment of CIRCUM-MENARCHEAL physical activity as a predictor of FOLLOW-UP post-menarcheal lean mass and strength, reporting total model ADJUSTED R², beta coefficients (95% confidence intervals).

Outcome	prePA/ Pre-menarcheal outcome[1]	prePA/ Post-menarcheal outcome[2]	circumPA/ Post-menarcheal outcome[2]
Dominant Hand			
Grip Strength	0.02	0.03	0.001
Arm Lean Mass	**0.10[c]**	**0.12[a]**	0.01
Leg Lean Mass	**0.03[a]**	**0.04[a]**	0.01
Sub-head Lean Mass	**0.06[c]**	**0.09[a]**	**0.01[a]**
Sit ups	**0.34[c]**	**0.27[c]**	0.006
Sub-head Fat Mass	**0.06[a]**	0.02	0.002

Data represent squared semi-partial correlation coefficients for focal physical activity (PA) variables and significance, ***[a]= p<0.05; [b]= p≤ 0.01; [c]= p≤0.001.***

[1] Adjusted for baseline GA, baseline standing height

[2] Adjusted for follow-up GA and follow-up standing height

[3] Adjusted for follow-up GA, baseline variable, and change in standing height

Table 3. Squared semi-partial correlation results for PA.

SPCC indicated that circumPA explained only 1% of post-menarcheal subLM variance (p<0.05).

Although subjects in our study participated in a variety of organized activities, about half of subjects participated in gymnastics training. To evaluate whether gymnast status affected our results, a categorical gym/non variable was added to baseline regression models (gym ≥4h/wk gymnastics participation). After accounting for physical activity, there was additional explanatory value for the gym/non variable only for sit-ups, with an adjusted R² change from 0.39 to 0.44 (p=0.012).

Discussion

In this cohort of early adolescent girls, *pre-menarcheal* organized physical activity participation was a significant predictor of lean mass and sit-up performance at both pre-menarcheal and post-menarcheal assessments. However, physical activity participation over a two-year *circum-menarcheal* window was not a strong independent predictor of these outcomes at the post-menarcheal assessment. In addition, we identified a negative association between *pre-menarcheal* physical activity and *pre-menarcheal* fat mass, but no significant association between physical activity (pre or circum) and *post-menarcheal* fat mass. We were surprised that circum-menarcheal physical activity was not a potent predictor of post-menarcheal lean mass, fat mass or strength, as we had hypothesized a strong influence of circum-menarcheal physical activity during this period of major somatic growth and maturation.

Regression analyses evaluating the explanatory value of circum-menarcheal activity were purposely designed to account for unmeasured factors in early childhood growth (e.g. genetics, diet and PREPA) through the inclusion of baseline status as a covariate. It was hoped that this practice would statistically isolate the contribution of circum-menarcheal activity to post-menarcheal outcomes. Several explanations for the lack of significant explanatory value of circum-menarcheal activity may apply. First, girls who exercised at a higher level pre-menarche may have attained greater lean mass/core strength (sit-ups) and lower fat mass from their elevated exercise level, setting them on a trajectory that was maintained throughout circum-menarcheal growth, compared to girls who had exercised at a lower level pre-menarche. Our finding that pre-menarcheal activity predicted post-menarcheal lean mass/core strength outcomes supports this hypothesis. Alternatively, it is possible that benefit from circum-menarcheal exercise is only evident in girls who *increase* their activity participation over the circum-menarcheal interval; we cannot evaluate this hypothesis effectively, as mean PREPA and mean CIRCUMPA did not differ significantly in our subjects (activity levels tracked across circum-menarche). Finally, it is possible that PA participation does not influence lean mass/fat mass/strength acquisition during circum-menarche and that somatic growth and maturation are the predominant modifiers of body composition and muscular function during this maturational phase. If this were the case, centering at menarche and adjusting for height and baseline status would explain the majority of variance. To elucidate the relationship between PA and lean mass and strength acquisition, further studies are necessary to evaluate larger groups of girls who participate in various levels of exercise pre-menarche, and who increase, decrease or maintain activity across the circum-menarcheal period.

There are several published reports evaluating lean and fat mass development across the entire span of pubertal maturation; all three have identified associations between adolescent physical activity and lean mass/fat mass at young adulthood. Cheng et al. evaluated 396 girls, aged 10-13 years at baseline; annual measurements were obtained and 236 girls provided follow-up data at a mean of 7.5 years post-baseline[14]. Repeated measures analyses from baseline to follow-up demonstrated tracking of bone, lean and fat mass from pre-puberty to early adulthood. Leisure time physical activity scores (LTPA), estimating prior 6-month activity level at baseline and follow-up, predicted 14% of variance in lean mass and 12% of variance in fat mass at young adulthood. Follow-up LTPA was a stronger predictor of lean and fat mass than baseline LTPA. As in the Cheng study, our results suggest tracking of lean and fat mass across menarche. However, in our cohort, pre-menarcheal physical activity participation predicted both pre- and post-menarcheal lean mass/fat mass/core strength outcomes, with almost no independent influence of circum-menarcheal physical activity on post-menarcheal traits.

Baxter-Jones et al. investigated the impact of habitual physical activity on total body and lean mass accrual over six years of adolescent growth in a group of 109 boys and 113 girls, aged 8-15 years at baseline[13]. Physical activity was assessed by questionnaire, 2-3 times per year; the annual mean was used as a time-varying covariate within multi-level models accounting for variability in height and biological maturity (based upon peak height velocity). Investigators identified a significant, independent statistical effect of habitual activity on total body and regional lean mass acquisition in both boys and girls. Although the authors note that these findings suggest the importance of adolescent PA in lean mass acquisition, it is unknown whether activity participation was more influential before, during or after PHV, as the pubertal phases were not evaluated separately. It is possible that *pre-pubertal* activity participation placed more active children on a higher trajectory than less active children, with resultant advantages maintained to young adulthood. Such a phenomenon would have yielded similar results to those of our analyses, if pre- and circum-menarcheal development had been isolated in their female subjects.

Volgyi et al. sought to determine if the amount and level of leisure-time physical activity (LTPA) during adolescence affected the quantity and distribution of lean mass and fat mass in early adulthood[15]. This study included 202 Finnish girls who were 10-13 years of age at baseline, divided into four groups based on amount of leisure time physical activity (LTPA, assessed by questionnaire) over the seven years of follow-up (low to low, low to high, high to low, and high to high groups). Girls with consistently higher LTPA (>5 h/wk), and girls who increased LTPA from low to high during puberty, had significantly greater lean mass at the age of 18 years compared to girls who stayed at a low level or decreased to a lower level. Because Volgyi's cohort was studied at two time points, seven years apart, it cannot be determined whether activity participation was more influential at any particular phase of growth (other than at adulthood, when high LTPA was associated with advantages in lean mass compared to low LTPA). Nonetheless, our results are consistent with the findings of Volgyi et al., as our cohort, on average, exercised at a level that would have been grouped as "high" in Volgyi's analysis, at both baseline and follow-up. Our findings appear to indicate a stronger influence of pre-menarcheal activity, with tracking of both PA and focal outcomes across menarche.

We hypothesized that circum-menarcheal physical activity participation would be negatively associated with fat mass development. We did identify a negative association between *pre-menarcheal* physical activity and *pre-menarcheal* fat mass, with PA explaining 6% of variation in fat mass at this time point. However, in contrast to Cheng, et al. who found that leisure time physical activity predicted 12% of variation in young adult fat mass, we found no significant association between physical activity (PRE or CIRCUM) and *post-menarcheal* fat mass. Volgyi, et al. noted no difference in fat mass between physical activity groups across adolescence, hypothesizing that the activity threshold (>5 h/wk LTPA) may have been too low. It is also possible that use of a dichotomous activity threshold did not allow for the greater potential explanatory value of a continuous activity variable. Similarly, in an analysis using multi-level modeling, Mundt et al. found no relationship between physical activity and fat mass development in females aged 8-19 years[16]. In addition to the explanations noted above for lean mass/core strength associations, it is also likely that our group of relatively lean girls did not provide adequate variation in fat mass to detect associations between physical activity and fat mass acquisition during circum-menarcheal growth. Evaluation in a cohort of more disparate body types and activity levels may identify associations that could not be isolated in our cohort.

Finally, our physical activity metric (h/wk of organized activity) does not discriminate among activity types, some of which may have greater influence on fat mass than others.

Interestingly, organized physical activity participation was not a significant predictor of dominant hand grip strength at baseline or follow up. Hand grip has previously been validated as an estimate of muscular fitness in children aged 6-12 years old[17]. In a cross-sectional study by Voss et al.[18], body composition, physical fitness and physical activity were compared in 3,036 Canadian and English children and adolescents. Height and body mass explained up to 40% of the variance in handgrip strength, but there was no significant association between strength and self-reported physical activity. Our findings are similar to those of Voss et al.; body size predicted grip strength, but physical activity did not. This is not altogether surprising, as organized physical activity participation is a non-specific indicator of dominant arm activity exposure. In contrast, sit-up capability was successfully predicted by physical activity participation, and, thus, may be a better marker for total body muscular fitness. These results corroborate our prior findings of a significant, positive correlation between sit-up capability and higher non-aquatic physical activity levels in a group of 114 females (60 ex/gymnasts and 54 non-gymnasts)[19].

Our study has several strengths, including detailed longitudinal assessment of physical activity associations with lean mass, fat mass and strength acquisition across a tight maturational window. Inclusion of gynecologic age and stature as covariates allowed us to statistically isolate the influence of pre- and circum-menarcheal physical activity on lean mass and strength during these important maturational phases. However, our study also has several limitations, including the specific nature of our cohort.

First, our cohort of adolescent females was highly active. Based on the United States Centers for Disease Control and Prevention Youth Risk Behavior Surveillance of 2013, only 37.3% of U.S. female students are physically active for a total of at least 60 minutes per day for 5 or more days per week[20]. Our study measured activity in annual mean hours per week, excluding school physical education classes. Using this metric, in our cohort, 59% of girls at baseline and 71% of girls at follow-up reported annual mean organized activity participation in excess of 5 h/wk, with group mean exposure of ~8 h/wk. Thus, we have limited ability to assess associations with "low" physical activity exposure or increasing or decreasing activity levels in this cohort. Second, only 14% of our subjects were either overweight or obese by BMI for age. Our percentage is much lower than was noted by Ogden et al., in a survey of the general population in 2011-12, reporting ~34% of girls aged 6-19 years as overweight or obese[21]. Thus, the composition of our cohort is not representative of the general population, and results cannot be extrapolated to populations with lower mean activity participation and/or a greater prevalence of overweight/obese subjects. Third, it is possible that aligning assessments by gynecological age reduces inter-individual variability in fat mass, because development of fat mass appears to be closely tied to achievement of menarche through the endocrine effects of circulating leptin levels[22-23]. Thus, aligning measurements by gynecological age may equalize fat mass across subjects, regardless of physical activity exposure.

We suspect that gymnastics participation provided a better metric of sit-up performance than did organized physical activity because of the consistently intense core strengthening programs in which gymnasts train, compared to the broader variability in training programs of other organized physical activities in which our subjects participated (dance, soccer, volleyball, etc.). However, the limited predictive value of gym/non status across regression models indicates a low likelihood that inclusion of gymnasts affected our overall results.

Finally, our work is limited by the metric we used to assess physical activity. Physical activity is difficult to assess, particularly in the pediatric population. Our questionnaire, recording participation in organized physical activity, has been shown to correlate strongly with coaches' logs in a subset of our population (gymnastics activity vs. coaches' logs, r> 0.97)[24]. Yet, the questionnaire may be less effective in other types of athletes or in non-athletes. Also, it does not record free play activities or activity intensity, and thus, may not accurately reflect between-subject variation in overall physical activity. Therefore, it is possible that our PA metric provides results that do not reflect the actual level of physical activity exposure (e.g. energy expenditure effects on fat mass) for these subjects.

In summary, our study provides a uniquely specific evaluation of circum-menarcheal lean mass, fat mass and strength development in females. Our results indicate the importance of pre-menarcheal physical activity in lean mass and core strength acquisition and suggest persistent benefit from pre-menarcheal exercise. Further study, evaluating cohorts with greater variability in activity level and body composition are necessary to corroborate these findings.

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