

## Short Communication

# Is breastfeeding related to bone properties? A longitudinal analysis of associations between breastfeeding duration and pQCT parameters in children and adolescents

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## Abstract

Nutritive and bioactive components of human milk could be involved in programming metabolic systems that affect bone growth throughout the life course. Bone properties in childhood and adolescence might differ, depending on breastfeeding duration. Thus, breastfeeding could be a relevant factor in the context of primary osteoporosis prevention. The prospective association between breastfeeding duration and bone properties was investigated using the data of 284 participants of the Dortmund Nutritional and Anthropometric Longitudinally Designed Study. Breastfeeding duration was assessed during infancy. Bone properties were measured by peripheral quantitative computed tomography (pQCT) at ages 5–23 years. Cortical volumetric bone mineral density, cortical bone mineral content, strength strain index, total cross-sectional area of the bone and cross-sectional area of the cortical bone were determined at the 65% site of the radius. Linear regression analyses were performed to check for differences in pQCT parameters of subjects who had not or shortly been breastfed (0–16 weeks) and subjects who had been breastfed for a long duration ( $\geq 17$  weeks). Multivariable models adjusted for age, gender, forearm length, muscle cross-sectional area, body mass index standard deviation score (SDS), height SDS and socio-economic status did not yield associations between breastfeeding duration and pQCT parameters. These findings suggest neither protective nor adverse effects of prolonged breastfeeding on bone health in childhood and adolescence. Influences of early nutrition on bone growth might be overridden by current effects of mechanical loads on bone physiology.

**Keywords:** breastfeeding, bone growth, pQCT, early nutrition programming.

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## Introduction

Breastfeeding as a factor amenable to primary osteoporosis prevention is currently under debate (Fewtrell 2006; Jones 2011). Bone characteristics throughout the life course might differ, depending on breastfeeding duration in infancy, possibly due to a role of nutritive or bioactive human milk compounds in early nutrition programming of bone metabolism (Fewtrell 2011; Jones 2011). However, current

mechanical and dietary factors strongly affect bone metabolism (Schoenau 2004; Schoenau & Fricke 2008) and may override early nutritional influences.

Follow-up studies of preterm infants have shown positive associations between breastfeeding duration and densitometric skeletal parameters at ages 5 and 20 years (Bishop *et al.* 1996; Fewtrell *et al.* 2009) but not at ages 9–12 years (Fewtrell *et al.* 1999). While positive associations between breastfeeding duration and bone properties in children and adolescents born

at term have been observed in two studies (Jones 2011; Molgaard *et al.* 2011), there were no such associations in three others (Young *et al.* 2005; Ganpule *et al.* 2006; Harvey *et al.* 2009). Studies of adult participants have not revealed a consistent relation between breastfeeding duration and bone properties (Cooper *et al.* 1997; Pearce *et al.* 2005; Laskey *et al.* 2007; Pirilä *et al.* 2011). Also, breastfeeding duration does not seem to be associated with fracture risk in adolescents and adults (Cooper *et al.* 2001; Jones *et al.* 2004), whereas one study yielded an inverse association between breastfeeding duration and fracture risk in children (Ma & Jones 2002).

With one exception (Laskey *et al.* 2007), dual energy X-ray absorptiometry (DXA) measurements were used in the studies mentioned earlier to determine bone properties, limiting inferences on bone quality or strength (Schoenau 2004; Binkley *et al.* 2008). Our objective was therefore to assess the relation between full-breastfeeding duration and skeletal parameters measured by peripheral quantitative computed tomography (pQCT) representing both geometric and material bone properties (Binkley *et al.* 2008; Rauch & Schoenau 2008).

## Materials and methods

Our study involved participants of the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study, which has been introduced in detail elsewhere (Kroke *et al.* 2004). The present study was approved by the ethics committee of the University of Cologne and the German Federal Office for Radiation Protection (Neu *et al.* 2001). In brief, pQCT measurements of 284 participants, aged

5–23 years were taken in 1998/1999. An XCT2000® device (Stratec Inc., Pforzheim, Germany) was positioned at a reference line that had a distance of 65% of the radius length to the ulnar styloid process. Cortical volumetric bone mineral density (vBMD<sub>cort</sub>), cortical bone mineral content (BMC<sub>cort</sub>), strength strain index (SSI), total cross-sectional area of the bone (CSA<sub>tot</sub>) and cross-sectional area of the cortical bone (CSA<sub>cort</sub>) were determined. The cross-sectional area of the muscle (MCSA) as a surrogate for muscular strength was also measured by pQCT. A second measurement of pQCT parameters was carried out at the so-called 4% site of the radius, close to the wrist. As bone at this site is formed more rapidly in childhood (Rauch & Schoenau 2005), we decided to use 65%-site parameters for our main analysis. Measurements were performed by trained personnel. Further details of the pQCT measurements have been described previously (Neu *et al.* 2001; Rauch & Schoenau 2008).

Full-breastfeeding duration in weeks was recorded by a dietician or a paediatrician during regular visits at 3, 6, 9 and 12 months after birth. Infants fed with human milk only, or with tea and water in addition, were defined as fully breastfed. Tanner pubertal stages according to genital or breast, or pubic hair development, were assessed by a study paediatrician. Anthropometric characteristics were assessed following standardised and quality monitored procedures (Kroke *et al.* 2004). Age- and sex-dependent standard deviation scores (SDS) for height and BMI were calculated using German reference data (Kromeyer-Hauschild *et al.* 2001).

Linear regression analyses to assess the association between full-breastfeeding duration (not/short, 0–16 weeks vs. long, ≥17 weeks) and pQCT parameters

### Key messages

- Bone characteristics throughout the life course might differ, depending on breastfeeding duration in infancy, possibly due to a role of nutritive or bioactive human milk compounds in early nutrition programming of bone metabolism.
- The present study was the first study to assess the prospective relationship between breastfeeding duration and bone properties in children and adolescents using pQCT. No associations between breastfeeding duration and bone properties were observed in participants aged 5–23 years.
- Overall, there is no clear evidence for an association between breastfeeding duration and bone properties in later life.

(continuous variables) were performed. The cut-off after 16 weeks of breastfeeding was set, as German public authorities recommend full breastfeeding for at least 4 months [National Breastfeeding Commission (Nationale Stillkommission am BfR) 2004]. Confounders were identified by literature review. They comprise essential factors that influence bone properties, i.e. gender, pubertal stage, bone length and height (Neu *et al.* 2002), muscle force (Schoenau & Fricke 2008) and body mass (Reid 2008). Regression model 1 was adjusted for age at pQCT (continuous), gender and forearm length. Model 2 was additionally adjusted for MCSA, BMI SDS, height SDS and maternal education (low, <12 years vs. high,  $\geq 12$  years) as proxy for the participants' socio-economic status. Multiplicative terms of breastfeeding variables and confounders, i.e. age (continuous), age groups (5–9, 10–13 and 14–23 years), Tanner stages, forearm length, gender, maternal education, MCSA, BMI SDS and height SDS were added to model 1 to test for interactions. Due to the participants' wide age range, analyses stratified by age groups (5–9, 10–13 and 14–23 years) were conducted in addition to the pooled main analysis, even though we observed no statistically significant interaction between breastfeeding duration and age groups. SAS 9.2 (SAS Institute Inc., Cary, NC, USA) was used. For all evaluations,  $P$ -values  $\leq 0.05$  were considered statistically significant.

## Results

### Characteristics

Breastfeeding and pQCT data were available for 147 female and 137 male participants of the DONALD Study. Table 1 presents characteristics of the study population by age and breastfeeding duration strata. In short, participants with a long breastfeeding duration were younger, in earlier pubertal stages and had lower values of anthropometric and pQCT parameters. These differences were small in 5–9-year-old children and more pronounced in 10–13 and 14–23-year-old children and adolescents. A higher maternal education was associated with longer breastfeeding.

### Main findings

In multivariable models adjusted for age, gender and forearm length, there were no significant associations between breastfeeding duration and pQCT parameters, neither in pooled analyses nor in analyses stratified by age groups (Table 2). Additional adjustments for MCSA, BMI SDS, height SDS and maternal education level hardly affected the associations between breastfeeding duration and pQCT parameters presented in Table 2 (data not shown). Including Tanner pubertal stages that were available for 254 of the subjects into the pooled regression analyses also had only a marginal influence on the association of breastfeeding duration and bone characteristics (data not shown). The non-significant trend for a positive association between longer breastfeeding and higher SSI values in the 14–23-year-old subjects in model 1 ( $P = 0.09$ ) was attenuated by further adjusting for MCSA, BMI SDS, height SDS and maternal education level ( $P = 0.16$ , data not shown). No significant associations were observed using pQCT parameters assessed at the 4% site of the radius as dependent variables in the described models (data not shown).

### Sensitivity analyses

Applying alternative breastfeeding duration categories, e.g. dichotomous variables with theory-driven cut-points after 12 weeks as used in previous studies (Laskey *et al.* 2007; Jones 2011), or after 25 weeks reflecting the World Health Organization (WHO) recommendation for exclusive breastfeeding, did not reveal significant associations between breastfeeding duration and pQCT parameters (data not shown). Using full-breastfeeding duration variables with three categories (e.g. 0–2, 3–16 and  $\geq 17$  weeks) instead of dichotomous variables did not yield significant associations either (data not shown). Additionally, adjusting for partial breastfeeding duration did not affect the results shown in Table 2 (data not shown). There were no significant interactions of breastfeeding duration with any of the adjustment variables (data not shown).

**Table 1.** General characteristics of the study population presented by age groups and full-breastfeeding duration categories

Age group	5–9 years		10–13 years		14–23 years		All participants	
	0–16 weeks	≥17 weeks	0–16 weeks	≥17 weeks	0–16 weeks	≥17 weeks	0–16 weeks	≥17 weeks
<i>N</i>	45	54	58	47	51	29	154	130
Females (%)	55.6	50.0	53.4	42.6	51.0	62.1	53.2	50.0
Age at pOCT	7.8 (±1.0)	7.6 (±1.3)	11.9 (±1.1)	11.7 (±1.1)	17.3 (±2.2)	15.9 (±1.5)	12.5 (±4.1)	10.9 (±3.5)
Tanner stage 1, <i>n</i> (%) <sup>*</sup>	38 (88.4)	41 (89.1)	6 (10.9)	9 (19.6)	–	–	44 (31.4)	50 (43.8)
Tanner stages 2–4, <i>n</i> (%) <sup>*</sup>	5 (11.6)	5 (10.9)	41 (74.6)	33 (71.7)	4 (9.5)	4 (18.2)	50 (35.7)	42 (43.9)
Tanner stage 5, <i>n</i> (%) <sup>*</sup>	–	–	8 (14.5)	4 (8.7)	38 (90.5)	18 (81.8)	46 (32.9)	22 (19.3)
High education <sup>†</sup> (%)	46.7	55.6	51.7	61.7	25.5	31.0	41.6	52.3
Weight (kg)	28.3 (±6.2)	26.6 (±5.7)	48.7 (±10.6)	43.6 (±11.3)	67.6 (±14.7)	61.4 (±10.6)	49.0 (±19.1)	40.5 (±16.3)
Height (cm)	130.2 (±8.2)	128.5 (±9.4)	157.4 (±8.2)	152.5 (±9.0)	174.9 (±8.9)	170.9 (±8.6)	155.3 (±19.6)	146.6 (±19.1)
Height SDS	0.3 (±0.9)	0.2 (±0.9)	0.7 (±1.0)	0.2 (±1.0)	0.4 (±1.0)	0.2 (±0.9)	0.5 (±1.0)	0.2 (±0.9)
Forearm length (cm)	19.9 (±1.5)	19.7 (±1.5)	24.6 (±1.5)	23.8 (±1.6)	27.3 (±1.9)	26.6 (±2.0)	24.1 (±3.3)	22.7 (±3.2)
BMI (kg m <sup>-2</sup> )	16.5 (±2.2)	15.9 (±1.6)	19.5 (±3.3)	18.5 (±3.3)	21.9 (±3.4)	20.9 (±2.5)	19.4 (±3.7)	18.0 (±3.2)
BMI SDS	0.1 (±1.0)	-0.1 (±0.8)	0.3 (±1.0)	0.0 (±1.2)	0.2 (±1.0)	0.0 (±0.8)	0.2 (±1.0)	0.0 (±1.0)
MCSA (mm <sup>2</sup> )	1771.5 (±256.3)	1745.1 (±365.6)	2538.6 (±434.5)	2374.0 (±459.0)	3422.8 (±851.9)	3242.0 (±694.2)	2607.3 (±869.1)	2306.4 (±751.6)
vBMD <sub>cort</sub> (mg cm <sup>-3</sup> )	984.7 (±46.1)	983.8 (±55.8)	1036.7 (±45.2)	1024.5 (±44.3)	1093.7 (±42.3)	1093.0 (±40.3)	1040.4 (±61.8)	1022.9 (±63.9)
SSI (mm <sup>3</sup> )	123.4 (±32.2)	122.3 (±40.7)	204.1 (±44.6)	187.9 (±53.0)	293.5 (±75.8)	280.7 (±58.8)	210.1 (±86.4)	181.3 (±78.3)
CSA <sub>tot</sub> (mm <sup>2</sup> )	79.6 (±13.7)	78.9 (±15.5)	102.7 (±15.8)	99.1 (±20.1)	124.6 (±24.5)	119.7 (±18.3)	103.2 (±25.6)	95.3 (±23.8)
CSA <sub>cort</sub> (mm <sup>2</sup> )	40.3 (±9.5)	39.2 (±10.3)	59.4 (±10.6)	54.3 (±12.8)	79.3 (±15.0)	76.1 (±12.9)	60.4 (±19.5)	52.9 (±18.4)
BMC <sub>cort</sub> (mg mm <sup>-1</sup> )	40.0 (±10.8)	38.9 (±11.6)	61.8 (±12.9)	55.9 (±14.9)	86.8 (±16.6)	83.2 (±14.8)	63.7 (±23.0)	54.9 (±21.7)

BMC<sub>cort</sub>, cortical bone mineral content; BMI, body mass index; CSA<sub>cort</sub>, cross-sectional area of the cortical bone; CSA<sub>tot</sub>, total cross-sectional area of the bone; MCSA, cross-sectional area of the muscle; pOCT, peripheral quantitative computed tomography; SDS, standard deviation scores; SSI, strength strain index; vBMD<sub>cort</sub>, cortical volumetric bone mineral density. Parameters presented as arithmetic means (standard deviations).

<sup>\*</sup> According to breast (female subjects) and genital (male subjects) development. Information available for 254 of 284 participants. <sup>†</sup> At least 12 years of maternal school education.

**Table 2.** Linear regression analyses on the association between breastfeeding duration and pQCT parameters

Age group	Breastfeeding duration	Adjusted means of pQCT parameters*						
		vBMD <sub>cor</sub> (mg cm <sup>-3</sup> )	SSI (mm <sup>3</sup> )	CSA <sub>tot</sub> (mm <sup>2</sup> )	CSA <sub>cor</sub> (mm <sup>2</sup> )	BMC <sub>cor</sub> (mg mm <sup>-1</sup> )		
5–23 years (all subjects)	<17 weeks (n = 154) <sup>†</sup>	1031.5	196.5	99.6	57.2	59.8		
	≥17 weeks (n = 130)	1032.9	198.1	99.8	56.8	59.6		
	Beta (95% CI)	1.47 (-8.95, 11.88)	1.66 (-8.17, 11.48)	0.23 (-3.47, 3.94)	-0.37 (-2.60, 1.86)	-0.28 (-2.92, 2.36)		
	P <sup>‡</sup>	0.78	0.74	0.90	0.75	0.83		
5–9 years	<17 weeks (n = 45) <sup>†</sup>	983.2	121.9	79.1	39.9	39.6		
	≥17 weeks (n = 54)	985.9	124.1	79.4	39.7	39.6		
	Beta (95% CI)	2.65 (-15.8, 21.11)	2.19 (-9.56, 13.95)	0.26 (-5.32, 5.84)	-0.19 (-3.20, 2.81)	0.01 (-3.39, 3.41)		
	P <sup>‡</sup>	0.78	0.71	0.93	0.90	1.0		
10–13 years	<17 weeks (n = 58) <sup>†</sup>	1034.6	197.7	101.0	57.7	59.9		
	≥17 weeks (n = 47)	1027.7	195.6	100.9	56.5	58.4		
	Beta (95% CI)	-6.85 (-24.49, 10.79)	-2.8 (-17.93, 13.78)	-1.28 (-7.81, 5.25)	-0.10 (-6.24, 6.03)	-1.23 (-4.98, 2.52)		
	P <sup>‡</sup>	0.44	0.80	0.97	0.52	0.51		
14–23 years	<17 weeks (n = 51) <sup>†</sup>	1088.3	282.2	121.4	77.2	84.1		
	≥17 weeks (n = 29)	1096.7	303.2	126.1	80.3	88.1		
	Beta (95% CI)	8.32 (-7.10, 23.74)	21.03 (-3.40, 45.46)	4.77 (-3.51, 13.04)	3.10 (-1.92, 8.12)	4.0 (-1.81, 9.80)		
	P <sup>‡</sup>	0.29	0.09	0.25	0.22	0.17		

BMC<sub>cor</sub>, cortical bone mineral content; CI, confidence interval; CSA<sub>cor</sub>, cross-sectional area of the cortical bone; CSA<sub>tot</sub>, total cross-sectional area of the bone; pQCT, peripheral quantitative computed tomography; SSI, strength strain index; vBMD<sub>cor</sub>, cortical volumetric bone mineral density. Linear regression models adjusted for age, forearm length and gender were calculated using general linear models. <sup>†</sup>The presented values are age-, gender- and forearm length-adjusted least squares means. <sup>‡</sup>Reference category: Breastfeeding duration of <17 weeks. <sup>§</sup>P for difference calculated by analysis of covariance.

## Discussion

Overall, this study did not reveal associations between breastfeeding duration and pQCT parameters, neither in analyses stratified by age groups nor in pooled analyses. Our study extends previous knowledge in that bone characteristics were assessed by pQCT, a method that allows an in-depth analysis of bone geometry and strength.

A limitation to our study is the wide age range of the participants at pQCT measurement. Grouping of subjects by pubertal stage was restricted due to the total number of 284 participants and missing data on pubertal status for some of the subjects. Also, we cannot rule out that our sample size, particularly in the stratified analyses, was insufficient to detect marginal differences between breastfeeding categories, as also evident from the confidence intervals for our estimates. Furthermore, we could only assess pQCT parameters at the radius. Finally, we did not account for potential confounders such as complementary feeding, other early life factors, genetic factors, fracture data, sunlight exposure, diet, activity or hormonal status in our evaluations. On the other hand, we could use well-defined exposure and end-point variables. First of all, we used pQCT to assess bone properties, at a comparatively low radiation dose. In contrast to the two-dimensional DXA parameters previously used in similar studies, we could revert to pQCT measures of bone size, three-dimensional bone properties and indices of bone strength and mineralisation. Furthermore, breastfeeding duration was recorded by trained personnel at tight intervals during infancy. Thus, the lag of time between full-breastfeeding cessation and breastfeeding assessment was short, minimising recall bias.

The hypothesis that prolonged breastfeeding might be associated with bone health in childhood and adolescence has mainly been derived from two epidemiological studies. First, findings of an Australian cohort study indicated consistent positive associations between breastfeeding duration and DXA parameters at ages 8 and 16 years in children born at term (Jones *et al.* 2000; Jones 2011). Also, results of a follow-up study of preterm infants suggested that breastfeeding might be related to later bone health at

ages 5 and 20 years (Bishop *et al.* 1996; Fewtrell *et al.* 1999, 2009). In agreement with the findings of these two studies, a correlation of breastfeeding duration and DXA parameters at age 17 years has recently been reported from a Danish study (Molgaard *et al.* 2011). In contrast, there was no association between breastfeeding duration and bone parameters at ages 4 and 6 years in three further prospective cohort studies (Young *et al.* 2005; Ganpule *et al.* 2006; Harvey *et al.* 2009). Further studies did not reveal positive associations between breastfeeding duration in infancy and bone properties in adulthood (Cooper *et al.* 1997; Pearce *et al.* 2005; Laskey *et al.* 2007), with one study even indicating a moderate inverse relationship between breastfeeding duration and bone properties in adult men (Pirilä *et al.* 2011). Moreover, there is no strong evidence for a relation between breastfeeding duration in infancy and fracture risk in later life (Cooper *et al.* 2001; Ma & Jones 2002; Jones *et al.* 2004).

Putting our findings in the context of the overall evidence, more research is needed to establish human milk consumption as a factor influencing bone parameters in later life. In line with theoretical concepts that highlight the responsiveness of bone properties to concurrently operating mechanical exposures (Schoenau 2004; Schoenau & Fricke 2008), our results and findings from several other cohorts (Cooper *et al.* 1997; Pearce *et al.* 2005; Young *et al.* 2005; Ganpule *et al.* 2006; Harvey *et al.* 2009; Pirilä *et al.* 2011) suggest that factors representing current physical loads on bones, i.e. height, BMI and especially muscular force, play a more important role for bone strength than breastfeeding duration in infancy. Yet, it appears worth noting that in our study and multiple other studies (Bishop *et al.* 1996; Cooper *et al.* 1997, 2001; Fewtrell *et al.* 1999, 2009; Jones *et al.* 2000, 2004; Pearce *et al.* 2005; Young *et al.* 2005; Ganpule *et al.* 2006; Laskey *et al.* 2007; Harvey *et al.* 2009; Jones 2011; Molgaard *et al.* 2011), no adverse effects of a long breastfeeding duration on skeletal parameters in later life were detected, despite slower growth and initially lower body mass of breastfed infants during the first months of life. Thus, and given the various advantages of breastfeeding for mothers and children, the inconclusive evidence on the link between



breastfeeding and later bone health does not challenge breastfeeding recommendations by the WHO and German authorities.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Contributions

TK evaluated and interpreted the data and drafted the manuscript. AK, AEB, ES and TR revised the manuscript. AK interpreted the data and was responsible for the conceptual design of the data analysis. TR interpreted the data and was responsible for the study design. ES was responsible for the pQCT performance, the data collection and the study design. AEB managed and interpreted the data and was responsible for the study design.

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