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Effect of early life physical growth on midlife vertebral dimensions — The Northern Finland Birth Cohort 1966 study

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ABSTRACT

Small vertebral size is an independent risk factor for osteoporotic vertebral fractures. Physical growth in early life is related to bone health in later life, but the relationship of early growth versus vertebral size has been inconclusively studied. Utilizing the Northern Finland Birth Cohort 1966 with a 47-year follow-up, we investigated how physical growth in early life is associated with midlife vertebral dimensions. We obtained several physical growth parameters of 1) birth (gestational age, length, weight, BMI), 2) infancy and childhood (peak height velocity (PHV), peak weight velocity (PWV), adiposity peak (AP), adiposity rebound (AR)), and 3) puberty (BMI at growth spurt take-off (TO), PHV, height change). We also studied 4) the ages at which AP, AR, pubertal TO and pubertal PHV occurred. The outcome variable, vertebral cross-sectional area (CSA), was obtained from magnetic resonance imaging scans at the mean age of 46.7 years ($n = 517$). Sex-stratified linear regression analyses were used with adjustments for gestational age, smoking, and education. Birth length/weight/BMI, and adult height/weight/BMI were also used as covariates, depending on the model. According to our results, birth weight ($p \leq 0.006$) and infant PWV ($p \leq 0.001$) were positively associated with midlife vertebral CSA among both sexes. Length/height variables were associated with vertebral size only before including adult height in the models, and became non-significant thereafter. Among women, BMIs at birth, AP, AR, and pubertal TO were positively associated with midlife vertebral CSA ($p < 0.05$), whereas among men, only high BMI at AR was associated with large vertebral size ($p = 0.028$). Gestational age and timing of growth were not associated with future vertebral CSA. We conclude that early life weight gain is positively associated with midlife vertebral CSA, and suggest that adult height may mediate the effect of height gain on vertebral size.

1. Introduction

Osteoporosis is a major global health problem [1] characterized by a significant decline in bone mass and strength [2], and low-energy vertebral fractures are among its most common clinical manifestations [3,4]. A systematic review [5] previously concluded that small vertebral size is an independent risk factor for osteoporotic vertebral fractures, indicating that further knowledge on the factors that affect vertebral size would be beneficial.

Recent reviews [6–8] have shown clear evidence that growth in childhood and puberty is related to bone health in later life. While most publications have focused on bone mineral density (BMD) and bone mineral content (BMC) rather than geometry as outcome measures, some studies have associated growth in early childhood [9,10] and puberty [11,12] with later bone size. However, the interest of these studies has centered on skeletal segments other than the spine.

Data on vertebral size are very scarce. As regards early childhood, a Danish birth cohort study [13] of 44 boys and 64 girls found that the dual X-ray absorptiometry (DXA)-derived bone area of the lumbar spine (L1–L5) at the age of 17 years was associated with birth weight and length, and length at the age of nine months. It was not, however, associated with change in weight or length between birth and age nine months. The results were adjusted for sex. A South African study

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[14] of 254 boys and 222 girls found no association between the DXA-derived lumbar spine (L1–L4) bone area at the age of 10 years and birth weight, length at the age of one, or weight at the age of one year. The results were adjusted for race, socioeconomic status, bone age, height at the age of 10 years, and weight at the age of 10 years. We could find no published data on the potential relationship between pubertal growth and vertebral size. Nevertheless, the importance of revealing critical growth periods in terms of long-term bone strength has been emphasized [15].

In this study, we aimed to examine how growth in early life is associated with vertebral dimensions in midlife, utilizing the Northern Finland Birth Cohort 1966 study (NFBC1966). We investigated growth parameters including gestational age; birth length, weight, and body mass index (BMI); infant peak height velocity (PHV) and peak weight velocity (PWV); childhood adiposity peak (AP) and adiposity rebound (AR); BMI at pubertal growth spurt take-off (TO); pubertal PHV; and pubertal height change. In addition, we analyzed the ages at which AP, AR, pubertal TO and pubertal PHV occurred. As for vertebral size, we obtained the axial cross-sectional area (CSA) of the fourth lumbar vertebra (L4) in midlife using magnetic resonance imaging (MRI) scans. We hypothesized that rapid and vigorous growth in early life was associated with large vertebral size in midlife. We present the expansions for abbreviated growth parameters, alongside other abbreviations, in Table 1.

2. Materials and Methods

2.1. Initiation and progression of the cohort study

The Northern Finland Birth Cohort 1966 is a prospective population-based cohort study from birth onwards [16]. The population initially consisted of pregnant women living in the two northernmost provinces of Finland (Oulu and Lapland) with expected dates of delivery between Jan 1 and Dec 31, 1966 ($n = 12{,}068$ mothers, $n = 12{,}231$ children, 96% of all births during 1966 in the area). The cohort participants have been followed since 1966. During childhood and early adolescence, and at the ages of 14, 31 and 46, clinical examinations and questionnaires were used to gather information regarding the participants' health status, medication and lifestyle habits.

2.2. Sample selection of the present study

At the age of 46, NFBC1966 participants with known addresses in Finland ($n = 10{,}321$) were invited to fill in a questionnaire and to take part in clinical examinations (attendance rate in both 57%; $n = 5861$). Those who attended the clinical examinations and were living in the Oulu region ($n = 1988$) were additionally invited to lumbar MRI. The MRI study population consisted of 1540 participants (77% of those invited to attend the imaging), as 448 participants did not attend due to 1) no show ($n = 409$), 2) claustrophobia ($n = 35$), 3) severe obesity preventing the use of the machine ($n = 3$), or 4) a pacemaker ($n = 1$). After the imaging, 1023 participants were further excluded from this study due to 1) difficulties in measuring vertebral dimensions (segmentation error, severe disc degeneration, endplate erosions, presence of spondylodesis or Schmorl's nodes; $n = 159$), 2) bone-affecting medication (calcium supplements and/or osteoporosis medication; $n = 42$), and 3) missing growth data ($n = 770$) or covariate data ($n = 52$). Therefore, the final eligible population was $N = 517$ participants (26% of those invited to attend the imaging).

Table 1
Summary of abbreviations.

Abbreviation	Explanation
AP	Adiposity peak
AR	Adiposity rebound
BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
CSA	Cross-sectional area
DXA	Dual-energy X-ray absorptiometry
effTE	Effective echo time
FOV	Field-of-view
frFSE	Fast-recovery fast spin-echo
L4	Fourth lumbar vertebra
MRI	Magnetic resonance imaging
NFBC1966	Northern Finland Birth Cohort 1966
PHV	Peak height velocity
PWV	Peak weight velocity
SD	Standard deviation
TO	Growth spurt take-off
TR	Repetition time

2.3. Assessment of growth

From their birth in 1966 to late puberty, the children's length/height (cm) and weight (g) were measured and documented repeatedly during health care visits (mean 25.7 times, of which 7.4 within the first 18 months). Length/height was measured to the accuracy of 1 cm, and weight was rounded up to the nearest 10 g. BMI values (kg/m^2) were calculated according to these height and weight measurements.

The growth curves of each individual were based on the repeated height, weight, and BMI measurements. Detailed description of the process is provided elsewhere [17]. The curves in early childhood were fitted using the Reed1 model [18,19], and the JPA2 growth model [20,21] was accordingly used for puberty. These models were chosen as best-fitting after comparisons against other models [17].

The growth curve features which were examined in the present study were chosen according to a previous study [17] utilizing the same NFBC1966 population. Gestational age was calculated as the time difference in weeks between the last menstrual period as reported by the mother, and the birth date of the newborn. Childhood AP and AR (kg/m^2) were determined from the previously well-characterized sex-specific childhood BMI-for-age curves [22,23] as the local maximum and minimum, respectively (Fig. 1). Age at AP and AR were then obtained from the same curves (Fig. 1). PHV (cm/year) in infancy and puberty, and PWV (kg/year) in infancy were determined as the local maxima of the height-velocity-for-age and weight-velocity-for-age curves [24], respectively (Fig. 2 for PHVs). Since infant PHV and PWV were reached very early during the neonatal period, specific ages at which they occurred were not recorded. The age at which pubertal PHV occurred was determined from the height-velocity-for-age curve (Fig. 2). Pubertal growth spurt TO point was determined as the point just before the pubertal increase in height velocity (Fig. 2). Estimations of height and weight at the exact point of pubertal TO were obtained using linear interpolation, which was based on the two closest measurements, one before and one after the TO point. Pubertal height change (cm) was calculated as the difference between adult height and height estimation

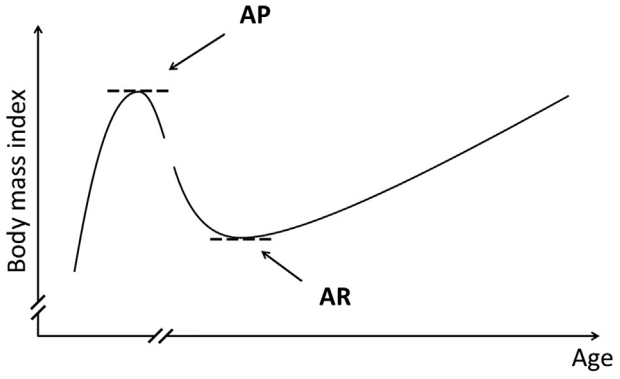

Fig. 1. Simplified BMI-for-age curve in childhood with its typical [23] characteristics. AP = adiposity peak, AR = adiposity rebound.