



## Review Article

# Low energy fractures in childhood: the association with an increased fracture risk in adulthood

Despoina Papadimitriou

Postgraduate Program "Metabolic Bone Diseases", National and Kapodistrian University of Athens, Medical School, Athens, Greece

## Abstract

This study aimed to investigate whether childhood fractures are associated with future risk of osteoporosis and fracture occurrence in adult life. Bone is a dynamic organ which is modified by bone modeling and remodeling. Peak bone mass is obtained in early adulthood and it is affected by a variety of modifiable and non-modifiable factors. In the last decades, childhood fractures have been increased by 35-65% due to many variable factors. Pediatric fractures are 10-25% of all pediatric injuries, their most common site is distal forearm and they are most frequent during the prepubertal and pubertal period of life. According to some cohort studies, childhood fractures are considered a risk factor for osteoporosis and future bone fragility. Most of the available data from published studies suggest that pediatric low-energy fractures are linked to decreased bone mass. However, based on our literature search the prognostic value of positive pediatric fracture history in osteoporosis and skeletal fragility is still debated.

**Keywords:** Childhood fractures, Fracture risk, Risk of osteoporosis

## Introduction

The composition of bone can serve the contradictory needs of stiffness, flexibility and lightness at the same time. The strength of bone is determined by its size, the quantity of bone tissue (g/area or g/volume), its quality (macroarchitecture and microarchitecture), the material composition and the repair of microcracks by bone turnover<sup>1</sup>.

Bone is not a static organ due to occurrence of continuous resorption and formation throughout life<sup>2,3</sup>. The processes of bone modeling and remodeling maintain the shape and strength of skeleton<sup>1</sup>. Bone size and shape are both affected by bone modeling, as this process includes bone production at one site and bone removal at another site within the same bone<sup>1</sup>. Bone remodeling is the replacement of mechanically old bone by bone resorption and the formation of new bone at the same site<sup>1</sup>. In early adulthood, once peak bone mass is obtained, remodeling is the superior proceeding throughout lifespan. During adolescence, the bone mass is increased because production of new bone tissue is greater than bone destruction. One quarter of peak bone mass is gained during the peak height velocity in puberty<sup>3</sup>. In the course of child growth, both muscle and lipid tissue expansion induce bone modeling and remodeling to meet the demands of the growing

skeleton<sup>3</sup>. Bone health and peak bone mass is influenced by modifiable and non-modifiable factors. Modifiable factors are the diet (calcium, vitamin D), physical activity, forces applied on the skeleton, puberty and hormonal status. Non-modifiable factors are genes, age, gender, ethnicity<sup>4</sup>.

A main contributing factor of the lifetime risk for osteoporosis is the magnitude of peak bone strength obtained by first years of adulthood. Bone strength depends on the peak bone mass (PBM) acquired and bone size, geometry, and microarchitecture accomplished through the childhood and adolescence. Genetic factors determine 60-80% of bone strength variability. However, the first two decades of life, ideal bone health is obligatory in order

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**Corresponding author:** Despoina Papadimitriou, Nikis 2, Kifisia 145 61, Athens, Greece

**E-mail:** nena.libra@hotmail.com

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to succeed the highest genetic potential of bone strength<sup>4</sup>. Childhood fracture risk is a complex and dynamic issue with numerous biological, behavioral, and environmental factors proposed to affect a child's fracture risk<sup>4</sup>. A 35 to 65% increase in pediatric fractures over the past four decades has been recorded in the bibliography<sup>3</sup>. Numerous factors may be at play here: possible decreased bone strength as a result of primary bone disease (i.e. osteogenesis imperfecta), secondary causes (i.e. diabetes, autoimmune diseases, cortisol etc), or factors mainly attributed to the force applied to the bones (i.e. falls, sports, abuse of the child etc).

Fractures are frequent in childhood and constitute 10-25% of all pediatric injuries. According to epidemiological studies, around 27-40% of girls and 42-50% of boys present at least one fracture during their childhood, which are corresponding to average annual incidence 103-165/10,000 for girls and 162-257/10,000 for boys<sup>5</sup>. The annual incident of fractures increased from ages 0 to 14, peaking in the 10 to 14 age range. Childhood fractures are predominantly located in distal forearm (25-35% of fractures)<sup>6</sup> and their typical mechanism is hyperextension injury while trying to avoid a fall<sup>7</sup>. Whereas finger fractures are the second most common fractures<sup>6</sup>. Fractures of femoral bone and lower extremities are rare during childhood, but there is an increased frequency of them in children with osteogenesis imperfecta<sup>7</sup>. Fractures due to abuse are especially common among infants (as they have not started to walk yet) and rib fractures are often related to abuse at any age<sup>7</sup>.

Our main question for this study was to investigate the hypothesis that fractures in adolescence may be associated with increased frequency of fractures later in life. Osteoporosis is a generalized skeletal disorder characterized by reduced bone mass and deterioration of bone architecture, thereby increasing the risk of fracture<sup>8</sup>. While osteoporosis is mainly encountered in individuals after the age of 50 and can be primary or secondary, postmenopausal osteoporosis has been regarded as a result not only of increased bone resorption due to the low levels of estrogen, but possibly of not adequate peak bone mass or bone strength attained during childhood or adolescence<sup>1</sup>. The possibility that fractures in early life have a prognostic value regarding osteoporosis and fractures in middle age and later has been acknowledged by various researchers and has been our working hypothesis for the present literature review.

## Materials and Methods

We conducted a search of the published literature using the PubMed (Medline) database using as keywords for an advanced search the expressions: fractures in childhood and adolescence; association between fractures in childhood and osteoporosis later in life. Inclusion criteria: publication date after the year 2000, papers in the English language, cohort studies either prospective

or retrospective that examined pediatric fracture as a risk factor for a fracture later in life. Exclusion criteria: papers regarding patients with osteoporosis in childhood (either primary or secondary), case reports or case-series, as well as reviews and conference papers.

## Results

Our primary search provided 67 articles. Of those, based in our inclusion and exclusion criteria, we included 6 studies.

Stephen R. Pye et al performed a prospective population-based study<sup>9</sup> in 2009 to determine if childhood fractures could predict fractures in later life. This study included both men and women above 50 years of age from population registers in 36 European Centers who were recruited for participation in European Prospective Osteoporosis Study (EPOS). Subjects were interviewed and completed a questionnaire about previous fractures (site, number, age and level of trauma). Prevalent vertebral deformities were detected by lateral spine radiographs. Participants were followed prospectively by annual post questionnaires, telephone or personal interview to determine the occurrence of clinical fractures. Any reported fracture had to be verified by X-ray, medical record or subject interview in order to be part of the final analysis. Mean follow-up time was 3 years. One part of participants had bone mineral density (BMD) measurements using DXA. A percentage of 36% of the participants had hip BMD measurements and 30% had spine measurements. The analysis included people aged 50-79 years due to the small number of subjects in the study cohort being over 80 years old. In this study, childhood fractures are defined as those that first occurred between the ages of 8 and 18 years because of concerns about report of fractures that happened earlier. A total of 6.451 men and 6.936 women were included in the analysis. At baseline, 11,6% of men and 11,2% of women had a extensive vertebral deformity. During follow-up, women had more incident limb fractures than men, for a total of 391 fractures in women and 140 in men. The occurrence of any childhood fracture was greater in men (8,9%) than in women (4,5%). Forearm fractures were the most frequent. However, information of childhood fractures was self-reported, thus introducing recall bias, and fractures above 18 years old are actually referred to fully grown individuals. According to this study, childhood fractures are not linked to future incident fractures and risk of prevalent vertebral deformity in either sex. The researchers could not find a statistical difference in bone mineral density (BMD) in adults with or without self-reported fractures in childhood (8-18 years old). This conclusion is contradictory to data from both cross-sectional and prospective studies suggest that a positive fracture history predicts a fracture event later in life<sup>10,11</sup>. There is evidence though that fractures during puberty are related to a lower bone mass. The results of this study

support the possibility that by growing and getting older the skeletal envelope fills and the childhood bone fragility and skeletal weakness does not continue in adult life<sup>9</sup>

In 2013, researchers Christian Buttazzoni et al reported results from a 27-year prospective controlled study<sup>12</sup>. They investigated if a pediatric fracture is a prognostic factor of low bone mass in young adulthood. All participants were Caucasian healthy individuals without any medical condition that could affect skeletal growth. Distal forearm BMD was measured with single-photon absorptiometry (SPA) in 47 boys and 26 girls (mean age 10 years) with an index fracture and in 41 boys and 43 girls (mean age 10 years) with no fracture. In the fracture group the skeletal evaluation was performed 40±25 days after the fracture event, in order to avoid the major influence of post-traumatic osteopenia. Children with a finger fracture had a significantly lower BMD than the children with no fracture. The subjects were assessed for an average of 27 years after the fracture event. The long duration of follow-up indicates that the participants have reached their peak bone mass. Bone mineral content (BMC) and bone mineral density (BMD) was measured by the same apparatus and at the same region at the baseline and at the follow-up. Anthropometric measurements (body weight, body height) and questionnaires about lifestyle, diseases and drugs were also performed both at baseline and follow-up. According to this study, boys with a fracture have a BMD deficit of -0.4 SD compared to boys with no fracture and the respective deficit in girls is -0.2 SD. These results are in close accordance to the conclusion of a systematic review and meta-analysis that included all articles published in 1965-2005 which found a mean BMD deficit of -0.3 SD in children with a fracture<sup>13</sup>. In this study, there were no changes in the BMC and BMD deficit from growth into adulthood, in participants with low, moderate or high energy trauma. Low BMD at childhood though is associated to low PBM in adulthood. In conclusion, a pediatric low-energy fracture in men was associated with low BMD and smaller bone size at the radius and tibia compared with controls. Defects in bone density and structure detected in adult women with a pediatric fracture were smaller in comparison to those seen in men and they had not any statistical significance related to their controls. According to published prospective observational studies<sup>10</sup>, it is accepted that a deficit of -0.4 SD would be associated with a 40% higher fracture risk than expected by age and the fracture risk in adult men with a positive fracture history in adulthood is more than 40% due to the smaller bone size. So, low-energy fractures in boys are strongly correlated to increase fracture risk in adulthood (due to low BMD) and increase risk to osteoporosis (due to low PBM).

In 2013, Amin and colleagues studied a population-based cohort<sup>14</sup> of 1776 children who had a distal forearm fracture in 1935-1992 in Olmsted County, MN, USA. The subjects of analysis (1086 boys and 690 girls) had a long-term follow-up to determine the risk for all types of fractures

on or after the age of 35 years. The median age at follow-up was 49 years and 48 years for men and women respectively. Any subsequent fracture was defined by medical records in the community. The cumulative incidence of a fracture on or after age 35 years was evaluated using the Kaplan Meier method. Over 40% of boys and girls had at least a fracture at any site during childhood. In conclusion, men but not women who had a distal forearm in childhood due to high or low energy trauma are related to an increased risk of future fragility fractures as adults. In particular, their risk of any fracture event is twofold greater compared to that expected in community men. It is understood that men with history of a previous childhood fracture in the forearm have a greater fracture risk not only in comparison to men that they have a negative history of previous fracture but also to women. Decreased bone strength as a remnant of childhood, high risk behavior or their combination may be the main factors that define higher fracture incidence in men with a distal forearm fracture in childhood. The results of the particular study is possible to be applied in the future in clinical level. This means that elderly men should be asked for history of a previous pediatric fracture in the distal forearm. Men with a positive fracture history should have a further check-up and the appropriate preventive measures to improve their bone health and prevent fractures.

## Discussion

Recent data suggest that both advantages and disadvantages in BMD obtained during growth may be reserved into adulthood. A childhood low-energy fracture is such a contributing factor for low BMD<sup>12</sup>. Most adult bone mass is obtained by the end of puberty, negative effects on the development of peak bone mass and structure during childhood and adolescence may be significant predictors on the risk of future osteoporosis<sup>14</sup>. Future bone health and the skeletal fragility in adult life is strongly associated with the quantity of bone that is "stored" in growth spurt through the first years of adult life<sup>3</sup>.

According to epidemiological studies the future fracture risk could be decreased by half if the peak bone mass (PBM) increases by 10%. One of the most effective ways for osteoporosis prevention is improving PBM during the third decade of life<sup>15</sup>. During their lifespan women's peak bone mass is reduced by 30% to 50%, whereas men's by 20% to 30%, so women have more vulnerable skeleton to osteoporotic fractures than men. The rhythm of bone gain though, is not the same during all stages of maturation, for example 26% of PBM is obtained during the 2 years of peak bone accretion in adolescence<sup>15</sup>.

According to studies, childhood fractures may be related to low peak bone mass (PBM) and might be markers for persistent bone fragility and higher risk for osteoporosis in adulthood. It is proven that the bone mineral content (BMC) of a previously fractured forearm is decreased about 10%<sup>16</sup>. Bone strength, is thought to be the basis of fracture

prevention. It is mainly affected by the following factors: bone size, bone mineral density and the organization of bone microarchitecture<sup>17</sup>. Consequently, accretion of peak bone strength must be upgraded during the growth spurt to decrease the risk of osteoporosis in adult life. This can be achieved by a healthy body mass index (since both obese and very thin children have been associated to fractures) which requires the appropriate for age intake of calories, protein, calcium, and vitamin D and adequate physical activity<sup>18</sup>.

Osteoporosis is the most significant process of bone loss in adulthood. However, the BMD accretion during growth predicts the vulnerability of skeleton in adult life, as according to recent data the half value of BMD at 65 years old people is determined by PBM<sup>12</sup>. Puberty is proposed as the most important period in bone production and it is the “bone bank” of future skeleton. Nearly half of bone mass, about 40%, is obtained during the 4 peripubertal years<sup>12</sup>, and peak bone mass is achieved into early adulthood<sup>3</sup>. In conclusion, although osteoporosis is thought as a geriatric disease, its roots may be in childhood. Most evidence-based results show a correlation between pediatric fractures and risk of fracture or osteoporosis in adult life<sup>10,11</sup>. However, some researchers have described childhood fractures as independent factors that do not predict osteoporosis or bone fragility later in life<sup>9</sup>. It is almost generally accepted, though, that low-energy fractures in puberty are highly linked to lower bone mass<sup>9</sup>. Finally according to significant studies, a possible fracture event and future osteoporosis, mainly in men, is predicted by positive fracture history during childhood<sup>12,14</sup>.

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