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Childhood Fractures Do Not Predict Future Fractures: Results From the European Prospective Osteoporosis Study

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on behalf of the EPOS Study Group

ABSTRACT: Childhood fractures are common. Their clinical relevance to osteoporosis and fractures in later life is unclear. The aim of this study was to determine the predictive risk of childhood fracture on the risk of fracture in later life. Men and women ≥50 yr of age were recruited from population registers for participation in the European Prospective Osteoporosis Study (EPOS). Subjects completed an interviewer administered questionnaire that included questions about previous fractures and the age at which the first of these fractures occurred. Lateral spine radiographs were performed to ascertain prevalent vertebral deformities. Subjects were followed prospectively by postal questionnaire to determine the occurrence of clinical fractures. A subsample of subjects had BMD measurements performed. Cox proportional hazards model was used to determine the predictive risk of childhood fracture between the ages of 8 and 18 yr on the risk of future limb fracture and logistic regression was used to determine the association between reported childhood fractures and prevalent vertebral deformity. A total of 6451 men (mean age, 63.8 yr) and 6936 women (mean age, 63.1 yr) were included in the analysis. Mean follow-up time was 3 yr. Of these, 574 (8.9%) men and 313 (4.5%) women reported a first fracture (any site) between the ages of 8 and 18 yr. A recalled history of any childhood fracture or forearm fracture was not associated with an increased risk of future limb fracture or prevalent vertebral deformity in either men or women. Among the 4807 subjects who had DXA measurements, there was no difference in bone mass among those subjects who had reported a childhood fracture and those who did not. Our data suggest that self-reported previous childhood fracture is not associated with an increased risk of future fracture in men or women.
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Key words: childhood fracture, prevalent vertebral fracture, incident limb fracture, epidemiology, prospective study

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INTRODUCTION

Childhood fractures are relatively common. The incidence increases during the peripubertal years during the period of rapid skeletal growth and is higher among boys than girls.[1] There is evidence from several studies that low bone mass is a predictor of future fracture. Thus, in a series of girls with distal forearm fracture, bone mass was lower than a group of matched controls.[2] The results of a systematic review of case-control studies and a recent prospective study suggested that there is an association between low BMD and fractures in children.[3,4] Such fractures seem therefore to be a marker of bone fragility in childhood.

There is strong evidence to suggest that fractures in later life are linked with an increased risk of future fractures.[5,6] There is some evidence that peri/premenopausal fractures are linked with an increased risk, and in one study, fractures as early as age 20 were linked with future fracture risk.[7–11] There is, however, to our knowledge no good evidence linking childhood fracture to the risk of fracture in later life. Such data are important—evidence that childhood fractures are linked with an increased risk of future fracture provides an important rationale for considering affected individuals for assessment and therapy to prevent further bone loss and reduce morbidity in later life. Also identification of a history of fracture in childhood as a risk predictor of future fracture would help inform the development of more targeted risk assessment tools. We used data from the European Prospective Osteoporosis Study (EPOS) to determine whether fractures reported in childhood were linked with an increased risk of fractures in later life.

The authors state that they have no conflicts of interest.

MATERIALS AND METHODS

Subjects

The subjects were recruited for participation in the European Prospective Osteoporosis Study (EPOS). The

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detailed methods concerning the baseline phase have been described elsewhere.[12] In brief, men and women ≥50 yr of age were recruited from population registers in 36 European centers. Stratified sampling was used with the aim of recruiting equal numbers of men and women in each of six 5-yr age bands: 50–54, 55–59, 60–64, 65–69, 70–74, and ≥75 yr. Subjects were interviewed using a structured interview that included questions about previous fractures. Subjects were asked ''Have you ever suffered from a broken bone (fractures).'' If yes, subjects were asked about the site of their previous fracture(s) (vertebral, hip, rib, forearm, other), number of fractures, the age of their first fracture (at each site), and the level of trauma (spontaneous, minor, or major trauma) for that fracture.

Lateral spinal radiographs were performed to ascertain prevalent vertebral deformities. The radiographs were evaluated morphometrically by one of three observers and the presence of vertebral deformity determined using the McCloskey-Kanis method.[13]

Follow-up

The subjects recruited in 29 centers were followed prospectively by annual postal questionnaire and in a further 3 centers by telephone or personal interview. However, because of a low follow-up rate, data from one center were subsequently excluded from the analysis. Subjects were asked to record details of any fractures sustained in the intervening period, including marking on a body manikin (included in a previously validated postal questionnaire) the position or site of their fractures.[14] Fractures reported were verified at each of the participating centers by the principal investigator by review of radiographs, medical record, or subject interview. From these sources, contemporary data to confirm or refute the occurrence and site of fracture were not available in 9% of cases. In these cases, the site of fracture was determined from the area marked by the subject on the manikin.[14]

BMD measurements

A subsample of 21 centers was able to measure BMD at the hip and or the spine at baseline or during follow-up in subsamples of between 20% and 100% of their available participants using DXA. The densitometers in each center were, with one exception (a Sopha fan-beam machine), pencil beam DXA machines made by Lunar, Hologic, or Norland. They were cross-calibrated using the European Spine Phantom (ESP).[15] The ESP is a semianthropomorphic phantom with three ''vertebrae'' of known densities 0.5, 1.0, and 1.5g/cm^2.[15] At least five measurements of the phantom were made on each machine, and a two-parameter empirically fitted linear or exponential calibration curve used to convert measured density values into standardized values, as previously described.[16] For the participants considered in this analysis, 4807 (36%) from 19 centers had hip BMD (femoral neck and/or trochanter) measurements, and 3998 (30%) from 14 centers had spine BMD measurements. Those who had a scan were slightly younger than those who did not (63.1 versus 63.6 yr); however, there was no difference in the proportion of subjects who reported a childhood fracture between the two groups.

TABLE 1. Occurrence of Recalled Childhood Fractures (Age 8–18 yr), Prevalent Vertebral Deformities, and Incident Limb Fractures in Men and Women

	Men (n = 6451) [n (%)]	*Women (n = 6936) [n (%)]*
Prevalent vertebral deformity	717 (11.6)	740 (11.2)
Any recorded adult incident fracture*	215 (3.3)	472 (6.8)†
Any recorded adult incident limb fracture	140 (2.2)	391 (5.6)†
Any fracture‡ aged 8–18 yr	574 (8.9)	313 (4.5)†
Forearm fracture aged 8−18 yr	239 (3.7)	130 (1.9)†

* Excludes incident vertebral deformities.
† $p < 0.05$.
‡ First reported fracture at any site (vertebra/hip/rib/forearm/other).

Analysis

The analysis was restricted to subjects 50–79 yr of age at baseline because the proportion of the study cohort above the age of 80 yr was small. We defined childhood fractures as those that first occurred between the ages of 8 and 18 yr. The younger age limit was chosen pragmatically because of concerns about recall of earlier fractures. In the prospective phase incident limb fractures were classified using the ninth edition of the International Classification of Diseases.[17] Cox proportional hazards model was used to assess the predictive risk of childhood fracture on the risk of nonvertebral fractures sustained during the EPOS follow-up study. Subjects contributed follow-up time (person years) from the date of the baseline survey until limb fracture, death, or the end of the study. In subjects who sustained more than one incident fracture of the same type during follow-up, the time to the first fracture event was used in the analysis. The results of this analysis were expressed as hazards ratios (HRs) and 95% CIs.

We looked also at the association between self-reported childhood fractures and prevalent vertebral deformity (identified from morphometry at the baseline survey). For this analysis, we used logistic regression with the results expressed as ORs and 95% CIs. All analyses were undertaken separately in men and women with adjustments made for center. Analyses were performed using the statistical package STATA.[18]

RESULTS

Subjects

A total of 6451 men (mean age, 63.8 ± 8.0 [SD] yr) and 6936 women (mean age, 63.1 ± 7.9 yr) were followed for a median of 3 yr (range, 0.4–5.9 yr), for a total of 41,042 person-years of follow-up. At baseline, 717 (11.6%) men and 740 (11.2%) women had evidence of a prevalent vertebral deformity (Table 1). During the follow-up period, there were 391 incident limb fractures in women and 140 in men.

TABLE 2. Number (%) of Men and Women With a History of Childhood Fracture By Age of First Fracture

Age (yr)	*Men [n (%)]**	*Women [n (%)]**
8	43 (7.5)	23 (7.3)
9	31 (5.4)	16 (5.1)
10	71 (12.4)	54 (17.3)
11	32 (5.6)	22 (7.0)
12	82 (14.3)	51 (16.3)
13	37 (6.4)	29 (9.3)
14	55 (9.6)	19 (6.1)
15	52 (9.1)	21 (6.7)
16	53 (9.2)	36 (11.5)
17	48 (8.4)	20 (6.4)
18	70 (12.2)	22 (7.0)

* Percentage is the number of fractures in each age band divided by the total number of fractures multiplied by 100.

Occurrence of childhood fractures

Childhood fractures between the ages of 8 and 18 yr were reported by 574 (8.9%) men and 313 (4.5%) women. Of these, forearm fractures were the most frequent (men = 239, women = 130; Table 1). Both history of ''any'' and forearm fractures were more common in men than women. The mean age for occurrence of any fracture was slightly greater in men than women (13.3 versus 12.8 yr ; $p < 0.05$). The frequency of occurrence of first reported fracture (any site) by age in both men and women is shown in Table 2. If an individual had sustained fractures at different sites (between 8 and 18 yr), the age of the earlier fracture was included.

Childhood fracture and risk of future fracture

There was no association between the occurrence of childhood fracture (any site) and future incident fracture or incident limb fracture in men and women (Table 3). Small numbers at individual fracture sites precluded analysis, for example, of the association between childhood forearm fractures and future fracture. The risk of incident fracture was not influenced by follow-up time. There was no association between the occurrence of childhood fracture and the risk of prevalent vertebral deformity (ascertained at the baseline survey) in either sex (Table 3).

Childhood fracture and BMD

In both men and women, BMD measurements at the spine and femoral neck were similar among those who did and did not report sustaining a fracture during childhood (Table 4). This was true also when analysis was restricted to those with a childhood forearm fracture.

DISCUSSION

In this prospective study, childhood fractures were not associated with an increased risk of subsequent limb or vertebral deformity.

Our study had several advantages: data concerning incident fractures were collected prospectively, it was population based, and it included both men and women. There are, however, several limitations that need to be considered when interpreting the results. Classification of childhood fractures at the baseline survey was based on self-report of events that occurred decades earlier and subject therefore to errors of recall. When compared with fracture rates in population-based studies from Scandinavia, the United Kingdom, and the United States, the reported fracture rates seem lower,[1,19,20] although the epidemiological pattern is similar in that fractures were more common in boys than girls and occurred at an older age in boys. In the United Kingdom, data from the General Practice Research Database suggest that around one third of boys and girls sustain at least one fracture before 17 yr of age, with a peak annual incidence in boys of ~3% and in girls of 1.5%.[1] There is evidence, however, that there has been a secular increase in the occurrence of fracture from several countries, which may in part explain the apparent difference.[19,20] In Rochester, MN, fracture rates from ages 0 to 34 yr increased by 32% in male residents and 56% in female residents between 1969–1971 and 1999–2001, with most of the excess occurring in those 0–20 yr of age.[20] In Malmo, Sweden, there was an increase in distal forearm fractures of ~60% in girls and 35% in boys between 1950 and 1979.[19] We cannot, however, exclude under-reporting as a possible cause. In our study, we asked about age at first fracture rather than specifically about childhood fractures, and it may be that, for some participants, these fractures may not have been considered relevant or important. Recall is likely to have been poor in relation to age of fracture; however, our main analysis was based on occurrence rather than timing of fracture. We looked separately at individuals with reported childhood fractures between 8 and 14 and 15 and 18 yr on the basis that recall may have been better for the later fractures; however, the results of the analyses looking at future fracture risk were similar for the two groups. The occurrence of a recent fracture may have influenced recall of childhood fracture; however, given that the study was prospective with incident fractures occurring after the baseline assessment, this would be relevant for prevalent vertebral deformities only and would tend if anything to bias the results in favor of a positive association.

Errors may also have occurred in the classification of incident fractures. To reduce the risk of over-reporting, fractures were where possible confirmed by either review of the radiograph or contemporary medical records or subject interview. In a small proportion of cases (9%), it was not possible to confirm fracture by any of these methods; however, restricting the analyses to those individuals in whom fractures were confirmed did not affect the results (data not shown). Given the study design, it was not possible to assess the degree of under-reporting. In a separate study, however, among 174 subjects with a known history of previous fracture, only 12 (7%) did not recall the event, and only 3% of subjects did not recall a hip or distal forearm fracture.[14] The effect of any under-reporting would tend to reduce the chance of finding any significant association between childhood fracture and future limb fracture. There is no gold standard for defining vertebral

TABLE 3. Influence of Childhood Fracture on Risk of Future Fracture in Men and Women

	Any incident fracture [HR† (95% CI)]*	*Incident limb fracture [HR† (95% CI)]*	*Prevalent vertebral deformity [OR‡ (95% CI)]*
Men			
Any fracture aged 8–18 yr			
No	Referent	Referent	Referent
Yes	1.1 (0.7, 1.7)	1.1 (0.6, 2.0)	0.8 (0.6, 1.1)
Women			
Any fracture aged 8–18 yr			
No	Referent	Referent	Referent
Yes	0.7 (0.4, 1.1)	0.7 (0.4, 1.3)	1.1 (0.8, 1.6)

* Excludes incident vertebral deformities.
† HR adjusted for center.
‡ OR adjusted for center.

TABLE 4. Influence of Childhood Fracture on BMD in Men and Women

	Men		*Women*	
	Any fracture 8–18 yr [mean (SD)]	*No fracture 8–18 yr [mean (SD)]*	*Any fracture 8–18 yr [mean (SD)]*	*No fracture 8–18 yr [mean (SD)]*
Femoral neck BMD (g/cm^2)	0.827 (0.159)	0.827 (0.142)	0.727 (0.137)	0.726 (0.137)
Trochanteric BMD (g/cm^2)	0.768 (0.144)	0.768 (0.139)	0.635 (0.138)	0.627 (0.124)
Spine BMD (g/cm^2)	1.036 (0.216)	1.063 (0.227)	0.919 (0.195)	0.923 (0.209)

deformity—we used a morphometric approach with good specificity and have shown a significant association between deformities defined using the method and low BMD.[13,21] Finally our results were derived from a predominantly white population in Europe who sustained childhood fractures over 50 yr ago, and the data should be extrapolated beyond this population with caution.

Data from both cross-sectional and prospective studies suggest that the presence of a prior fracture is a strong predictor of future fracture.[5,6] The risk seems greater for vertebral deformity predicting subsequent vertebral deformity, although there is an increased risk for any fracture.[5] The increased risk seems in part related to, although independent of, BMD.[6] In several studies, peri/premenopausal fractures have been shown to predict the risk of future fracture.[7–11] The mechanism by which fracture increases risk of future fracture is unknown, although it is thought in part to relate to reduced bone fragility and possibly an increased risk of falls. To our knowledge, there are no data concerning the relationship between childhood fracture and future fracture risk. Our data suggest no increased risk of future fracture or prevalent vertebral deformity linked with childhood fracture. Information was available on incident vertebral deformities; however, the numbers were too small to allow any meaningful analyses.

There is evidence that fractures during adolescence are linked with a reduced bone mass.[2–4] Whereas BMC continues to accrue during growth, there is dissociation between increase in height and mineralization of the skeleton. This corresponds to the time of peak fracture occurrence in childhood. The higher risk of fracture in boys would suggest that trauma plays an important role also in determining susceptibility to these fractures. It is possible that with increasing age the skeletal envelope fills and therefore childhood bone fragility does not track into later life. This is supported by our findings showing no increased fracture risk linked with childhood fracture and, in the subsample with measurements, no association with BMD.

What are the implications of our findings? Our data relate to fractures that occurred many years ago and may not necessarily be relevant to current childhood fractures. Further cross-sectional and prospective studies are required looking at the predictive risk of childhood fractures, which have occurred more recently and fractures in late life. Until such results are available, it would seem prudent to optimize lifestyle factors relating to skeletal growth among children who sustain childhood fractures. In assessment of fracture risk among older men and women, however, our data would suggest that a recalled history of fracture during childhood is not an important determinant of fracture risk.

In conclusion, this study showed that childhood fractures do not seem to be linked with a significant increase risk of future fracture. In assessment of future fracture risk, a history of childhood fracture does not seem to be important.

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