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Alimentary Tract

Pediatric-onset inflammatory bowel disease poses risk for low bone mineral density at early adulthood

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ABSTRACT

Background: Inflammatory bowel disease (IBD) is known to pose a risk for low bone mineral density (BMD) in children and adults. We aimed to evaluate the impact of pediatric-onset IBD on BMD in adulthood.
Methods: Records of pediatric-IBD patients were retrospectively reviewed for documentation of dual-energy X-ray absorptiometry (DXA) scans in adulthood. BMD was expressed as z-score.
Results: Sixty one patients were included. Mean (±SD) age at diagnosis was 14.7 (±2.4) years. Mean age at first DXA scan in adulthood was 23.9 years (±4.8). Median BMD z-score was −1.2 SD (IQR, −1.8 to −0.4), significantly lower than expected in normal population ($p < 0.001$). Osteopenia (BMD z-score ≤−1 SD) was noted in 44.3% (n = 27), and osteoporosis (BMD z-score ≤−2.5 SD) in 8.2% (n = 5). Bone-status showed no correlation with age, disease severity, vitamin D status at diagnosis, IBD subtype or duration of disease. Positive correlation ($r = 0.306$) was identified between low weight z-score at diagnosis and abnormal bone-status in adulthood. Among 36 patients with multiple DXA scans, there was no significant change in BMD during follow-up of 2.4 years.
Conclusions: Osteopenia and osteoporosis are frequent in adult IBD patients with pediatric-onset disease and correlates with low weight z-score at diagnosis.

1. Introduction

Inflammatory bowel disease (IBD) is known to pose a risk for metabolic bone diseases, including osteopenia, osteoporosis, poor growth and high prevalence of fractures [1]. The pathogenesis of bone disease in IBD patients is multifactorial, including the impact of inflammatory cytokines on bone homeostasis, the effects of medical therapies such as corticosteroids on bone metabolism, the consequences of poor nutritional status, lack of physical activity, and environmental factors including smoking [2–4].

Bone mass is accrued mostly during childhood, and reaches its peak by the end of the second decade of life. Most studies refer to peak bone mass accrual by the age of approximately 18 and 20 years, in females and males respectively [5], but some reported further bone mass accrual until the age of 23 years [6].

The onset of IBD during childhood and adolescence may compromise final bone mineral density (BMD) via negative effect on growth and development, as well as the potential detrimental impact on the normal process of bone mass accrual, in this critical period. Most studies reporting the prevalence and risk factors of metabolic bone disease in IBD were performed on adult population, thus lacking data regarding the effect of pediatric-onset IBD on bone mass accrual and BMD at early adulthood.

The aim of this study was to evaluate the impact of pediatric-onset IBD, on BMD at early adulthood.

2. Methods

2.1. Patients

We conducted a retrospective chart review of all pediatric onset IBD patients, diagnosed between the ages 2–17 years at the Schneider Children's Medical Center of Israel Between 1981 and 2013 who had documentation of dual energy X-ray absorptiometry (DXA) scans at early adulthood. Diagnosis of IBD was performed according to accepted criteria [7,8]. Data were retrieved from both pedi-

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atric medical charts (Schneider Children's Medical Center) and adult medical charts for patients followed-up into adulthood (Rabin Medical Center).

For this study adult age was defined as the average age of peak bone mass accrual-18 years for females and 20 years for males [5]. In addition we analyzed the changes in BMD in patients who had more than one DXA scan during follow-up years, regardless of the age at which the scan was performed.

The study protocol was approved by the Rabin Medical Center Internal Review Board which represents both the Schneider Children's Medical Center and the Rabin Medical Center.

2.2. Description of variables

Age at onset; gender; anthropometric measurements; laboratory findings; medical treatments and clinical characteristics of the disease were thoroughly investigated by reviewing medical records. Disease activity was assessed using the Harvey Bradshaw Index (HBI) for CD and the Pediatric UC Activity index (PUCAI) for UC.

2.3. Bone mineral density measurements

Bone mineral density was measured by Dual Energy X-Ray Absorptiometry (DXA), (LUNAR DPX 5548 till 2006, and LUNAR IDEXA ME + 200181 from 2007). DXA was performed on lumbar spine L1–L4 and femoral neck routinely, with addition of total-body DXA in all children, and in some adults according to clinical request. The BMD was expressed as z-score, calculated using the lower measurement between lumbar and femoral-neck BMD for each patient. Osteopenia was defined as z-score ≤ -1 SD whereas osteoporosis was defined as z-score of ≤ -2.5 SD.

2.4. Statistical analysis

Categorical variables were described as frequency and percentages. Continuous variables were evaluated for normal distribution using histogram and Q–Q plots. Chi square test and Fisher's exact test were used to evaluate the impact of categorical variables at diagnosis on early adulthood bone status. Independent sample T test and Mann–Whitney test were used for continuous variables. Correlations between continuous variables were assessed using Pearson Correlation Coefficient. One Sample Chi-square test and One Sample Binomial test were used to compare the bone status of the study cohort with that of the normal population.

Multivariable logistic regression using backward-likelihood ratio method was used to evaluate the association between various potential predictors (gender, age at diagnosis, diagnosis, weight z-scores, low vitamin D, years to peak BMD), and bone status. Univariate and multivariate linear mixed models were used to assess changes in BMD during follow-up.

$p < 0.05$ was considered as statistically significant. All tests were two-tailed.

SPSS version 23 (IBM Corp. Armonk, NY) was used for all statistical analysis.

3. Results

Sixty one patients with DXA scans performed during early adulthood were included in the study (31 males, 50.8%). The study group was composed of 42 patients diagnosed with Crohn's disease (CD) and 18 patients with Ulcerative Colitis (UC). Mean (±SD) age at diagnosis was 14.7 (±2.4) years, and mean age at first DXA scan in adulthood was 23.9 years (±4.8).

There were no significant differences between UC and CD patients regarding: male to female ratio; age at diagnosis; weight, height and BMI z-scores at diagnosis; age at first DXA scan in adulthood; mean BMD z-score, prevalence of osteopenia and osteoporosis. There was a greater portion of clinically severe disease, (defined by PUCAI for UC patients, and HBI for CD patients) among the UC group-70.6%, compare to 33.3% of the CD patients ($p = 0.01$). Low vitamin D status (defined as 25-Hydroxy Vitamin D <50 nmol/L) was observed in 20.3% of the patients (n = 12) at time of IBD diagnosis.

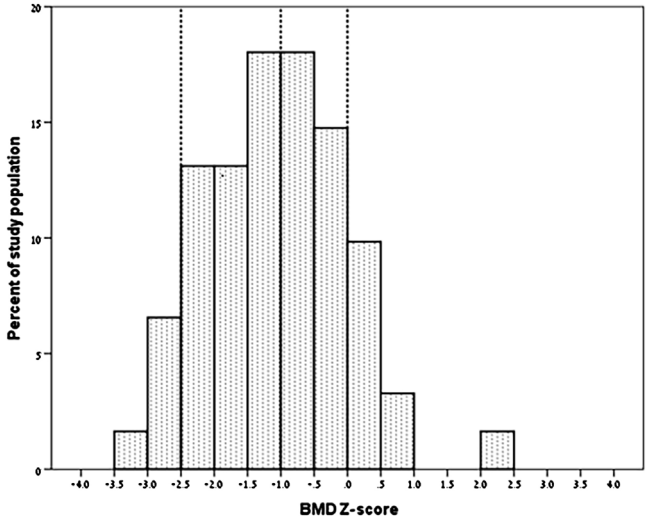

Fig. 1. Bone mineral density (BMD) distribution in adulthood. BMD distribution demonstrates a median BMD z-score of −1.2 SD (IQR, −1.8 to −0.4) with 44.3% (n = 27) patients showing osteopenia, and 8.2% (n = 5) osteoporosis.

Results of BMD distribution are demonstrated in Fig. 1. The median BMD z-score was −1.2 SD (IQR, −1.8 to −0.4), significantly lower than the median of zero expected in normal population ($p < 0.001$). Overall, abnormal BMD (z-score ≤ -1 SD) was found in 52.5% of the patients (n = 32), with 44.3% (n = 27) identified with Osteopenia, and 8.2% (n = 5) with Osteoporosis.

Table 1 outlines the association between baseline and follow-up parameters with bone status, categorized as either normal (>−1 SD), or abnormal (≤ -1 SD). Except for weight z-score, no other diseases' or patients' parameters at diagnosis showed any correlation to the bone status at early adulthood, including age and gender; disease type (Crohn's vs. UC); disease severity at diagnosis; vitamin D status at diagnosis, or the duration of disease until adulthood or until first DXA scan in adulthood.

Furthermore, the course and severity of the disease during follow up, as reflected by rates of exacerbations, hospitalizations and need for surgical treatments-did not demonstrate any association with final BMD (as outlined in Table 1). Moreover, the rates of corticosteroids courses per year were similar: 0.7 courses per year of follow-up in the group of patients with normal adulthood BMD, vs. 0.85 courses per year in the group with abnormal adulthood BMD ($p = 0.42$). The prevalence of anti-TNF exposure was 68% in both groups.

Using multivariable logistic regression analyses, a positive correlation was found, after adjustment for age at diagnosis, between weight z-score at diagnosis and BMD z-score at early adulthood, $r = 0.306$ ($p = 0.017$). Median weight z-score at diagnosis was −0.8 (IQR, −1.8 to −0.15) for patients with abnormal bone status, versus −0.33 (IQR, −0.9 to 0.47) for patients with normal bone status (Fig. 2).

During follow-up, 36 patients had more than one DXA scan. Mean (±SD) age at first DXA scan was 17.8 years (±4.7), and median time between first and second DXA scan was 2.4 years (IQR, 1.6–4.5).