

Evaluation of Bone Mineral Density in a Cohort of Children with Growth Hormone Deficiency

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BACKGROUND

- Growth Hormone (GH) has an important role on both linear growth and bone turnover during childhood
- GH deficiency (GHD) may cause secondary osteoporosis associated with low bone mineral density (BMD), impairment of bone turnover, and increased fracture risk

AIMS OF THE STUDY

- To assess the BMD using the dual energy x-ray absorptiometry (DEXA) in a cohort of children with GHD
- To evaluate associations between BMD and both auxological and biochemical data before the start of recombinant human GH (rhGH) therapy

PATIENTS AND METHODS

- 193 patients (aged 9.68 ± 3.27 years, 58% males, 75% pre-pubertal) with GHD were recruited in the study
- In all patients, before the start of rhGH therapy, we collected
 - auxological data [chronological age (CA), height (Ht), z-score body mass index (BMI), growth velocity (GV), sitting Ht, SPAN, pubertal status, target Ht (TH)]
 - biochemical data (IGF-1, IGFBP-3, and bone metabolism indices)
 - DEXA of lumbar spine (L1-L4), bone age (BA), and brain nuclear magnetic resonance (NMR) imaging
- BMD was expressed as z-score according to the International Society for Clinical Densitometry (ISCD)
- Data were analyzed using non-parametric statistical analysis (STATISTICA software, StatSoft Inc, Tulsa, OK, USA)

RESULTS

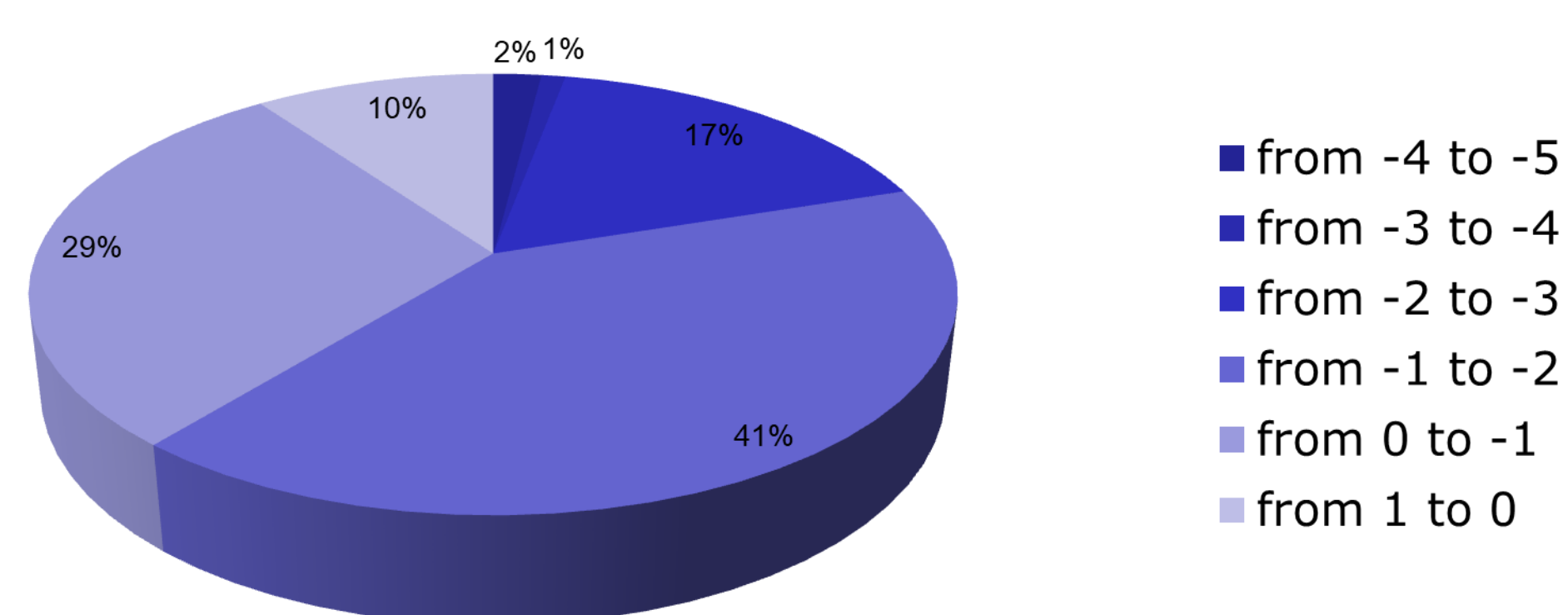
1. Auxological data

	All patients (193)	Male (112)	Female (81)
CA (yrs.)	9.68 ± 3.27	9.96 ± 3.50	9.29 ± 2.89
Ht (SDS)	-2.59 ± 0.61	-2.48 ± 0.47	-2.73 ± 0.74 *
GV (SDS)	-1.74 ± 1.75	-1.87 ± 1.80	-1.56 ± 1.68
TH (SDS)	-0.80 ± 0.75	-0.71 ± 0.75	-0.94 ± 0.74
Ht correct for TH (SDS)	-1.50 ± 0.79	-1.49 ± 0.75	-1.52 ± 0.85
z-score BMI (SDS)	-0.97 ± 1.16	-0.93 ± 1.12	-1.03 ± 1.23
BA – CA (yrs.)	-1.83 ± 0.94	-2.06 ± 1.02	-1.57 ± 0.77 *
SPAN/Ht ratio	0.95 ± 0.22	0.96 ± 0.21	0.93 ± 0.24
Sitting Ht/Ht ratio	0.51 ± 0.10	0.51 ± 0.11	0.52 ± 0.09

- Females had significantly lower Ht SDS respect to males
- The discrepancy between BA and CA resulted significantly higher in males compared to females

* p < 0.05

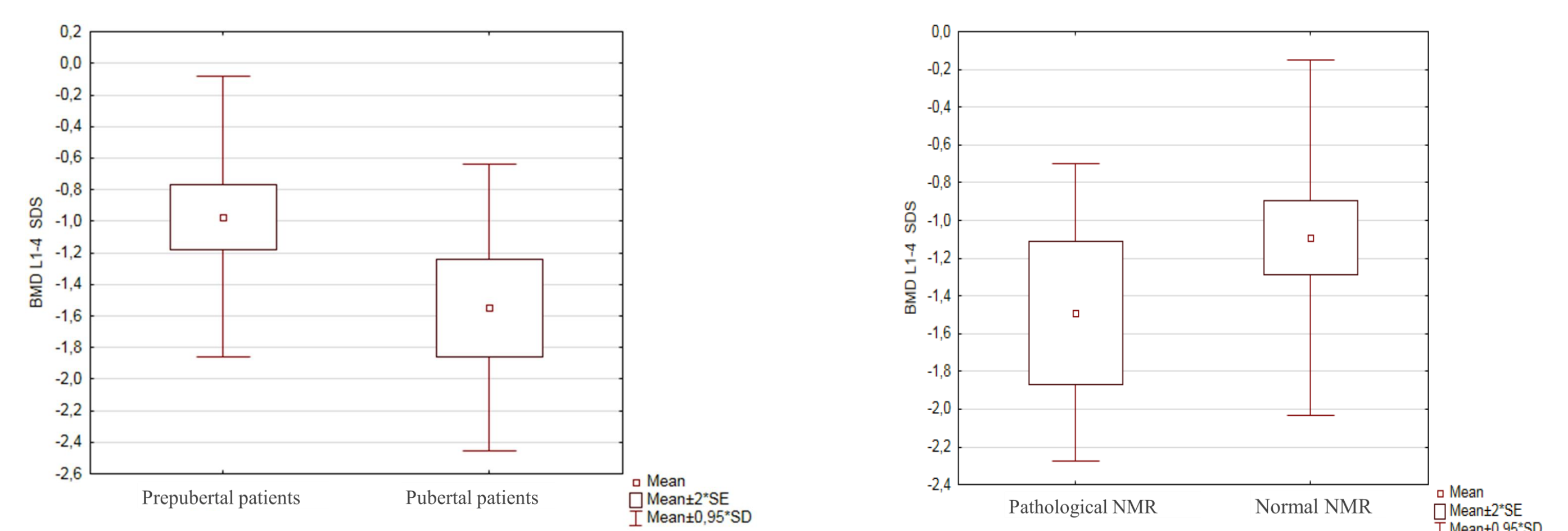
2. BMD data (a)



In all population study, mean BMD SDS was «low for age» according to ISCD, but not pathological (-1.15 ± 0.97)

3. BMD data (b)

- BMD SDS values were significantly lower in pubertal patients respect to pre-pubertal ones ($p < 0.001$) and in patients with pathological brain NMR imaging respect to with normal NMR one ($p = 0.03$)



4. Correlations

- BMD values (g/cm^2) were significantly and positively correlated with Ht SDS ($R 0.20$, $p < 0.05$), z-score BMI ($R 0.24$, $p < 0.05$), and IGF-1 levels ($R 0.33$, $p < 0.05$)
- BMD SDS values were significantly and positively correlated with TH SDS ($R 0.28$, $p < 0.05$) and z-score BMI ($R 0.36$, $p < 0.05$); they were significantly and negatively correlated with CA at time of GHD diagnosis ($R -0.40$, $p < 0.05$)
- No association between BMD values and bone metabolism indices was demonstrated

5. Multiple Regression Analysis

- z-score BMI ($\beta 0.023$, $p 0.008$) was identified as an independent positive predictor factor for pre-therapy BMD SDS
- CA at diagnosis of GHD ($\beta -0.12$, $p 0.007$) was found to be an independent negative predictor factor for pre-therapy BMD SDS

CONCLUSIONS

- Our data demonstrated that patients with diagnosis of GHD at pubertal period had a lower BMD than pre-pubertal ones. This data probably is a consequence of the mild bone demineralization due to the GHD itself. This data support the necessity to start the rhGH therapy as early as possible to promote an optimal bone growth.
- In our study, patients with pathological brain NMR had a lower BMD respect to patients with a normal NMR. This can be the consequence of a more severe phenotype secondary to structural abnormalities of the hypothalamic-pituitary region.
- DEXA might be considered a useful diagnostic tool to complete the diagnosis in GHD patients and to optimally guide therapeutic strategies. Moreover, DEXA should be repeated at the end of treatment in order to evaluate the effects of rhGH therapy on bone metabolism.