Differentiation of growth hormone effects on metacarpal bone and bone age in children with growth hormone deficiency

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Aim:

To track the effect of growth hormone on bone geometry and maturation in children with growth hormone deficiency (GHD).

Patients and Methods:

602 non-dominant hand X-rays from 178 short prepubertal children (122 boys) with GHD undergoing GH treatment were analyzed for changes in metacarpal thickness (T), width (W), length (L), medullar diameter (M), area bone mineral density (BMD) and bone age (BA) from 1 year preceding until 4 years after start of GH treatment using BoneXpert, a fully automatic image analysis software.

Results:

- Chronological age (CA)-related standard deviation scores (CASDS) revealed strong and significant stimulatory effects on T, L and W, ranking in this order, and no effect on M.
- T also increased significantly in terms of height- and BA-related standard deviation scores (HSDS and BASDS), while L and W increased nonsignificantly in this regard. BMD showed a significant increase for CA, BA and height.
- Catch-up growth was strongest in the 1st year and, by BASDS, the more pronounced for a parameter the greater the baseline deficit was for that parameter.
- BA change was slower than change of T and height during the 1st year and thereafter faster, showing the same gain in terms of CASDS as thickness after 4 years.

Table: T, W, L, M and BMD expressed in terms of BASDS, CASDS and HSDS (mean ± SD) over time relative to start of GH treatment
p-values for differences relative to the previous year: *: p<0.05; **: p<0.01; ***: p<0.001

Years from GH start	-1	0	1	2	3	4
N (boys)	39 (32)	79 (56)	123 (89)	143 (95)	123 (84)	95 (64)
T BASDS	-1.04±0.78	-1.04±0.88	-0.24±0.99***	-0.34±1.00	-0.42±1.00	-0.51±1.09
T CASDS	-2.03±0.78	-2.01±0.89	-1.15±1.01***	-0.95±0.97	-0.89±0.96	-0.84±1.11
T HSDS	-0.84±0.87	-0.85±0.94	-0.21±1.05***	-0.16±1.05	-0.19±1.04	-0.32±1.05
W BASDS	-0.25±0.90	-0.34±0.89	-0.05±0.98*	-0.12±1.07	-0.20±1.06	-0.19±1.06
W CASDS	-1.12±0.84	-1.18±0.85	-0.84±0.94**	-0.67±0.96	-0.64±0.98	-0.53±0.98
W HSDS	0.08±0.96	-0.04±0.93	0.05±0.95	0.09±0.97	0.05±0.93	0.05±0.93
L BASDS	-0.55±0.80	-0.47±0.94	-0.07±1.07**	-0.18±1.07	-0.36±1.03	-0.40±0.92
L CASDS	-2.02±0.72	-1.93±0.72	-1.50±0.77***	-1.15±0.80***	-1.08±0.82	-0.93±0.82
L HSDS	0.13±1.09	0.13±0.91	0.16±0.96	0.37±0.96	0.26±1.07	0.18±1.06
M BASDS	0.28±0.90	0.21±0.91	0.09±0.96	0.08±0.99	0.05±0.98	0.11±0.95
M CASDS	-0.07±0.87	-0.11±0.87	-0.22±0.92	-0.14±0.95	-0.13±0.94	-0.04±0.90
M HSDS	0.49±0.95	0.38±1.00	0.15±0.96	0.16±0.97	0.16±0.96	0.23±0.93
BMD BASDS	-1.07±0.82	-1.10±0.93	-0.24±1.02***	-0.35±1.06	-0.45±1.06	-0.53±1.14
BMD CASDS	-2.20±0.82	-2.20±0.94	-1.27±1.05***	-1.05±1.00	-0.98±1.00	-0.91±1.13
BMD HSDS	-0.85±0.96	-0.89±1.01	-0.19±1.11***	-0.12±1.08	-0.17±1.07	-0.29±1.07
Height BASDS	-0.79±0.85	-0.74±0.94	-0.30±1.09**	-0.54±1.14	-0.64±1.10	-0.61±1.02
Height CASDS	-2.74±0.64	-2.68±0.68	-2.09±0.66***	-1.78±0.77***	-1.59±0.77*	-1.31±0.77*
BA CASDS	-1.96±0.73	-1.92±0.90	-1.79±0.97	-1.23±0.99***	-0.96±0.90*	-0.74±0.84

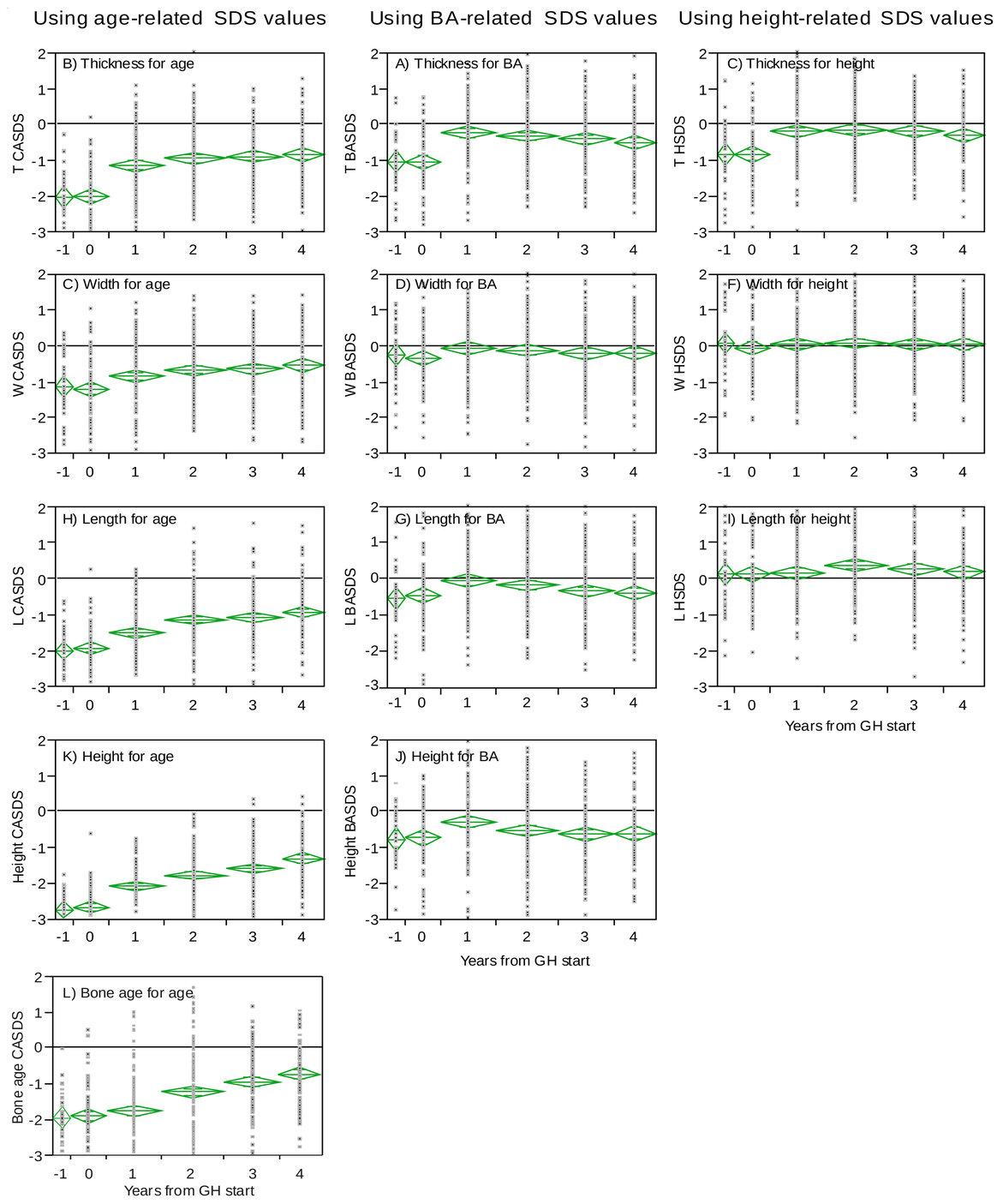

Figure: T, W, L, expressed in terms of BASDS (a-c), CASDS (d-f) and HSDS (g-i), as well as height BASDS and CASDS (j-k), and BA CASDS (l) versus years relative to start of treatment (both genders pooled). The relative width of each year-segment of the X-axis is proportional to the quantity of data in that year. Each measurement is represented by a dot. The diamonds portray the mean (middle horizontal line), 95% CI (vertical diamond span).

The children in our study had thinner metacarpals than normal children regardless of whether they were matched for CA ($p < 0.0001$), BA ($p < 0.0001$) or height ($p < 0.0001$). After the start of GH treatment we see a general trend towards the normal in all four metacarpal dimensions as well as BMD, regardless of whether children of equal CA, BA or height are compared.

Conclusion

- While it takes many years of GH treatment for the height of children with GHD to normalize, their metacarpal thickness normalizes for height within the first year of treatment.
- The strongest and statistically most significant effect of GH treatment on metacarpal bone is not elongation but increase in cortical thickness as a result of subperiosteal bone deposition. This adds to the evidence that GH treatment enhances not only growth but rapidly increases fracture resistance in GHD children.
- In children with GHD, GH leads to a significant catch-up in BA only from the 2nd year onwards.
- Bone geometry and bone age assessment with BoneXpert can contribute to monitoring skeletal development in children with growth hormone deficiency (GHD) undergoing GH treatment.

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