Growth hormone therapy in patients with SGA short stature improves body composition by increasing muscle mass and bone mineral density rather than decreasing fat mass.

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【Background】 Children born SGA have been implicated to be at higher risk for subsequent obesity[1] ;however, the body composition, especially fat distribution, in SGA short stature (SGA-SS) patients and the effects of growth hormone (GH) therapy on body composition in SGA-SS have not been fully studied. In this study, we evaluated the body composition of SGA-SS children without catch-up and examined the effect of GH treatment on the body composition of SGA-SS children.
【Purpose】 To investigate the effects of GH treatment on body fat mass, body fat distribution, muscle mass and bone density in children with SGA-SS.
【Methods】 Thirty pre-pubertal subjects with SGA-SS (14 boys and 16 girls, mean age at GH commencement 4.1+/- 1.1 years old) were included. Data on cumulative dose of GH, height (HT)-SDS, BMI-SDS, IGF-1 SDS, body composition by DXA analysis, and fat distribution by abdominal CT analysis obtained before and 1-year after GH treatment were retrospectively evaluated based on medical records. Parameters of body composition included percent fat mass (%FM) and percent muscle mass (%MM). Bone size-corrected volumetric lumbar BMD (vBMD) was calculated.
Statistical analysis was performed using paired t-test or Pearson's correlation analysis.

Basic data of the subjects

	All(n=30)	Male(n=14)	Female(n=16)
Gestational age(week)	35.1±4.3	35.2±4.8	35.0±3.8
Birth HT-SDS	-2.6±1.0	-2.9±1.0	-2.3±0.9
Birth weight-SDS	-2.9±1.0	-3.0±1.0	-2.8±1.1
Start age(y.o)	4.1±1.1	4.4±1.2	3.9±1.0
Start HT-SDS	-2.8±0.4	-2.8±0.4	-2.7±0.4
Start weight-SDS	-2.4±0.5	-2.4±0.5	-2.4±0.5
Visceral fat (㎠)	4.2±1.0	4.0±1.0	4.4±1.0
Subcutaneous fat (㎠)	11.4±7.1	7.4±4.6	14.6±7.2
Start BMI-SDS	-1.5±1.2	-1.8±1.3	-1.3±1.0

Correlation between HT-SDS and each parameter before GH treatment

Start HT-SDS	Univariate analysis		Corrected by age and gender	
	Correlation coefficient(R)	P value	Standard partial regression coefficient(β)	P value
Birth weight-SDS	**0.42**	**0.020**	**0.42**	**0.024**
Birth HT-SDS (n=25)	0.09	0.667	0.07	0.762
Gestational age	-0.16	0.410	-0.13	0.512
Start weight-SDS	**0.40**	**0.029**	**0.39**	**0.038**
Start %fat	**-0.58**	**0.0007**	**-0.79**	**0.0001**
Start %MM	**0.59**	**0.0006**	**0.79**	**＜0.0001**
Start vBMD	0.11	0.557	0.16	0.45
Start IGF-1 SDS(n=28)	0.06	0.768	0.13	0.56

Both visceral fat mass and subcutaneous fat mass were not as high as those in normal children before the start of treatment in SGA-SS patients.
HT-SDS before GH treatment showed a positive correlation with birth weight, start weight, muscle mass, and a negative correlation with body fat percentage.
In addition, body fat percentage before GH treatment showed positive correlation with gestational age, and negative correlation with height and muscle mass.

Comparison of various data at start and the first year of treatment

	Start	One year	P-value
Height(cm)	89.6±6.8	98.9±6.7	<0.001
HT-SDS	**-2.8±0.4**	**-1.9±0.6**	**<0.001**
Weight(kg)	11.0±1.7	13.5±1.9	<0.001
Weight-SDS	-2.4±0.5	-1.8±0.5	<0.001
BMI	13.7±1.2	13.7±1.2	0.91
BMI-SDS	-1.5±1.2	-1.3±1.0	0.10
IGF-1	100.1±34.3	208.6±61.9	<0.001
IGF-1 SDS	-0.2±1.0	1.7±1.2	<0.001
% fat	**21.5±4.3**	**16.2±3.2**	**<0.001**
Visceral fat (㎠)	4.2±1.0	5.3±1.9	0.004
Subcutaneous fat (㎠)	11.4±7.1	9.4±6.4	0.34
MM/Total(%)	**74.6±4.2**	**80.0±3.1**	**<0.001**
vBMD	**0.60±0.11**	**0.64±0.10**	**0.007**

Δ height-SDS and correlation of each parameter

	Δ height SDS			
Analysis method	Univariate analysis		Corrected by age and gender	
	Correlation coefficient (R)	P value	Standard partial regression coefficient(β)	P value
Start weight-SDS	0.07	0.706	0.09	0.656
Start HT-SDS	-0.12	0.517	-0.09	0.631
Start BMI-SDS	0.27	0.153	0.20	0.326
Start %MM	-0.36	0.051	-0.35	0.116
Start vBMD (n=29)	0.14	0.465	0.09	0.646
Δ %fat	-0.31	0.100	-0.29	0.150
Δ %MM	0.20	0.297	0.16	0.429
Δ vBMD (n=29)	-0.16	0.415	-0.20	0.300
Start IGF-1 SDS (n=28)	0.18	0.364	0.15	0.48
Δ IGF-1 SDS (n=28)	0.24	0.195	0.22	0.275
GH dose(n=28)	0.38	0.048	0.41	0.051

One year of GH treatment increased height SDS, muscle mass, and vBMD, and significantly reduced body fat percentage. Visceral fat and subcutaneous fat were not decreased.

No significant factors correlated with height gain could be identified. Changes in %fat were negatively correlated with GH dose.

【Discussion】

GH & growth：GH increases IGF-1 production primarily in the liver. IGF-1 stimulates the proliferation and differentiation of chondrocytes and has a growth promoting effect, and also stimulates the proliferation of osteoblasts to increase bone mass. In fact, GH treatment significantly increased IGF-1 in children with SGA-SS, but there was no correlation between the increase in IGF-1 and the growth-promoting effect.

GH & lipolysis： GH is known to promote lipolysis in adipose tissue, and GH supplementation is known to reduce body fat in pediatric GHD and adult GHD [2)3)4)5)] However, in this study, the visceral/subcutaneous fat mass in SGA-SS children was in the normal range before GH treatment, and the effect of GH to reduce fat mass was not clear.

Effects of GH on muscles： GH has the effect of increasing protein synthesis in muscle directly and indirectly through IGF-1. [6)]

【Conclusion】GH therapy in children with SGA-SS increased HT-SDS and this was associated with improvement of body composition by increasing muscle mass and bone mineral density rather than reducing fat mass.

Reference
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CONFLICT OF INTEREST
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I declare that I have no potential conflict of interest.

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