

Impact of -202 IGFBP-3 Promoter Polymorphism on Growth Responses in Korean Children with Idiopathic Short Stature

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Disclosure Statement

Seung Yang, Kyung Hee Yi, Eun Young Kim and Il Tae Hwang have no relevant financial relationships to disclose or conflicts of interest to we solve.

Introductions and Objectives

Our previous study showed no correlation between -202 A/C IGFBP-3 promoter polymorphism and Δ height SDS in children with growth hormone deficiency. We investigated the influences of the -202 IGFBP-3 polymorphism on 1-year follow-up outcomes of GH treatment in Korean children with ISS.

Methods

Data was obtained from 81 children with idiopathic short stature (peak serum growth hormone (GH) \geq 7.0 ng/mL by GH stimulation test with 2 different stimulants). They were treated with GH for at least 1 year between 2014 and 2016. 69 of them were analyzed polymorphism of -202 IGFBP-3 promoter region (A or C). Their height velocity during GH treatment, serum insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) concentrations before and after GH treatment, respectively. Children with chronic disease, known syndromic disease and small for gestational age (SGA).

Results

Table 1. Baseline Characteristics of Subjects Studied

	ISS (N=81)
Sex	
Male No. (%)	44 (54.3%)
Female No. (%)	37 (45.7%)
Chronologic age (y)	8.4 \pm 3.0
Bone age (y)	6.6 \pm 3.1
Chronologic age - Bone age (y)	1.8 \pm 1.1
BMI (kg/m ²)	16.0 \pm 2.14
Genotype (N=69)	
AA No. (%)	48 (69.6%)
AC No. (%)	17 (24.6%)
CC No. (%)	4 (5.8%)
GH (IU/kg/week)	0.78 \pm 0.14
MPH SDS	-0.697 \pm 0.742

Table 2. Characteristics of 69 prepubertal children before and after treatment according to -202 A/C IGFBP-3 genotypes.

	Baseline			After 1 year		
	AA (n=48)	AC & CC (n=21)	P	AA (n=48)	AC & CC (n=21)	P
Age (y)	8.6 \pm 3.0	8.2 \pm 2.8	0.571			
Sex (M/F)	25/23	12/9	0.698			
GH (IU/kg/wk)	0.79 \pm 0.14	0.79 \pm 0.17	0.993			
Height SDS	-2.140 \pm 0.613	-2.380 \pm 3.506	0.098	-1.517 \pm 0.588	-1.631 \pm 0.525	0.447
BMI SDS	-3.271 \pm 1.460	-2.870 \pm 1.234	0.276	-3.067 \pm 1.444	-2.808 \pm 1.492	0.499
IGF-1 (ng/mL)	162 \pm 80	144 \pm 68	0.376	284 \pm 135	233 \pm 95	0.077
IGF-1 SDS	-0.784 \pm 0.781	-0.858 \pm 0.673	0.707	0.299 \pm 1.293	-0.124 \pm 0.802	0.172
IGFBP-3 (ng/mL)	4,115 \pm 1,000	3,562 \pm 879	0.032	4,887 \pm 1,066	4,401 \pm 949	0.077
IGFBP-3 SDS	2,234 \pm 1,197	1,609 \pm 1,682	0.084	3,074 \pm 1,534	2,539 \pm 1,709	0.202
*Ratio	0.038 \pm 0.011	0.040 \pm 0.015	0.404	0.057 \pm 0.021	0.052 \pm 0.144	0.285

*Ratio = IGF-1/IGFBP-3

IGF-1, insulin like growth factor 1; IGFBP-3, insulin-like growth factor binding protein 3; SDS, standard deviation

Fig. 1. There is an ethnic difference in C allelic frequency

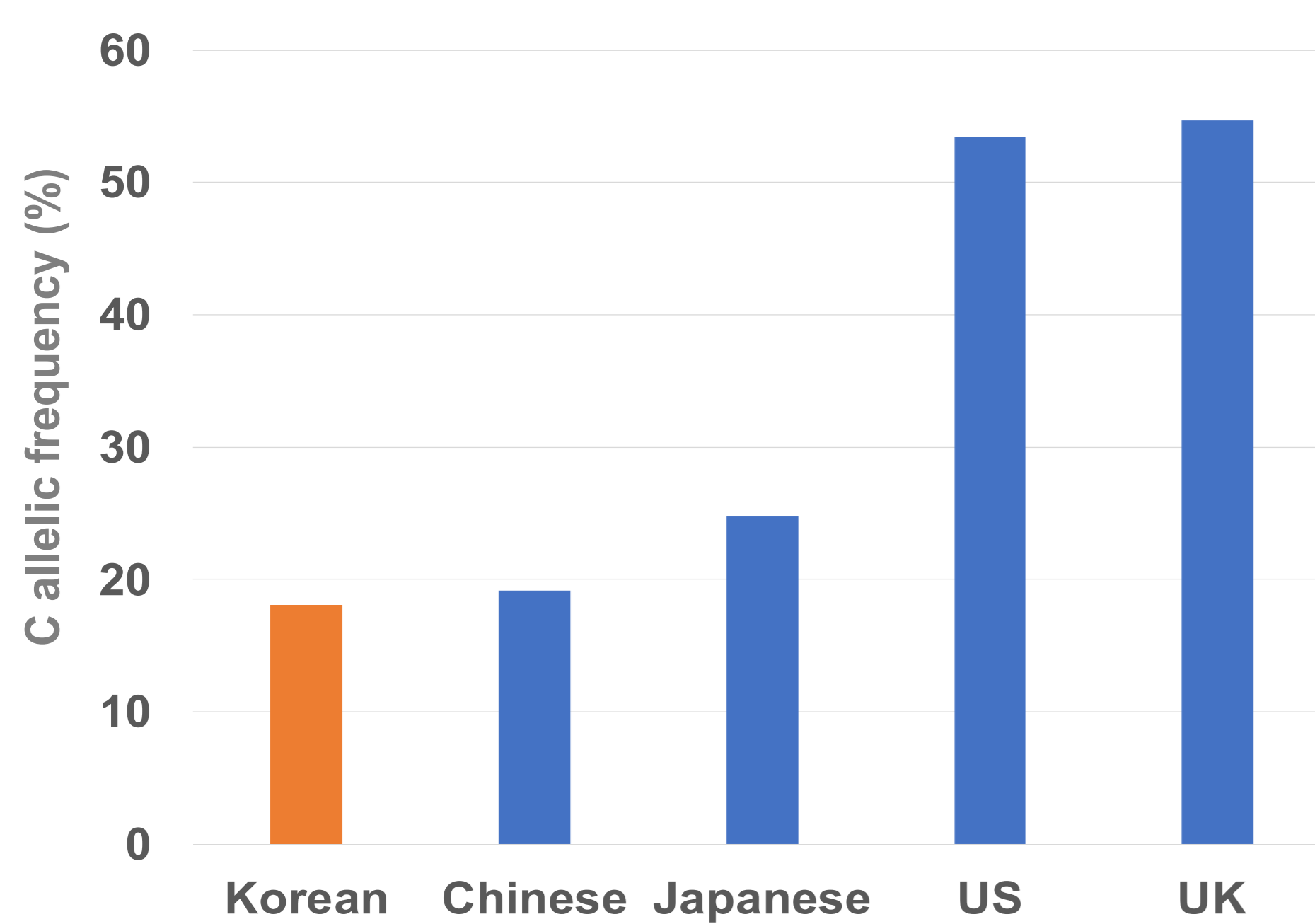


Fig. 2. Δ Height SDS level is no significant difference according to allele

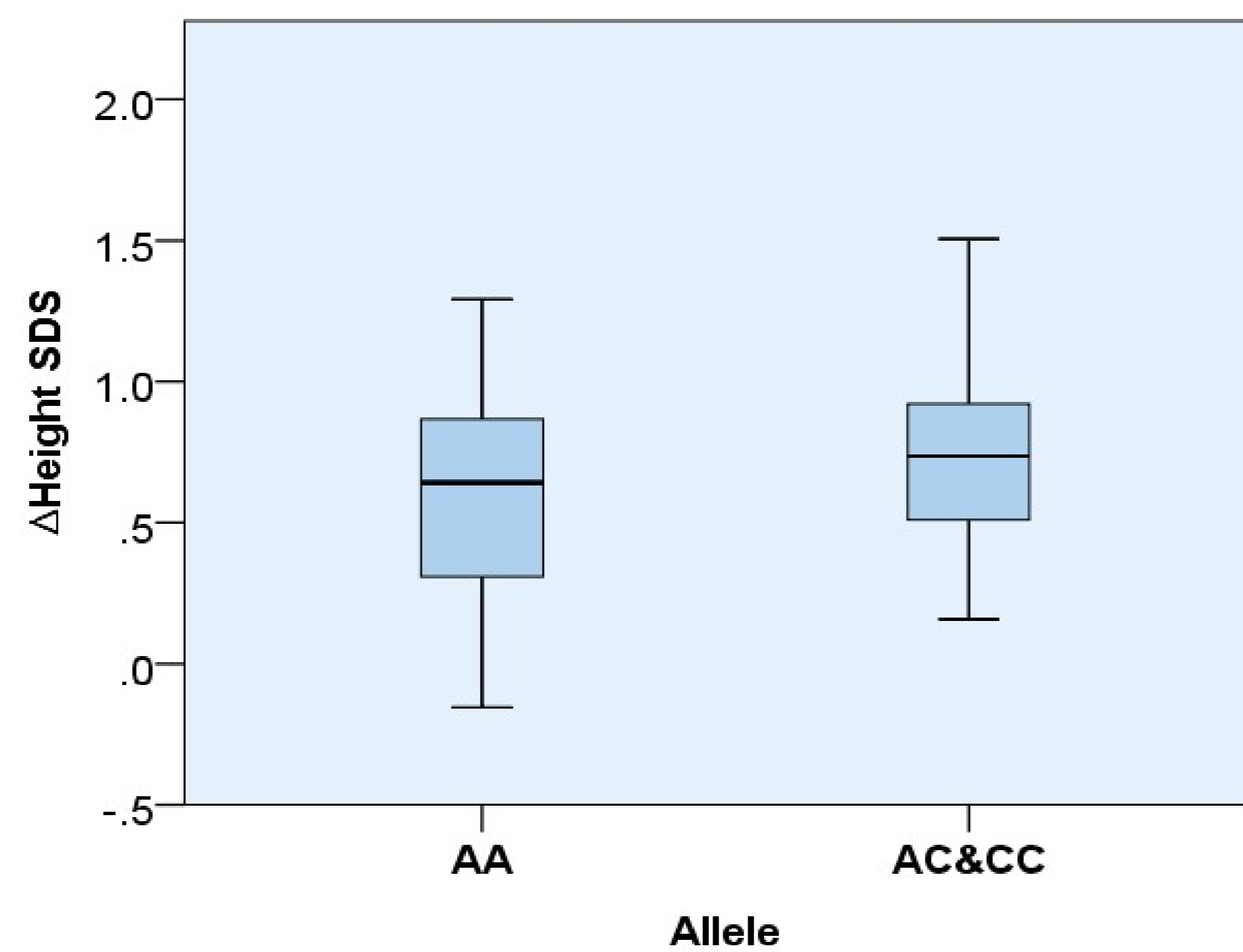


Fig. 3. Δ IGF-1 SDS level is no significant difference according to allele

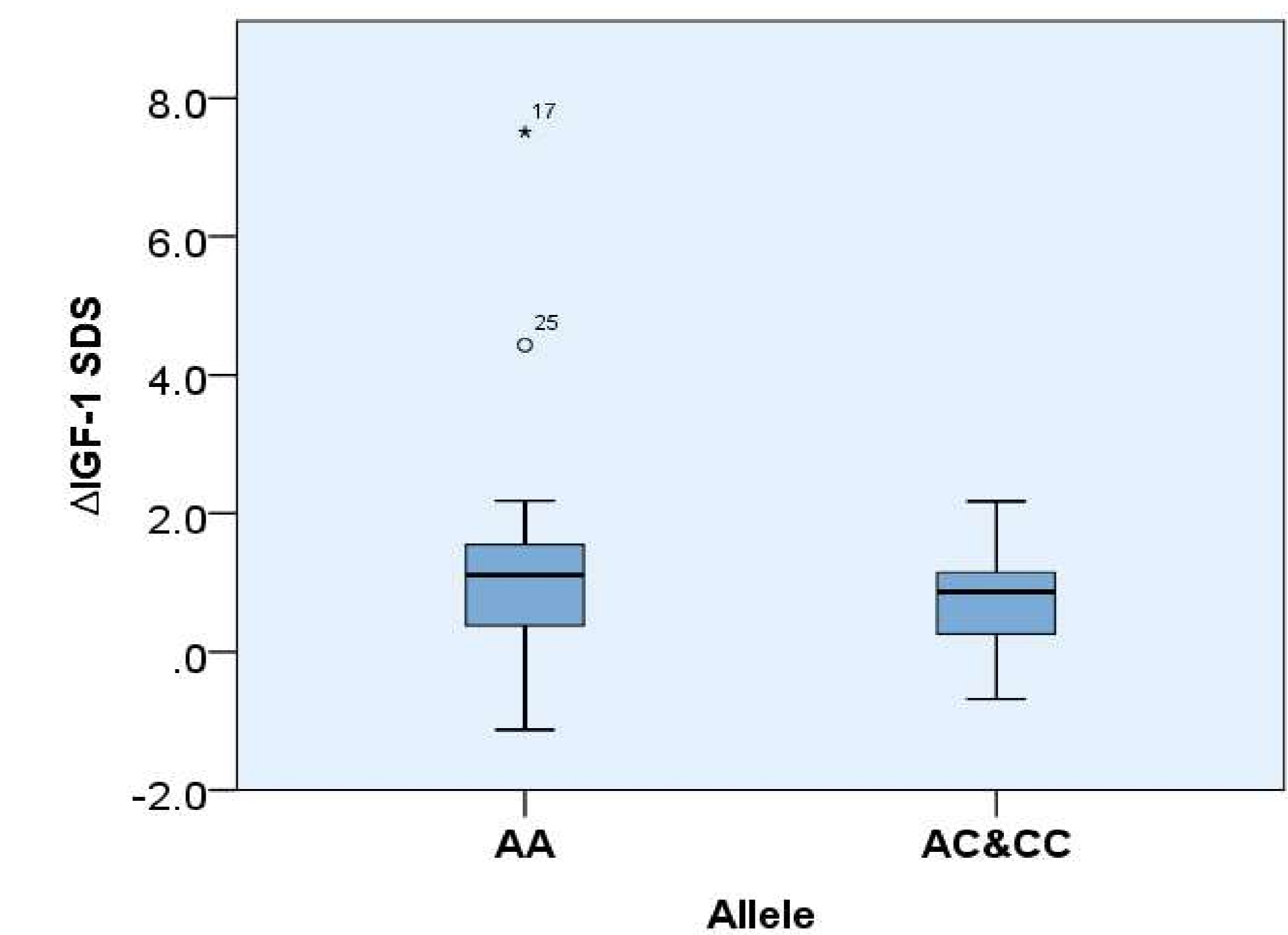


Fig. 4. Δ IGFBP-3 SDS level is no significant difference according to allele

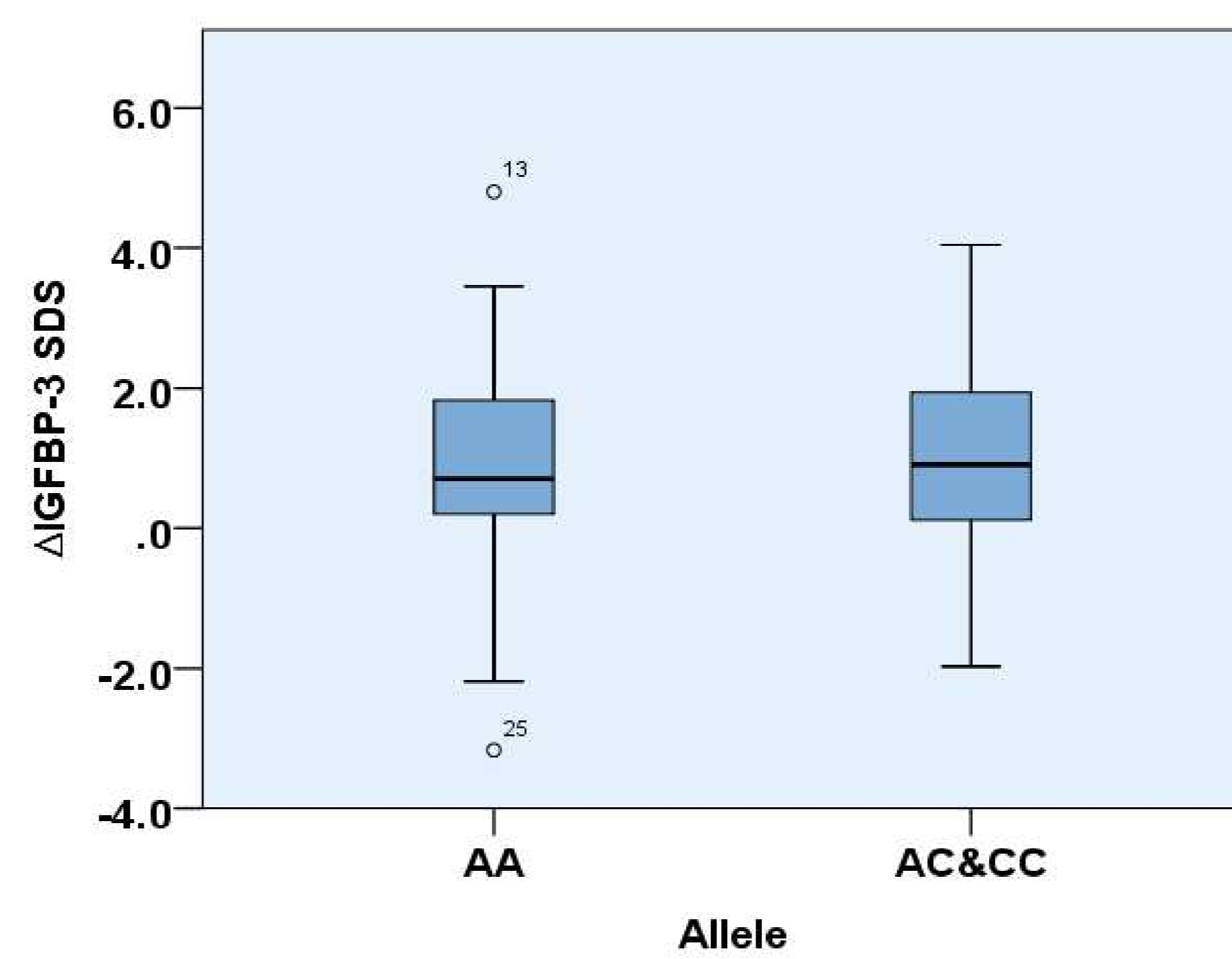
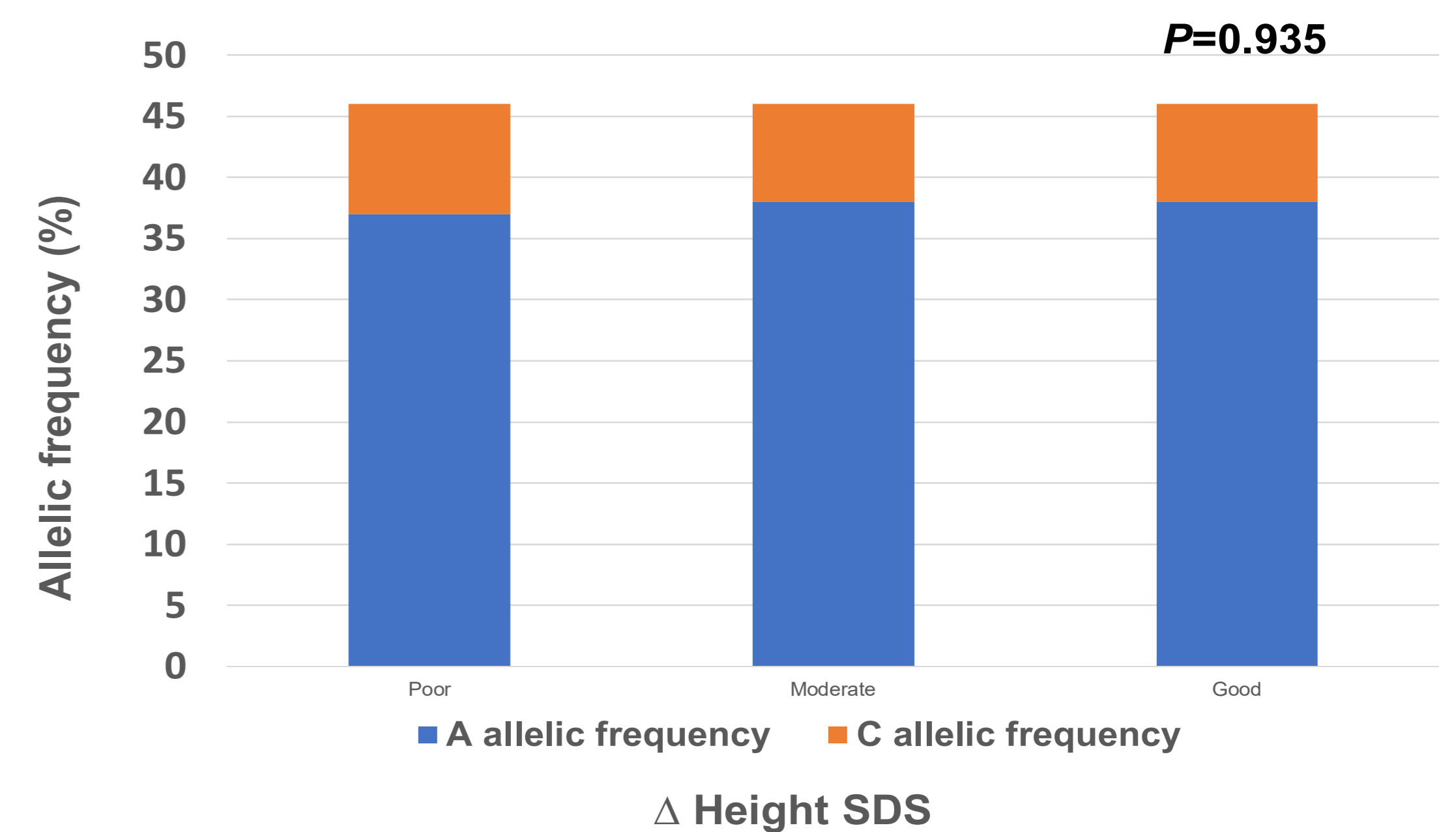


Fig. 5. There is no difference of allelic frequency among poor, moderate and good response group. P=0.935



Conclusions

The results suggest that -202 IGFBP-3 promoter polymorphism may not be a major factor in GH treatment in Korean children with ISS.