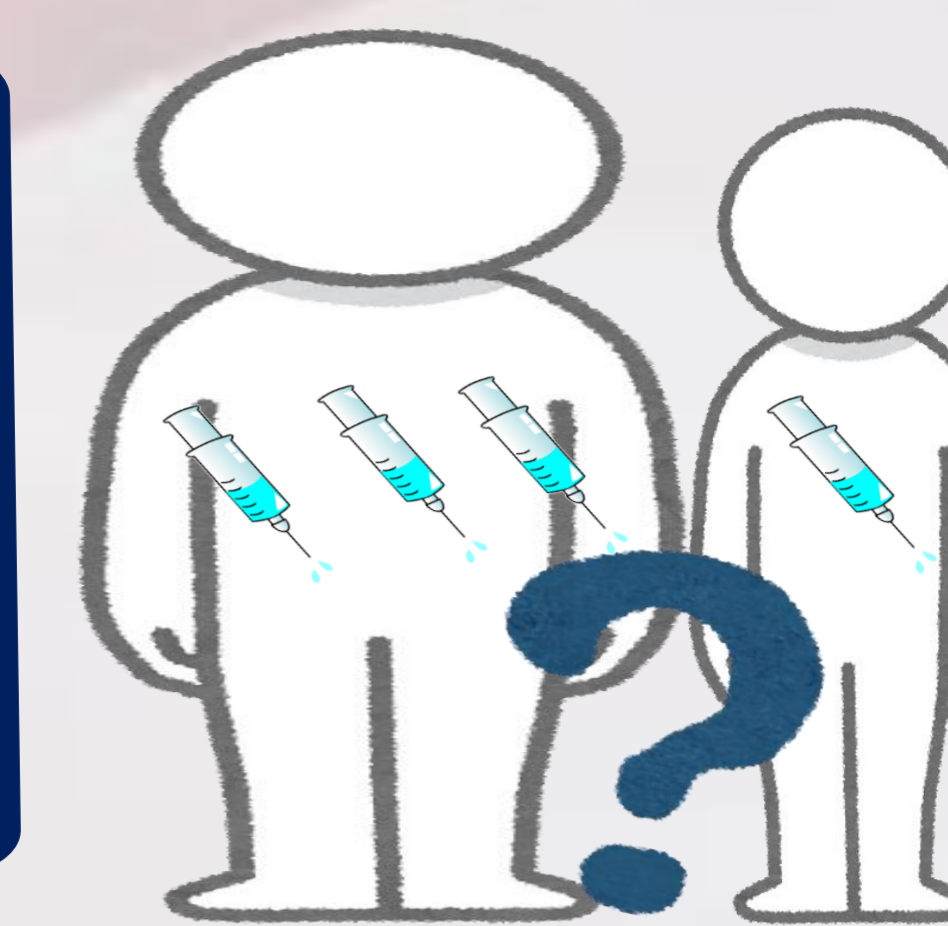


Is weight-based adjustment of factor VIII dosage required for underweight or overweight Japanese patients with hemophilia A?

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Introduction

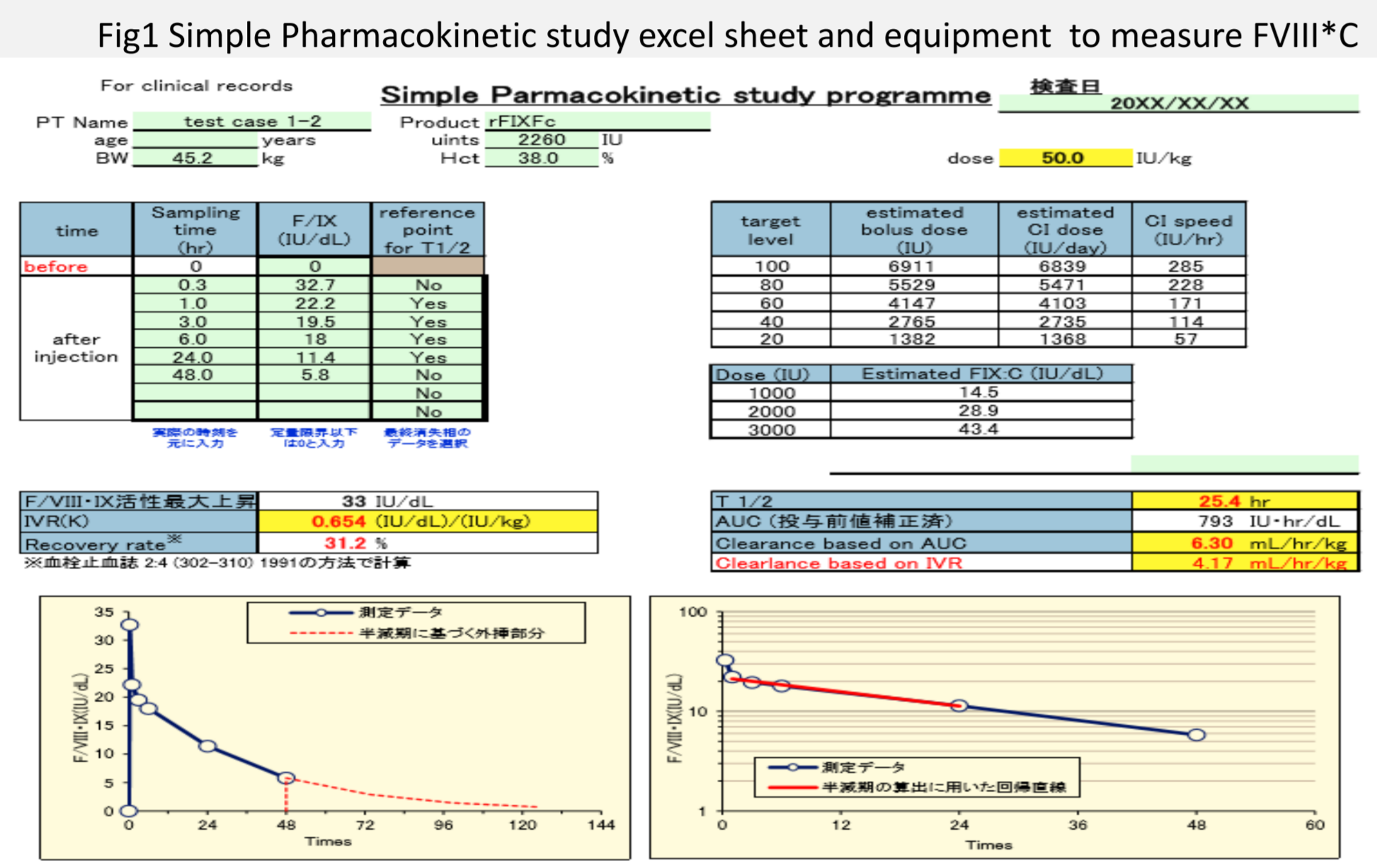
In treatment of patients with hemophilia, optimal dosing of factor is calculated by the formula based on the body weight. However, there are several reports warning the possible overtreatment in obese patients.

Objective

This study was aimed to investigate if the dosing of factor VIII (FVIII) should be adjusted based on weight in underweight or overweight Japanese patients

Patients & Methods

Patients : The study included 74 patients with hemophilia A who underwent a simple FVIII pharmacokinetic study in our hospital using Excel sheet. (Fig1) Measurements points are before (0) and 30 minutes (0.5), six hours (6), 24 hours (24) after administration. FVIII increment was calculated using FVIII:C at two points (0 and 0.5). Half-life was also calculated using FVIII:C at three points (0.5, 6 and 24). And FVIII recovery in each group was evaluated using the following formula: [body weight (kg) x observed FVIII increase (%) / administered dose (IU)]. FVIII increment was expressed as a percentage in FVIII per unit of FVIII per kg infused.

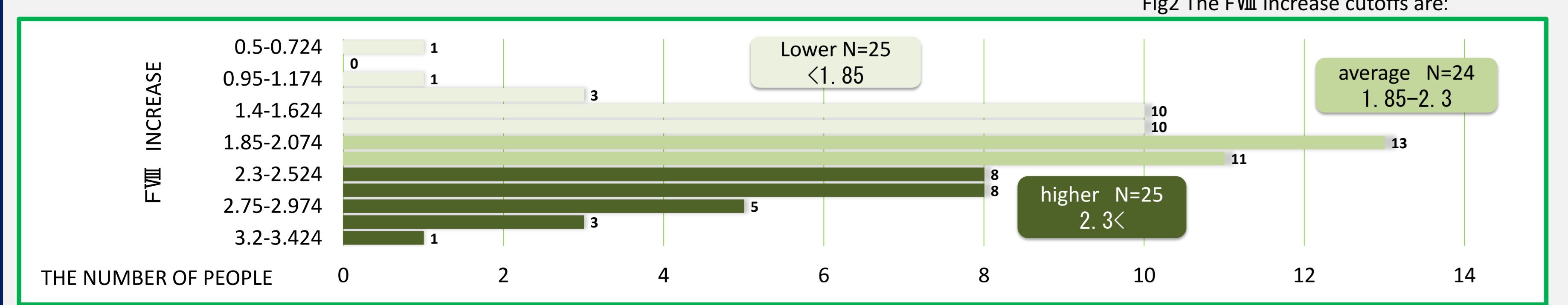


Groups : Subjects were divided to three groups according to BMI: **“lean”** group (BMI<18.5, n=6), **“normal”** group (18.5 ≤ BMI < 25, n=55) and **“obese”** group (25 ≤ BMI, n=13). (table1).

Table1 The BMI cutoffs are:

Groups	BMI (kg/m ²)	The number of people	WHO class	BMI (kg/m ²)
Lean	<18.5	6 (6)	Underweight	<18.5
Normal	18.5 ≤ BMI < 25	55 (55)	Healthy weight	18.5–24.9
Obese	25 ≤	(10)	Pre-obese state	25.0–29.9
		(2)	Obesity grade I	30.0–34.9
		(1)	Obesity grade II	35.0–39.9
		(0)	Obesity grade III	≥40

The subjects were also divided to 3 groups according to the distribution of FVIII increment (%); **“lower”** group (recovery < 1.85%, n=25), **“average”** group (1.85 ≤ recovery ≤ 2.30%, n=24) and **“higher”** group (recovery > 2.3%, n=25).



Statistical analysis : Variables were analyzed using the Kruskal-Wallis test and a P value < 0.05 was considered statistically significant.

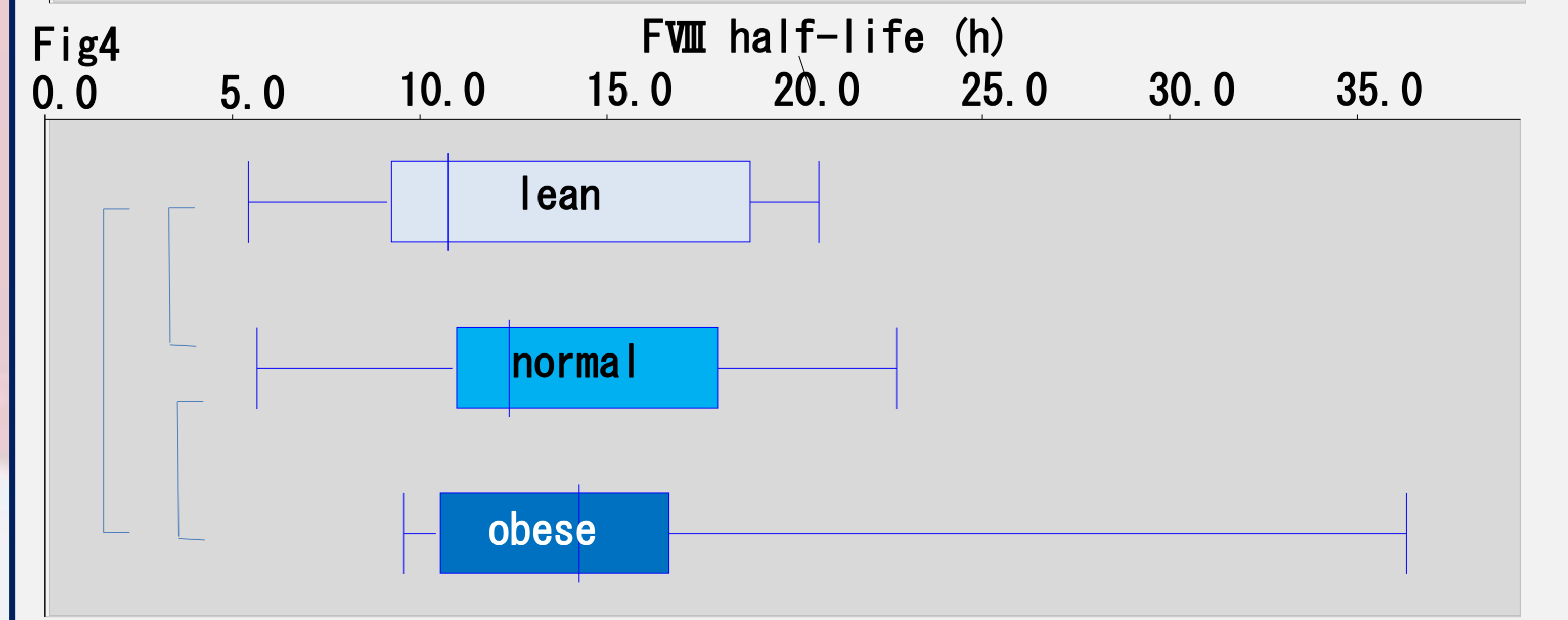
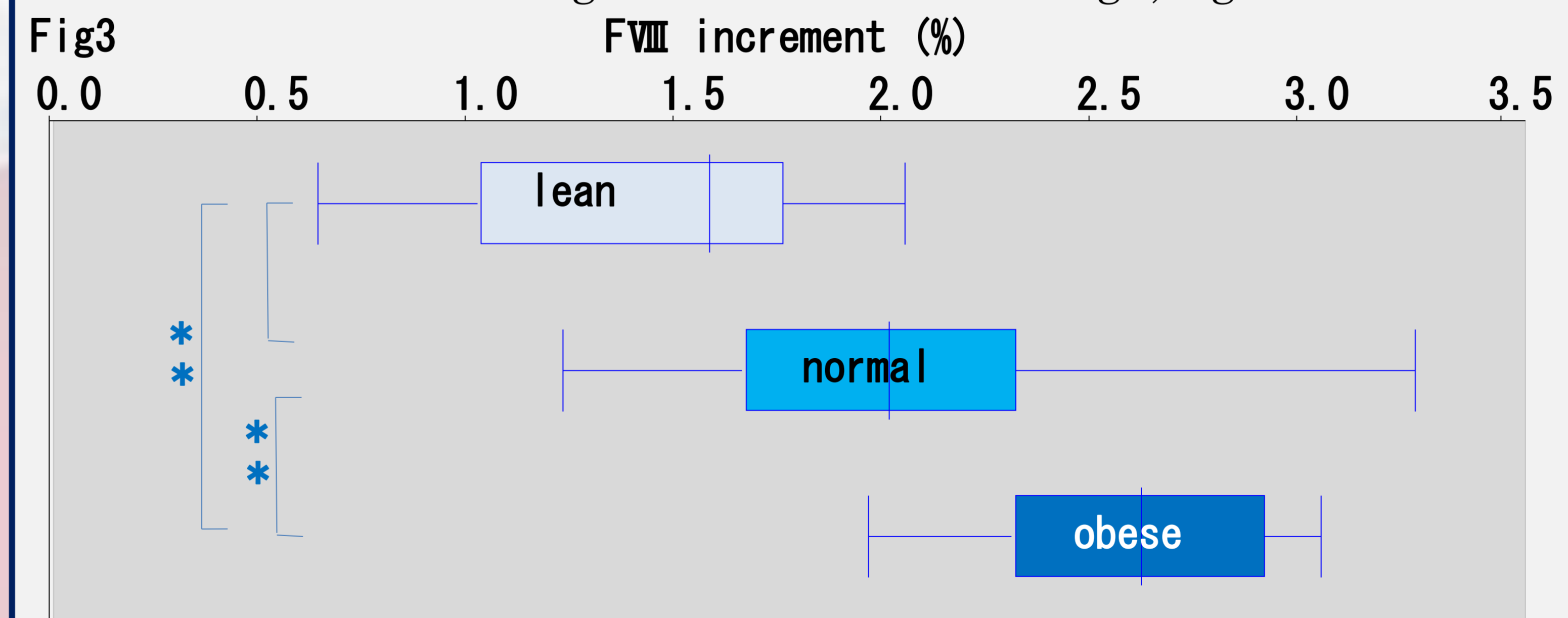
Results

As for age and height, there were no significant differences among two types of three groups which were lean, normal and obese group and lower, average and higher group.

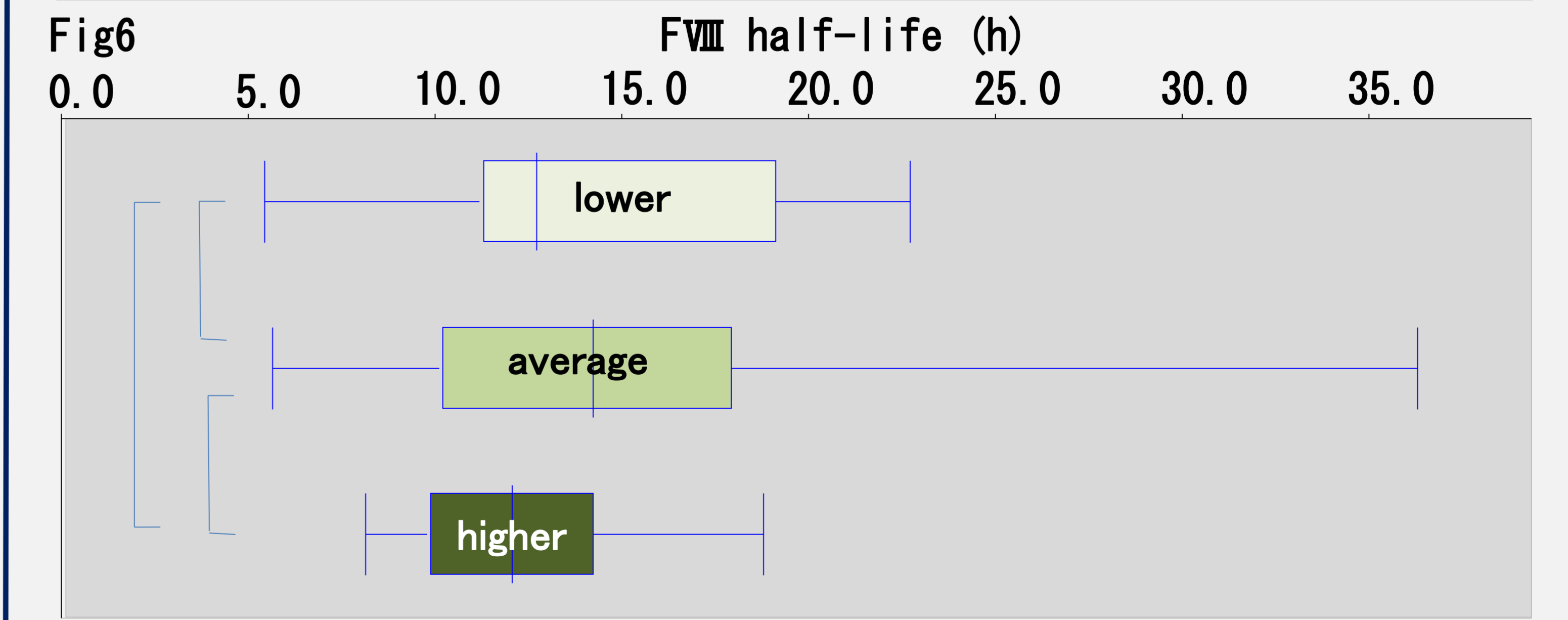
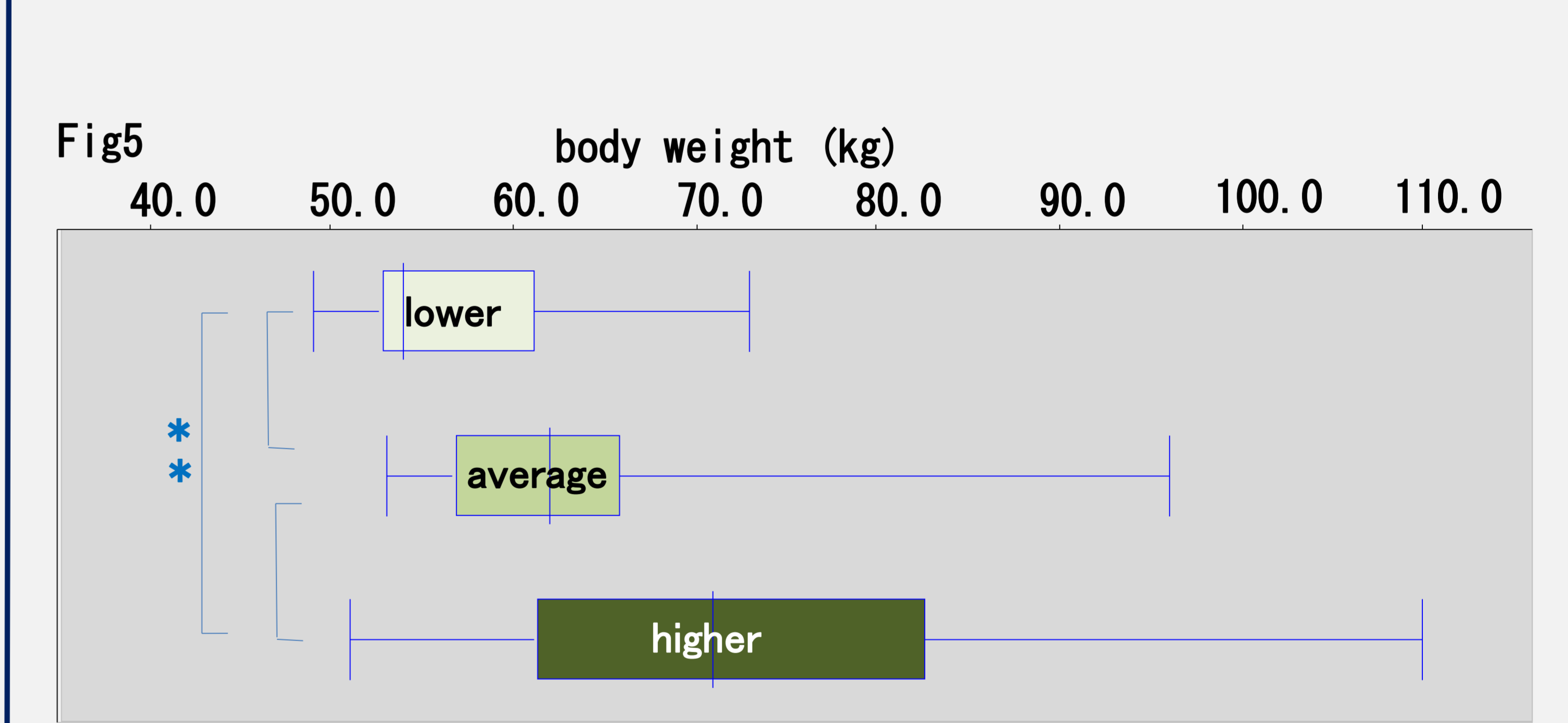
Table2 Baseline and clinical patient characteristics (N=74)

Lean	normal	obese	Variables	Over all (Average ± SD)	lower	average	higher
39.8 ± 13.9	40.5 ± 13.0	38.6 ± 11.3	Age (years)	40.1 ± 12.7	41.9 ± 11.6	40.3 ± 14.2	38.0 ± 12.2
1.70 ± 0.1	1.68 ± 0.1	1.72 ± 0.1	Height (m)	1.69 ± 0.1	1.67 ± 0.1	1.69 ± 0.1	1.72 ± 0.1
51.5 ± 2.4	60.6 ± 6.3	84.7 ± 10.5	Body Weight (kg)	64.1 ± 12.1	57.2 ± 7.1	62.9 ± 9.1	72.2 ± 13.9
63.4 ± 3.9	62.5 ± 5.3	64.9 ± 3.6	Ideal Body Weight (kg)	63.0 ± 4.9	61.5 ± 5.0	62.6 ± 4.9	64.9 ± 4.5
17.9 ± 0.3	21.4 ± 1.6	28.7 ± 3.2	Body mass index (Kg/m ²)	22.4 ± 3.6	20.4 ± 2.0	22.2 ± 3.3	24.4 ± 4.2
1.45 ± 0.5	2.04 ± 0.4	2.61 ± 0.3	FVIII increments (%)	2.10 ± 0.5	1.55 ± 0.3	2.07 ± 0.1	2.67 ± 0.3
12.6 ± 5.6	13.7 ± 4.4	15.1 ± 6.9	FVIII half-life (h)	13.8 ± 5.0	14.6 ± 4.7	14.6 ± 6.5	12.3 ± 3.1

« The group which I distributed at BMI »
FVIII increase was significantly higher in obese group compared with normal or lean group (P < 0.0001), while there was no significant difference between lean and normal group. There was a tendency for half-life to be longer in patients with higher BMI, however there was no significant difference. (Fig3, Fig4)



« The group which I distributed at FVIII increase »
BMI and Body weight was significantly higher in higher group compared with lower group (P < 0.0001), while there was no significant difference between lower and average group. (Fig5, Fig6)



Conclusions

In the previous studies, ideal body weight should be considered in the dose calculations instead of actual body weight and the relationship between half-life of FVIII and body weight wasn't discussed. Our results also suggest that adjustment of dose of FVIII may be required in obese Japanese patients. Furthermore, ours suggested that there may be no correlation between half-life of FVIII and BMI. We think that the adjustment by ideal body weight may be important to determine administration dose, but not to determine administration interval for Japanese patients with hemophilia A.

