

## Overall prevalence of feline overweight/obesity in Japan as determined from a cross-sectional sample pool of healthy veterinary clinic-visiting cats in Japan

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**Abstract:** Many veterinarians feel that feline obesity is increasing in prevalence within Japan, but are unsure as to what real rate of obesity prevalence exists currently. The objectives of this study are twofold. First, we sought to determine the ratio of overweight/obese cats, as determined via body condition score (BCS), based on a cross-sectional pool of healthy cats. Second, using a uniform method of biochemical measurement for cat plasma collected all over Japan, we sought to construct cross-sectional working reference ranges of plasma metabolites using age, BCS, and sex as classifying factors. Overall, the rate of overweight and obese cats (BCS of >3) was 56%, whereas obese cats (BCS >4) constituted 42% of our pool. Aging leads to an increased risk of developing lipid metabolism and kidney issues. Increases in BCS and age both carry increased risk of insulin resistance development. Moreover, increases in BCS bring about a higher risk of developing lipid metabolism problems, which may lead to the development of high cholesterol and triglyceride lipidemia, accompanied by higher levels of free fatty acids. Males appear to have a higher risk than females of developing higher BCS and body weight values, in addition to higher insulin and lower adiponectin values.

**Key words:** Obesity, overweight, indoor only cats, obesity ratio

### 1. Introduction

Overweightness and obesity are major concerns for the global companion animal population, as is the case with humans. The American Veterinary Medical Association reported that about 33,000 veterinarians were responsible for diagnosing approximately 840 overweight or obese cats and dogs in their respective animal hospitals in 1998 (1). In addition, 52% of 136 cats recruited by house-to-house survey in the United Kingdom (2) and 40% of vet-visiting cats in Glasgow (3) were deemed to be overweight/obese. The latest data in the United States indicate that 19%–29% and 6%–8% of cats are overweight and obese, respectively (4).

Many clinical veterinarians in Japan also feel that feline obesity is increasing in prevalence within Japan. However, with very little data or none regarding healthy domestic cats being readily available in Japan, veterinarians are currently unsure as to what real rate of obesity prevalence exists. One reason for this is because owners do not feel the necessity to bring in their overweight cats to the animal hospital without any apparent symptom(s) of disease. Furthermore, compounding the problem is the fact that owners may regard overweight or obese cats as

being physically appealing and cute, without truly seeing the potential health risk associated with overweight/obesity to their animals. For example, obesity can induce a low-grade inflammatory response (5), and accumulated excess fat can result in inadequate secretion of adipokines and dysfunction in metabolic organs. In addition, feline obesity increases the risks of diabetes mellitus, hepatic lipidosis, neoplasia, urinary tract disease, oral cavity and gastrointestinal disease, dermatoses, and lameness (6). Obesity-induced dyslipidemia in cats has the same health consequences as in humans.

As such, the objectives of this study are twofold. First, we sought to determine the rate of overweight/obese cats, as determined via body condition score (BCS), in Japan, based accordingly on a cross-sectional pool of healthy cats that were presented to 18 different veterinary clinics across Japan. Second, using a uniform method of biochemical measurement for cat plasma collected all over Japan, we sought to determine plasma biochemical parameter reference values from healthy indoor client-owned cats, using the same cross-sectional pool of healthy cats. In doing so, we also investigated whether age, BCS, and sex could significantly influence changes in plasma

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biochemical parameter values. In the process, cross-sectional working reference ranges of plasma metabolite values of house cats in Japan, using age, BCS, and sex as classifying factors, could be produced and used as a reference by clinical veterinarians.

## 2. Materials and methods

### 2.1. Animals

Over 200 cats that were presented to 18 different veterinary clinics across Japan (Tokyo, Ibaraki, Chiba, Osaka, and Fukuoka) from 2008 to 2013 were eligible for our study. All animal hospitals are located in residential regions near large urban areas. All cats were evaluated by 18 veterinarians and 27 cats were deemed to be ineligible due to existing disorders, such as liver failure, kidney failure, and diabetes mellitus, based on examinations and clinical signs, and were therefore excluded from our study. Thus, 190 cats (89 females, 101 males; age, 0.6–19 years) were actually included in our study.

Purebred cats included Abyssinian (female (F)  $n = 3$ , male (M)  $n = 3$ ), American shorthair (F-7, M-15), Chinchilla (F-3, M-2), Japanese domestic cats (F-18, M-14), Norwegian Forest cat (M-3), Persian (F-2, M-2), Turkish Angora (F-1, M-2), Scottish Fold (F-1, M-3), American Curl (M-1), British shorthair (M-1), Egyptian Mau (F-1, M-1), Exotic Shorthair (M-1), Japanese bobtail (M-2), Maine Coon (M-1), Ocicat (F-1, M-1), Russian Blue (M-2), Selkirk Rex (M-1), Siamese (F-1, M-1), Mix (F-38, M-37), and unreported/unknown (F-11, M-10). The subjects were diagnosed to be clinically healthy according to the physical evaluation and clinical signs as assessed by the attending veterinarian, who scored them on a 5 point BCS scale [1, very thin; 2, underweight; 3, ideal; 4, overweight, and 5, obese] (7), based on palpation and inspection.

To investigate the effects of aging, cats were divided into six age group categories based on 2010 AAFP/AAHA Feline Life Stage Guidelines (8): kitten (0–6 months), junior (7 months to 2 years), prime (3–6 years), mature (7–10 years), senior (11–14 years), and geriatric (>15 years). When analyzing age as a factor, cats were divided into 3 main groups: young (consisting of kitten and junior animals), mature (consisting of prime and mature animals), and elderly (consisting of senior and geriatric animals). In addition, when analyzing BCS as a factor, cats were originally classified according to their BCS on a 5-point scale and then subsequently grouped into 1 of 3 main groups for our study: thin to underweight (BCS of <3), ideal (BCS of 3), and overweight/obese (BCS of >3). Animal body weight (BW) was measured individually at each animal hospital.

Ethical approval was obtained from the Nippon Veterinary and Life Science University Animal Research

Committee. Written informed consent was obtained from the owners of the animals in this study.

### 2.2. Blood sampling

Postprandial blood samples (at least 4 h after the last meal) were collected from the cervical vein into heparinized plastic tubes. Blood samples were immediately centrifuged at  $1700 \times g$  for 10 min at 4 °C and subsequently were stored at -25 °C until further use.

### 2.3. Analysis of plasma metabolite parameters

Plasmametabolites, hormone and adipokine concentrations, and enzyme activities were measured. Plasma glucose (Glu), triglyceride (TG), total cholesterol (T-cho), total protein (TP), blood urea nitrogen (BUN), and creatinine (Cre) concentrations, as well as lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) activities, were measured using an Olympus AU680 autoanalyzer (Olympus Corporation, Tokyo, Japan) with the manufacturer's reagents. Free fatty acids (FFAs), adiponectin, and insulin were determined with an NEFA-C test (Wako Pure Chemical Industries, Inc., Tokyo, Japan), mouse and rat adiponectin ELISA kit (Otsuka Pharmaceutical Co., Tokyo, Japan), and an Lbis cat insulin kit (Shibayagi Co., Gunma, Japan), respectively.

### 2.4. Statistical analysis

Values are expressed as means  $\pm$  95% confidence interval. Nonparametric reference intervals (RIs) were determined using Analyse-It statistical add-in software for Microsoft Excel (v 4.00.1, Analyse-It Software, Ltd., Leeds, UK). Multivariate linear regression analysis was performed to determine the effect of age, BCS, and sex on plasma analyses. Statistical significance was determined by Kruskal–Wallis multiple comparison ANOVA (Dunn's method). All tests were performed using Sigmaplot (Version 11.2, Build 11.2.0.5, Systat Software Inc., San Diego, CA, USA). The significance level was set at  $P < 0.05$ .

## 3. Results

### 3.1. Prevalence of overweight/obesity

In order to determine the prevalence rate of overweight/obesity of cats in Japan, a cross-sectional pool of 190 healthy cats that were presented to 18 different veterinary clinics across Japan was examined. Cats were divided into 5 different BCS categories, with BCS scores of 3, 4, and 5 being equal to ideal, overweight, and obese body condition. Out of 190 cats examined, 14% (27/190) were overweight while 42% (80/190) were obese, with an overall prevalence rate of 56% (107/190) for being overweight/obese (Table 1).

### 3.2. Combined reference intervals

For reference interval calculations, all cats, including both sexes and regardless of age or BCS, were combined. All records, after outlier investigation, were used to determine

**Table 1.** BCS ratio of cross-sectional pool of Japanese cats.

	BCS <3		BCS 3		BCS >3	
	(n)	Rate	(n)	Rate	(n)	Rate
Kitten (0–6 months)	9	81.8%	2	18.2%	0	0.0%
Junior (7 months to 2 years)	0	0.0%	13	65.0%	7	35.0%
Prime (3–6 years)	4	6.6%	15	24.6%	42	68.9%
Mature (7–10 years)	3	5.6%	19	35.2%	32	59.3%
Senior (11–14 years)	2	6.1%	8	24.2%	23	69.7%
Geriatric (>15 years)	4	33.3%	4	33.3%	4	33.3%
Total	22		61		107	

Obesity rate (BCS >4 (n = 80)): 42%.

Overweight and obese rate (BCS >3 (n = 107)): 56%.

95% reference intervals. Descriptive statistics (Table 2) and visual examination (histograms provided in the Figure) were used to explore the data. The Shapiro–Wilk test (9) was applied to each biochemical parameter to test for the hypothesis of normality. Since all parameters exhibited a nonnormal distribution pattern, nonparametric reference intervals were calculated.

### 3.3. Influence of age, BCS, or sex on parameter values

Table 3 lists all the P-values for each individual factor (age, BCS, or sex) that may have had an influence on plasma parameter values measured. Age appears to significantly affect TG (P = 0.009), with a tendency to influence BCS (P = 0.074). BCS appears to significantly affect BW (P < 0.001) and TG (P = 0.022), with a tendency to be affected by age (P = 0.074). Lastly, sex has a tendency to affect LDH (P = 0.062). Parameter reference ranges according to age (Table 4), BCS (Table 5), and sex (Table 6) are further elaborated.

## 4. Discussion

Remarkably, more than half (~56% of 190 cats) of the vet-visiting cats in this study were overweight or obese, which is in line with and nearly double the obesity rate previously reported in the United Kingdom (52%) (2) and United States (19%–29%) (4), respectively. However, the obesity rate (BCS >4) in vet-visiting cats was ~42% (80 of 190 cats), which exceeded our expectations and is roughly 5 times the rate reported for the United States (6%–8%) (4). There are a multitude of factors to help explain this greater incidence of feline overweight and obesity in Japan as compared to the United States. One major characteristic is that the majority of cats in Japan are considered to be indoor cats, which rarely leave their owners' homes.

As of 2011, the Tokyo Metropolitan Government Bureau of Social Welfare and Public Health reported that 1,110,000 cats were living in Tokyo, and 860,000 of them (~77%) were indoor-only cats (10). Because it is easier for people living in the city to have indoor-only cats than dogs, the trend in the number of indoor cats has been steadily rising, whereas indoor-outdoor and stray cats tend to be steadily decreasing in Japan (10). As such, indoor-only cats may be commonly overfed, as a sign of owner affection, and allowed a minimum amount of exercise. Furthermore, compounding the problem is the fact that owners may regard overweight or obese cats as being physically appealing and cute, without truly seeing the potential health risk associated with overweight/obesity to their animals. Interestingly, approximately 60% of all animals in the prime (3–6 years), mature (7–10 years), and senior (11–14 years) age groups were overweight or obese. This contrasts with approximately 25% of prime (3–6 years), mature (7–10 years), and senior (11–14 years) animals and over 60% of junior (7 months to 2 years) animals having ideal BCS. This would indicate that aging is an important factor to consider in contributing to the overall prevalence of overweight/obesity. In addition, since this study comprised client-owned animals, standardization of diet and housing was not possible. Instead, the animals were kept under a variety of situations and fed a variety of commercial diet regimens. However, due to the large number of animals from a variety of management conditions, we think that this is a good representation of the cat population kept in Japan.

With very little data or none regarding healthy domestic cats being readily available in Japan, veterinarians are currently unsure as to what reference value ranges for plasma metabolites should be used in healthy domestic

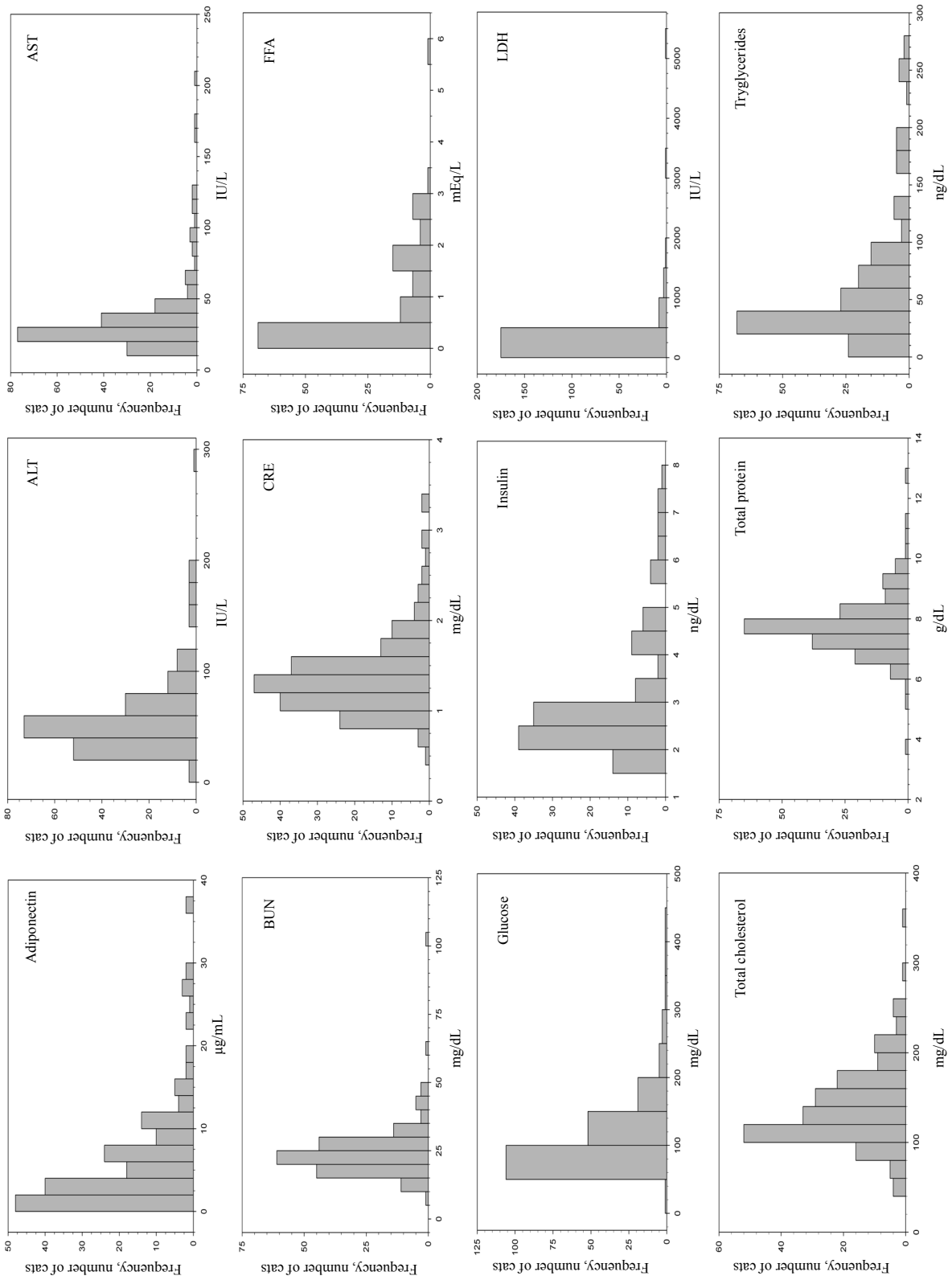
**Table 2.** Descriptive statistics for the observations from cross-sectional pool of Japanese cats used in the reference interval.

Analytes	Number of observations	Normality of distribution	Median Mean	Minimum value Maximum value	Reference values	
					2.5% limit (90% CI)	97.5% limit (90% CI)
Glucose (mg/dL)	189	Not normal	95.5	18	55.1	266
		P < 0.0001	110.4	432	(51.2–55.1)	(266–375.8)
Insulin (ng/mL)	130	Not normal	2.63	1.62	1.81	7
		P < 0.0001	3.08	7.89	(1.62–1.81)	(7.00–7.58)
Adiponectin (µg/mL)	177	Not normal	4.05	0.02	0.32	27.69
		P < 0.0001	6.48	37.14	(0.13–0.32)	(27.69–36.00)
Triglycerides (mg/dL)	179	Not normal	39	8	12.6	248.7
		P < 0.0001	60.2	278	(10.1–12.6)	(248.7–261.5)
Total cholesterol (mg/dL)	180	Not normal	129	44	62	242
		P < 0.0001	138.5	341	(54–62)	(242–287.3)
Free fatty acids (FFAs) (mEq/L)	116	Not normal	0.307	0.008	0.021	2.863
		P < 0.0001	0.799	5.55	(0.008–0.021)	(2.863–4.443)
Total protein (g/dL)	189	Not normal	7.6	3.7	6	9.9
		P < 0.0001	7.72	12.5	(5.43–6)	(9.9–11.07)
BUN (mg/dL)	189	Not normal	22.95	8.6	12.81	45.71
		P < 0.0001	24.44	103.2	(11.6–12.81)	(45.71–59.51)
Creatinine (mg/dL)	189	Not normal	1.31	0.56	0.83	2.64
		P < 0.0001	1.38	3.26	(0.70–0.83)	(2.64–3.79)
LDH (IU/L)	190	Not normal	128.5	24	40	1150.5
		P < 0.0001	229	5006	(31.9–40.0)	(1150.50–2968.30)
AST (IU/L)	190	Not normal	27	10	16.23	124.75
		P < 0.0001	35.8	201.3	(12.21–16.23)	(124.75–173.18)
ALT (IU/L)	189	Not normal	48	10	20	170.9
		P < 0.0001	58.7	283	(13.2–20)	(170.9–196.2)

cats. In this study, we took the opportunity to survey and create cross-sectional working reference value ranges for plasma metabolites commonly used to survey and diagnose metabolic health state. All of our plasma samples were derived from vet-visiting cats not showing any signs of disease, thereby providing a partial cross-sectional glimpse of healthy cats in Japan (Table 2). We elected to construct a working reference value range to include overweight and obese cats, since they were deemed to be healthy and not showing any signs of disease, to better reflect the actual cat population encountered by veterinarians in Japan. However, age, BCS condition, and sex can have a profound impact on the reference value range of plasma metabolite values in healthy cats (Table 3).

Therefore, we also examined the influence of these factors and constructed reference value ranges according to each factor.

Aging had meaningful impacts on adiponectin, BUN, BCS, BW, Cre, insulin, and T-cho values (Table 4), which would all indicate that aging animals are at a greater risk of developing obesity-related health risks. BW and BCS values tended to increase with age. Insulin values were increasing whereas adiponectin values were decreasing with age, which are all signs of possible insulin resistance development. Insulin resistance is frequently observed in cats, unlike in dogs (11). Cats, with their tendency to develop insulin resistance, are considered a good animal model for studying the onset mechanism of metabolic



**Figure.** Histograms illustrating the distribution of the observations used for the reference interval calculations for the 12 parameters described in Table 2 in a cross-sectional pool of healthy cats that were presented to 18 different veterinary clinics across Japan.

**Table 3.** Multivariate linear regression analysis.

Analyte	Age	BCS	Sex
Glucose (mg/dL)	0.947	0.329	0.471
Insulin (ng/mL)	0.804	0.672	0.728
Adiponectin ( $\mu\text{g/mL}$ )	0.843	0.825	0.257
Triglycerides (mg/dL)	0.009 <sup>a</sup>	0.022 <sup>b</sup>	0.615
Total cholesterol (mg/dL)	0.360	0.577	0.593
FFAs (mEq/L)	0.681	0.929	0.827
Total protein (g/dL)	0.112	0.389	0.856
BUN (mg/dL)	0.866	0.270	0.309
Creatinine (mg/dL)	0.93	0.382	0.662
LDH (IU/L)	0.658	0.597	0.062
AST (IU/L)	0.457	0.934	0.225
ALT (IU/L)	0.152	0.585	0.783
BW (kg)	0.292	<0.001 <sup>b</sup>	0.356
Age (years)	N/A	0.074	0.738
Sex	0.738	0.181	N/A
BCS (out of 5)	0.074	N/A	0.181

Values are presented as P-values for each factor.

<sup>a</sup>: Indicates significance of age ( $P < 0.05$ ) on analyte.

<sup>b</sup>: Indicates significance of BCS ( $P < 0.05$ ) on analyte.

**Table 4.** Reference value ranges of analytes as filtered by age category.

Analyte	Young	Mature	Elderly	P-values
	Kitten (0–6 months) (n = 11) Junior (7 months to 2 years) (n = 20)	Prime (3–6 years) (n = 60) Mature (7–10 years) (n = 54)	Senior (11–14 years) (n = 33) Geriatric (>15 years) (n = 12)	
Glucose (mg/dL)	112.81 $\pm$ 19.95	108.05 $\pm$ 9.49	112.76 $\pm$ 18.37	0.352
Insulin (ng/mL)	2.9 $\pm$ 0.36	2.92 $\pm$ 0.31	3.43 $\pm$ 0.47 <sup>b</sup>	0.034
Adiponectin ( $\mu\text{g/mL}$ )	8.27 $\pm$ 2.51	6.31 $\pm$ 1.43 <sup>a</sup>	5.46 $\pm$ 1.50 <sup>a</sup>	0.053
Triglycerides (mg/dL)	51.47 $\pm$ 11.35	95.04 $\pm$ 25.40	47.46 $\pm$ 12.39	0.139
Total cholesterol (mg/dL)	109.31 $\pm$ 9.80	139.39 $\pm$ 7.18 <sup>a</sup>	154.07 $\pm$ 17.06 <sup>a</sup>	<0.001
FFAs (mEq/L)	0.76 $\pm$ 0.35	0.76 $\pm$ 0.23	0.94 $\pm$ 0.42	0.476
Total protein (g/dL)	7.50 $\pm$ 0.22	7.80 $\pm$ 0.18	7.68 $\pm$ 0.33	0.312
BUN (mg/dL)	20.83 $\pm$ 1.95	22.56 $\pm$ 0.93	31.01 $\pm$ 4.46 <sup>b</sup>	<0.001
Creatinine (mg/dL)	1.07 $\pm$ 0.08	1.32 $\pm$ 0.05 <sup>a</sup>	1.74 $\pm$ 0.17 <sup>ac</sup>	<0.001
LDH (IU/L)	359.5 $\pm$ 213.92	151.47 $\pm$ 32.46 <sup>ad</sup>	319 $\pm$ 222.95	0.001
AST (IU/L)	50.82 $\pm$ 15.38	29.28 $\pm$ 2.63 <sup>ad</sup>	40.20 $\pm$ 9.99	0.002
ALT (IU/L)	62.29 $\pm$ 16.36	55.26 $\pm$ 5.81	62.87 $\pm$ 13.60	0.432
Age (years)	1.42 $\pm$ 0.21	6.49 $\pm$ 0.46 <sup>a</sup>	13.38 $\pm$ 0.68 <sup>b</sup>	<0.001
BW (kg)	3.29 $\pm$ 0.32	4.67 $\pm$ 0.34 <sup>a</sup>	3.93 $\pm$ 0.54 <sup>a</sup>	<0.001
BCS (out of 5)	3.08 $\pm$ 0.19	3.7 $\pm$ 0.14 <sup>a</sup>	3.5 $\pm$ 0.23 <sup>a</sup>	<0.001

P-values indicate significant differences in the median values among the treatment groups.

<sup>a</sup>: Indicates significance when compared to the 'Young' category ( $P < 0.05$ ; Kruskal–Wallis multiple comparison ANOVA (Dunn's method)).

<sup>b</sup>: Indicates significance when compared to 'Young' and 'Mature' categories ( $P < 0.05$ ; Kruskal–Wallis multiple comparison ANOVA (Dunn's method)).

<sup>c</sup>: Indicates significance when compared to 'Mature' category ( $P < 0.05$ ; Kruskal–Wallis multiple comparison ANOVA (Dunn's method)).

<sup>d</sup>: Indicates significance when compared to 'Elderly' category ( $P < 0.05$ ; Kruskal–Wallis multiple comparison ANOVA (Dunn's method)).

**Table 5.** Reference value ranges of analytes as filtered by BCS category.

Analyte	Thin	Ideal	Overweight	P-values
	BCS <3 (n = 22)	BCS 3 (n = 61)	BCS >3 (n = 107)	
Glucose (mg/dL)	94.32 ± 18.61	109.82 ± 13.09	113.96 ± 11.17	0.075
Insulin (ng/mL)	2.58 ± 0.42	2.55 ± 0.36	3.32 ± 0.31 <sup>b</sup>	0.001
Adiponectin (µg/mL)	10.37 ± 3.42	9.56 ± 2.29	3.95 ± 0.85 <sup>b</sup>	<0.001
Triglycerides (mg/dL)	44.77 ± 14.52	40.31 ± 7.34	76.87 ± 13.59 <sup>b</sup>	0.001
Total cholesterol (mg/dL)	114.59 ± 14.89	118.26 ± 9.16	154.51 ± 8.58 <sup>b</sup>	<0.001
FFAs (mEq/L)	0.43 ± 0.27	0.98 ± 0.29 <sup>a</sup>	0.75 ± 0.29	0.021
Total protein (g/dL)	8.21 ± 0.58	7.63 ± 0.28	7.67 ± 0.15	0.194
BUN (mg/dL)	25.24 ± 5.83	23.98 ± 1.78	24.45 ± 1.86	0.496
Creatinine (mg/dL)	1.43 ± 0.31	1.29 ± 0.08	1.43 ± 0.08	0.069
LDH (IU/L)	339.55 ± 179.88	332.54 ± 195.75	144.66 ± 19.68 <sup>b</sup>	0.02
AST (IU/L)	55.16 ± 19.79 <sup>c</sup>	36.07 ± 5.96	31.32 ± 4.48	<0.001
ALT (IU/L)	69.64 ± 29.76	59.34 ± 11.46	58.06 ± 6.36	0.776
Age (years)	6.52 ± 2.80	6.41 ± 1.15	7.88 ± 0.77 <sup>b</sup>	0.03
BW(kg)	3.08 ± 0.27	3.54 ± 0.21	5.46 ± 0.40 <sup>b</sup>	<0.001
BCS (out of 5)	2.38 ± 0.12	3.00 ± 0.00 <sup>a</sup>	4.11 ± 0.10 <sup>b</sup>	<0.001

P-values indicate significant differences in the median values among the treatment groups.

<sup>a</sup>: Indicates significance when compared to the 'Thin' category (P < 0.05; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

<sup>b</sup>: Indicates significance when compared to 'Thin' and 'Ideal' categories (P < 0.05; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

<sup>c</sup>: Indicates significance when compared to 'Ideal' category (P < 0.05; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

**Table 6.** Reference value ranges of analytes as filtered by sex.

Analyte	Females (n = 89)	Males (n = 101)	P-values
Glucose (mg/dL)	110.42 ± 11.17	110.38 ± 11.15	0.667
Insulin (ng/mL)	2.85 ± 0.32	3.23 ± 0.33 <sup>b</sup>	0.086
Adiponectin (µg/mL)	8.19 ± 1.78	4.93 ± 1.06 <sup>a</sup>	<0.001
Triglycerides (mg/dL)	72.57 ± 19.70	69.93 ± 14.32	0.747
Total cholesterol (mg/dL)	114.59 ± 14.89	140.56 ± 8.25	0.128
FFAs (mEq/L)	0.77 ± 0.24	0.80 ± 0.26	0.884
Total protein (g/dL)	7.69 ± 0.18	7.74 ± 0.21	0.719
BUN (mg/dL)	25.30 ± 1.75 <sup>c</sup>	23.57 ± 2.02	0.075
Creatinine (mg/dL)	1.37 ± 0.09	1.39 ± 0.09	0.928
LDH (IU/L)	259.50 ± 132.71	201.61 ± 52.17	0.256
AST (IU/L)	37.25 ± 5.44	34.27 ± 5.74 <sup>a</sup>	0.041
ALT (IU/L)	65.40 ± 10.66	54.92 ± 6.51	0.129
Age (years)	7.08 ± 0.98	7.42 ± 0.86	0.562
BW(kg)	3.52 ± 0.25	4.91 ± 0.38 <sup>a</sup>	<0.001
BCS (out of 5)	3.34 ± 0.15	3.73 ± 0.16 <sup>a</sup>	<0.001

P-values indicate significant differences in the median values among the treatment groups.

<sup>a</sup>: Indicates significance when compared to the 'Female' category (P < 0.05; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

<sup>b</sup>: Indicates significance when compared to 'Female' category (P < 0.10; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

<sup>c</sup>: Indicates significance when compared to 'Male' category (P < 0.10; Kruskal-Wallis multiple comparison ANOVA (Dunn's method)).

syndrome in humans (12). In addition, aging appears to have a detrimental effect on lipid and renal metabolism, which may lead to the development of high cholesterol lipidemia and kidney failure with aging in healthy cats. T-Chol, BUN, and Cre values of healthy cats were markedly elevated with aging, with these values being highest in the geriatric group. In addition, ALT, AST, LDH, triglycerides, and total protein values seem unaffected by aging in healthy cats, unlike in healthy dogs.

BCS also had a meaningful impact on adiponectin, BW, FFAs, insulin, T-cho, and triglyceride values (Table 5), which would all indicate that healthy animals with high BCS values are at a greater risk of developing obesity-related health risks. BW values tended to increase with BCS. Insulin values were also increasing whereas adiponectin values were decreasing with BCS, which are all signs of possible insulin resistance development. In addition, BCS appears to have a detrimental effect on lipid metabolism, which may lead to the development of high cholesterol and triglyceride lipidemia, accompanied by higher levels of FFAs, which would exacerbate the condition.

Lastly, sex had a meaningful impact on adiponectin, BCS, BW, and insulin values (Table 6). Healthy male cats were heavier in weight than females and also tended to have corresponding higher BCS values. In addition, male cats had higher insulin and lower adiponectin values than female cats, which would indicate a higher risk of developing insulin resistance. In addition, male cats had a tendency to have higher total cholesterol levels, which might be indicative of a higher risk of also developing high cholesterol lipidemia, which would be corroborated by greater BW and BCS values in males than females.

Overall, this study has a number of limitations. First, the data were gathered from only 18 practices across Japan, and henceforth we should have recruited more practices into our study to increase the amount of samples. Collecting more samples would help increase the accuracy of the working parameter reference value ranges, in addition to allowing us to possibly factor in breed influence on parameter values. However, since the collected samples were from cats living in both city and rural areas, our results accurately reflect a representative cross-section of the current prevalence rate of overweight and obese cats in Japan. Second, we were unable to collect information regarding the reproductive status of cats. Previous risk factors found in overweight or obese cats can be divided into factors such as sex, reproductive status, and breed (13–15). These factors have been postulated to contribute directly or indirectly to positive energy balance and subsequent weight gain. In future experiments, we should collect samples from healthier cats, with a focus on noting reproductive status, and continue to investigate overweight and obese rates in healthy Japanese cats. Lastly, the effect

of cat breed on parameter values could not be factored. We did not have a sufficient amount of samples collected to examine breed influence. Forty percent of our samples were from mixed cats and 11% were unknown; henceforth, our parameter reference range values are currently dominated by mixed-breed animals. Breed has been documented as a risk factor found in overweight or obese cats (15) and has been postulated to contribute directly or indirectly to positive energy balance and subsequent weight gain. In fact, breed has been implicated as a possible predilection for aberrations in lipid metabolism, as in the case with Burmese animals (16). Therefore, in the future, we hope to be able to collect more samples and be able to have equal amounts of samples from various breeds for better overall representation. Ideally, we would like to produce working parameter reference values based accordingly on age, BCS, breed, sex, or reproductive status in the future.

In conclusion, the rate of overweight and obese cats (BCS >3) in Japan was ~56%, with obese cats (BCS >4) accounting for 42% of all cats surveyed in our study. When examining a cross-section pool of healthy cats in Japan, aging, BCS, and sex were observed to all have an impact on certain plasma metabolite values. Aging is very important and it is necessary for owners to consider and ensure adequate contents/quantity of diet and exercise to meet each cat's requirement, depending on their ages. Weight management in Japanese cats appears to be extremely important starting at prime age (3–6 years). In addition, there is a necessity for owners to understand that Japanese cats have increased rates of developing lipid metabolism and kidney issues associated with aging. Increases in BCS and age both carry increased risk of insulin resistance developing in healthy cats. Moreover, increases in BCS value bring about higher risks of developing lipid metabolism problems, which may lead to the development of high cholesterol and triglyceride lipidemia, accompanied by higher levels of FFAs, which could exacerbate the condition. Lastly, males appear to have a higher risk than females of developing higher BCS and BW values, in addition to higher insulin and lower adiponectin values, which might lead to a higher risk of developing insulin resistance. In addition, male cats have a tendency to have higher total cholesterol levels, which might be indicative of a higher risk of also developing high cholesterol lipidemia.

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