

Table 1. Baseline data of adult-aged (10-15 months old) and middle-aged (17-21 months old) WHHLMI rabbits.

	JW	WHHLMI	
	Adult-aged	Adult-aged	Middle-ages
Body weight (Kg)	3.58±0.10 (10)	3.33±0.04 (46)	3.53±0.05 (52)
Abdominal Circumference (cm)	38.3±0.9 (10)	38.3±0.40 (46)	39.4±0.42 (52)
BMI (kg/cm/cm x 10000)	25.5±1.4 (10)	25.4±0.54 (40)	26.2±0.48 (49)
Fat accumulation (g)			
Mesenteric fat	48.1±9.8 (9)	69.8±4.6 (46)	92.2±6.5 (52) * [†]
axillary fat	19.0±3.3 (9)	17.6±1.6 (37)	17.3±1.3(50)
Inguinal fat	22.0±2.6 (9)	27.3±1.8 (37)	33.0±2.4 (50)*
Fasting blood sugar (mg/dL)	129±2.3 (10)	130±2.3 (35)	117±1.8 (37) * [†]
Fasting IRI (ng/mL)	0.82±0.09 (10)	1.29±0.28 (25)	1.60±0.34 (34)
HOMA-IR	6.12±0.72 (10)	10.2±2.4 (25)	11.2±2.6 (34)
Matsuda-ISI at IVGTT	2.89±0.41 (10)	3.08±0.37 (21)	3.66±0.75 (17)
Matsuda-ISI at OGTT	2.73±0.32 (10)	3.56±0.46 (21)	3.28±0.57 (18)
Serum total cholesterol (mg/dL)	15.0±1.8 (8)	820±39 (41)*	761±27 (42)*
VLDL-cholesterol (mg/dl)	3.5±1.8 (8)	88.7±10.5 (16)*	107±17 (17)*
LDL-cholesterol (mg/dL)	2.5±0.4 (8)	773±34 (16)*	730±35 (17)*
HDL-cholesterol (mg/dL)	9.0±1.5 (8)	13.7±1.1 (16)	13.7±1.1 (17)
Serum Triglyceride level (mg/dL)	44.9±6.8 (8)	331±34 (40)*	323±32 (41)*
VLDL-triglyceride (mg/dL)	21.5±5.1 (8)	47.1±5.2 (16)*	67.3±13.7 (17)*
LDL-triglyceride (mg/dL)	4.5±1.9 (8)	196±13 (16)*	230±19 (17)*
HDL-Triglyceride (mg/dL)	24.1±2.3 (8)	18.6±2.1 (16)	17.9±1.2 (17)
Whole TG/HDL-cholesterol	11.3±5.3 (8)	18.1±1.8 (16)	27.1±4.6 (17)*

Systolic blood pressure (cmHg)	116±6.5 (5)	122±3.1 (16)	121±4.3 (15)
Diastolic blood pressure (cmHg)	87.5±2.9 (5)	85.0±1.8 (16)	79.0±2.3 (15)
% surface lesion area of aorta	0	75.1±3.4 (46)*	88.2±0.8 (52)* [†]
Serum CRP (µg/mL)	7.6±0.7 (7)	34.7±5.9 (20)	86.2±40 (17)

Values in parentheses represent the number of rabbits analyzed. Data are represented as the mean ± SEM.

Statistical analyses were carried out with Scheffe's multiple comparison test. *, P<0.05 (vs JW); †, P<0.005 (vs adult-aged WHHLMI rabbits). BMI, Body mass index ($=[\text{bodyweight}]/[\text{length between shoulder and buttocks}]^2 \times 10,000$); IRI, immunoreactive insulin; HOMA-IR, homoeostasis model assessment of insulin resistance [19]; IVGTT, intravenous glucose tolerance test; Matsuda-ISI, Matsuda-insulin sensitivity index [20]; OGTT, oral glucose tolerance test; VLDL, very low-density lipoprotein; LDL, low-density lipoprotein; HDL, high density lipoprotein; CRP, C-reactive protein

Table 2. Correlation between accumulation fat and physical or physiological parameters of adult-aged (11-15 months old) and middle-aged (17-21 months old) WHHLMI rabbits.

	Adult-aged rabbits						Middle-aged rabbits					
	Mesenteric fat			Subcutaneous fat*			Mesenteric fat			Subcutaneous fat		
	n	R	P-value	n	R	P-value	n	R	P-value	n	R	P-value
Age	46	0.013	ns	37	0.373	0.014	52	-0.078	ns	50	-0.005	ns
Body weight	46	0.349	0.002	37	0.405	0.007	52	0.682	<0.001	50	0.481	<0.001
Abdominal circumference	46	0.327	0.027	37	0.319	0.037	52	0.646	<0.001	50	0.440	0.001
BMI (kg/cm/cm x 10000)	46	0.112	ns	34	0.306	0.055	50	0.541	<0.001	49	0.240	ns
Subcutaneous fat	37	0.363	0.017				50	0.649	<0.001			
Blood pressure												
Systolic	16	-0.200	ns	15	0.129	ns	15	0.343	ns	13	0.083	ns

Diastolic	16	-0.310	ns	15	-0.021	ns	15	0.257	ns	13	0.245	ns
Average	16	0.319	ns	15	-0.042	ns	15	0.268	ns	13	0.176	ns
% surface lesion area of aorta	46	0.331	0.025	37	0.043	ns	52	-0.085	ns	50	-0.176	ns

*Sum of inguinal fat and axillary fat were used as subcutaneous fat. Correlation analyses were carried out with Pearson's correlation test. A value of

P<0.05 was considered statistically significant. ns, not significant

Table 3. Correlation between accumulation of fat and biochemical parameters of adult-aged (11-15 months old) and middle-aged (17-21 months old) WHHLMI rabbits.

	Adult-aged rabbits						Middle-aged rabbits					
	Mesenteric fat			Subcutaneous fat*			Mesenteric fat			Subcutaneous fat		
	n	r	P-value	n	r	P-value	n	r	P-value	n	r	P-values
Fasting blood sugar	21	-0.162	ns	15	0.331	ns	37	0.352	0.033	32	0.206	ns
Fasting IRI	21	0.520	0.016	15	-0.197	ns	34	0.493	0.003	32	0.535	0.002
HOMA-IR	21	0.479	0.028	15	-0.160	ns	34	0.502	0.002	32	0.442	0.011
Matsuda-ISI at IVGTT	21	-0.335	ns	15	0.1180	ns	17	-0.570	0.018	15	-0.353	ns
Matsuda-ISI at OGTT	21	-0.307	ns	15	0.145	ns	17	-0.570	0.017	15	-0.646	0.009
Lipoprotein cholesterol												
VLDL	19	-0.331	ns	16	-0.184	ns	17	0.834	<0.001	15	0.475	0.074

LDL	19	-0.032	ns	16	0.119	ns	17	0.570	0.021	15	0.689	0.005
HDL	19	-0.280	ns	16	-0.219	ns	17	-0.555	0.026	15	-0.271	ns
Whole cholesterol	19	-0.110	ns	16	-0.071	ns	17	0.701	0.002	15	0.667	0.007
Lipoprotein triglyceride												
VLDL	19	0.236	ns	16	-0.134	ns	17	0.855	<0.001	15	0.399	ns
LDL	19	0.138	ns	16	0.025	ns	17	0.825	<0.001	15	0.309	ns
HDL	19	0.410	ns	16	0.625	0.010	17	0.066	ns	15	0.146	ns
Whole triglyceride	19	0.233	ns	16	0.020	ns	17	0.836	<0.001	15	0.367	ns
Whole TG/HDL cholesterol	19	0.268	ns	16	0.187	ns	17	0.781	<0.001	15	0.238	ns
Serum CRP	20	0.455	0.044	17	0.211	ns	17	0.601	0.023	12	0.139	ns

*Sum of inguinal fat and axillary fat were used as subcutaneous fat. Correlation analyses were carried out with Pearson's correlation test. A value of

P<0.05 was considered statistically significant. ns, not significant

Table 4. Correlation between fasting IRI and physical or biochemical parameters in WHHLM

rabbits

	Adult-aged rabbits			Middle-aged rabbits		
	n	r	P-value	n	r	P-value
Body weight	21	0.133	ns	18	0.488	0.047
Abdominal Circumference	21	0.190	ns	18	0.389	ns
Body mass index	21	-0.192	ns	16	0.403	0.012
Lipoprotein cholesterol						
VLDL	18	-0.287	ns	16	0.552	0.027
LDL	18	-0.234	ns	16	0.658	0.006
HDL	18	-0.158	ns	16	-0.416	ns
Lipoprotein triglyceride						
VLDL	18	0.454	ns	16	0.818	0.005
LDL	18	0.324	ns	16	0.690	<0.001
HDL	18	-0.125	ns	16	0.054	ns
Whole TG/HDL-Ch	18	0.303	0.22	16	0.719	0.002
Blood pressure						
Systolic	15	0.218	ns	14	0.109	ns

Diastolic	15	-0.315	ns	14	0.002	ns
Average	15	-0.320	ns	14	0.030	ns
Aortic lesion area	21	0.326	ns	18	-0.184	ns
Serum CRP	19	0.0912	ns	16	0.825	<0.001

Correlation analyses were carried out with Pearson's correlation test. A value of $P < 0.05$ was considered statistically significant.

Figure legends

Figure 1. Visceral fat accumulation in WHHLMI rabbits and immunohistochemical staining of mesenteric adipose tissue. Panels A and B show photographs of the accumulation of intraperitoneal fat (A) and mesenteric fat in a WHHLMI rabbit (female, 18 months old) and Panels C and D show those of a Japanese white rabbit (male, 15 months old). Panels E-H show photomicrographs of immunohistochemical staining of mesenteric adipose tissue of the WHHLMI rabbit. RAM-11, an antibody specific for rabbit monocytes/macrophages, MCP-1, an antibody specific for monocyte chemoattractant protein 1; CRP, antibody for C-reactive protein.

Figure 2. Glucose tolerance test of rabbits aged 10-15 months old. Panels A and B show blood sugar levels and serum immunoreactive insulin (IRI) levels (B) during oral glucose tolerance tests (OGTT) and panels C and D show those during intravenous glucose tolerance tests (IVGTT) (C, D). Panels E to H show results of OGTT and Panels I to L, results of IVGTT. Hatched triangles and bars indicate normal rabbits; open circles and bars indicate WHHLMI rabbits with fasting IRI levels less than 0.7 ng/mL; Closed circles and bars indicate WHHLMI rabbits with fasting IRI levels greater than 1.2 ng/mL. Data are presented as the mean \pm standard error of the mean. Statistic analyses were carried out with Scheffe's multiple comparison test. *, $P < 0.05$ (compared with normal rabbits); †, $P < 0.05$ (compared to WHHLMI rabbits with low fasting IRI levels); BS, blood sugar; IRI, immunoreactive

insulin; HOMA-IR, homeostasis model assessment insulin resistance [19]; Matsuda-ISI ,
Matsuda-insulin sensitivity index [20]

Figure 3. Glucose tolerance test of WHHLMi rabbits aged 17-21 months old. Panels A and B show blood sugar levels and serum immunoreactive insulin (IRI) levels (B) during oral glucose tolerance tests (OGTT) and panels C and D show those during intravenous glucose tolerance tests (IVGTT) (C, D). Panels E to H show results of OGTT and Panels I to L, results of IVGTT. Open circles and bars indicate WHHLMi rabbits with fasting IRI levels less than 0.7 ng/mL; Closed circles and bars indicate WHHLMi rabbits with fasting IRI levels greater than 1.2 ng/mL. Data are presented as the mean \pm standard error of the mean. Statistic analyses were carried out with Student's t-test or Welch's t-test. Statistical significance was set at $P < 0.05$. BS, blood sugar; IRI, immunoreactive insulin; HOMA-IR, homeostasis model assessment insulin resistance [19]; Matsuda-ISI, Matsuda-insulin sensitivity index [20]

