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Relationship between the adiponectin-leptin ratio and parameters of insulin resistance in subjects without hyperglycemia

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Abstract

We previously reported that the adiponectin-leptin (A/L) ratio was more efficacious as a parameter of insulin resistance than adiponectin or leptin alone, and a more sensitive and reliable marker of insulin resistance than homeostasis model assessment (HOMA-R) as the fasting plasma glucose (FPG) level elevated in type 2 diabetes mellitus. In this study, we examined the usefulness of the A/L ratio as compared to HOMA-R for assessing insulin resistance in Japanese subjects without hyperglycemia. A total of 411 Japanese adults without hyperglycemia (205 men, aged 49 ± 10 years; 206 women, aged 48 ± 10 years) were enrolled. We investigated the correlation between fasting serum insulin level, FPG, leptin or adiponectin, and body mass index (BMI), fat mass (FM), triglycerides (TGs), high-density lipoprotein (HDL) cholesterol, or preheparin serum lipoprotein lipase (LPL) as parameters of insulin resistance. Next, we examined the relationships between parameters of insulin resistance and the A/L ratio or HOMA-R. By simple regression of the correlation between serum insulin level, FPG, leptin or adiponectin, and each parameter of insulin resistance, the best correlation coefficients were seen in leptin (men, $r = 0.501$; women, $r = 0.667$) as compared with BMI, in leptin (men, $r = 0.658$; women, $r = 0.747$) as compared with FM, in adiponectin ($r = -0.285$) in men and leptin ($r = 0.299$) in women as compared with TGs, in adiponectin (men, $r = 0.405$; women; $r = 0.442$) as compared with HDL cholesterol, and in adiponectin (men, $r = 0.228$; women, $r = 0.452$) as compared with LPL. By simple regression of the correlation between A/L ratio or HOMA-R and each parameter of insulin resistance, the highest correlation coefficients were seen with the A/L ratio except HDL cholesterol in men. Next, we carried out multiple linear regression to analyze the association between A/L ratio or HOMA-R and FM, TGs, HDL cholesterol, and LPL, excluding BMI, simultaneously. In men, the A/L ratio was significantly correlated with FM and TGs, and HOMA-R was significantly correlated with FM. This model explained 34% of the variance in the A/L ratio and 17% of the variance in HOMA-R. In women, the A/L ratio was significantly correlated with FM and LPL, and HOMA-R was significantly correlated with FM and LPL. This model explained 39% of the variance in A/L ratio and 14% of the variance in HOMA-R. In conclusion, the present study suggested that the A/L ratio might be more useful than HOMA-R to accurately assess insulin resistance in subjects without hyperglycemia.

1. Introduction

Adipose tissue is not only a source of energy but also plays an important role in the development of insulin resistance, type 2 diabetes mellitus, hyperlipidemia, and their complications through the secretion of various hormone-like substances [1]. From 1995 to 1996, adiponectin was originally identified independently by 4 groups using different approaches [2-5]. Plasma adiponectin concentration has been reported to decrease as the body mass index (BMI) increases and to correlate negatively with insulin resistance [6-9].

In 1994, Zhang et al [10] reported the first successful cloning of leptin complementary DNA by the positional cloning method. Leptin was identified as the gene of the ob/ob mouse with genetic obesity syndrome. Paradoxically, plasma leptin concentration has been reported to increase significantly in obese subjects and in proportion to the degree of adiposity. Thus, a positive correlation with insulin resistance and leptin can correspondingly be used as a

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sensitive chemical marker for the diagnosis of obesity and obesity-related diseases [11,12].

The ratio of leptin to adiponectin has been recently proposed as a potential index for comprehensively identifying obesity in cynomolgus monkeys [13] and/or as a potential atherogenic index in obese patients with type 2 diabetes mellitus [14,15]. Moreover, the adiponectin-leptin (A/L) ratio has been reported to predict insulin sensitivity [16] and cardiovascular risk in HIV-infected patients [17].

It is important to measure insulin resistance because it plays a role in the development of atherosclerosis and diabetes mellitus. Although the hyperinsulinemic euglycemic clamp [18,19] and steady-state plasma glucose value [20] are the gold standards to estimate insulin resistance, they involve complicated procedures. The homeostasis model assessment (HOMA-R) is a convenient means to evaluate insulin resistance [21,22], although some limitations restricting its clinical use have been reported [23,24]. Hyperglycemia can adversely affect glucose homeostasis by interfering with insulin action and/or β-cell function, which is termed glucotoxicity [25]. The mechanism by which hyperglycemia causes insulin resistance is not completely understood, but several hypotheses have been proposed. Besides insulin resistance in the state of elevated blood glucose, there is a secondary insulin resistance due to activity of the hexosamine pathway [26-29] or an excessive accumulation of normal products of glucose metabolism, such as diacylglycerol [30,31]. Originally, HOMA-R was the method to effectively evaluate insulin resistance in the situation where insulin secretion capacity is sustained to some extent. However, in the situation where endogenous insulin secretion capacity is inhibited because of aging or glucotoxicity caused by elevated blood glucose level, it is difficult to accurately evaluate insulin resistance by HOMA-R. We previously reported that the A/L ratio was a more useful parameter of insulin resistance than adiponectin or leptin alone, and a more sensitive and reliable marker of insulin resistance than HOMA-R as the fasting plasma glucose (FPG) level elevated in patients with type 2 diabetes mellitus [16].

Because insulin resistance has recently attracted attention as a factor that may relate BMI, hypertriglyceridemia, hypo high-density lipoprotein (HDL) cholesterol [32,33], and metabolic syndrome [34,35], we investigated the correlation between the A/L ratio or HOMA-R and these parameters of insulin resistance to examine whether the A/L ratio was more useful than HOMA-R for assessing insulin resistance in subjects without hyperglycemia.

2. Subjects and methods

2.1. Subjects

Four hundred eleven Japanese adults (205 men and 206 women) without endocrine disease, significant renal or hepatic disease, coronary artery disease, cerebrovascular disease, or diabetes mellitus, and those receiving medication for diabetes mellitus, hyperlipidemia, or hypertension who underwent annual health examination at Mitsui Memorial Hospital for from January 2005 to May 2005 were enrolled in this study. Table 1 shows the clinical and laboratory data of the subjects.

Table 1
Clinical and laboratory data of the subjects distributed

	Men (n = 205)	Women (n = 206)
Age (y)	48.7 ± 9.7	47.9 ± 9.8
FM (kg)	22.2 ± 4.6	25.4 ± 5.5*
BMI (kg/m^2)	23.5 ± 2.6	20.8 ± 2.7*
HbA_{1c} (%)	5.0 ± 0.4	5.0 ± 0.3
FPG (mg/dL)	94.3 ± 6.5	88.8 ± 7.7*
IRI (μU/mL)	5.3 ± 3.2	4.7 ± 2.2**
HDL-cholesterol (mg/dL)	57.6 ± 13.3	68.6 ± 12.8*
LPL (ng/mL)	48.8 ± 23.2	59.8 ± 18.3*
TGs (mg/dL)	101.3 ± 39.9	74.2 ± 29.7*
Adiponectin (μg/mL)	8.8 ± 3.3	14.4 ± 6.3*
Leptin (ng/mL)	4.0 ± 2.3	7.3 ± 3.8*
HOMA-R	1.3 ± 0.8	1.1 ± 0.6**
A/L ratio	3.1 ± 2.7	2.9 ± 2.8

Data are presented as mean ± SD. HbA_{1c} indicates glycosylated hemoglobin.

* $P < .0001$ vs men.

** $P < .05$.

The present study was conducted according to the principles expressed in the Declaration of Helsinki. Informed consent was obtained from each subject after full explanation of the purpose, nature, and risk of all procedures used.

2.2. Study design

The subjects were divided according to sex, and the relationship between each parameter (BMI, fat mass [FM], triglycerides [TGs], HDL cholesterol, and preheparin serum lipoprotein lipase [LPL]) and adiponectin, leptin, fasting plasma insulin level (IRI), or FPG were examined. Next, the correlation between the A/L ratio or HOMA-R and each parameter (BMI, FM, TGs, HDL cholesterol, and LPL) were examined and we compared the coefficient of the correlation between each parameter and A/L ratio with that of the correlation between each parameter and HOMA-R.

2.3. Measurement

After a 10- to 12-hour overnight fast, a blood sample was obtained to determine FPG, IRI, leptin, adiponectin, HDL cholesterol, and TGs. Plasma glucose and lipids were measured by enzymatic methods using an automated analyzer (HITACHI 7350 Analyzer, Tokyo, Japan). The plasma concentrations of adiponectin were measured by a sandwich enzyme-linked immunosorbent assay (ELISA) system (adiponectin ELISA kit, Otsuka Pharmaceutical, Tokyo, Japan) as reported previously [36]. The plasma concentrations of leptin were measured by using a commercially available kit based on radioimmunoassay (RIA) (human leptin RIA kit, Cosmic, Tokyo, Japan). The concentrations of LPL in preheparin serum were measured by sandwich ELISA as previously described [37]. For the

assay, a kit from Daiichi Pure Chemicals (Tokyo, Japan) was used. The plasma concentrations of insulin were measured by using an RIA kit (Insulin Riabead II Kit, Abbott, Tokyo, Japan). The insulin resistance index as assessed according to the homeostasis model approach was calculated as follows [21, 22]: HOMA-R = IRI × FPG/405, where IRI is in microunits per milliliter and FPG is in milligrams per deciliter. Hemoglobin A_{1c} was measured by high-performance liquid chromatography. BMI was calculated as weight divided by the square of height in meters. FM was measured by using a bioelectrical impedance method [38] using a body fat analyzer (TBF-210, Tanita, Tokyo, Japan).

2.4. Statistical analyses

All statistical analyses were performed with the Statview 5 system (Abacus Concepts, Berkeley, CA) for Apple computer. The Wilcoxon signed rank test was used where appropriate for comparisons of clinical parameters between men and women. Relationships were analyzed by simple correlation. Next, to analyze the association between A/L ratio or HOMA-R and FM, TGs, HDL cholesterol, and LPL simultaneously, we carried out multiple linear regression. All values are mean ± SD, and a value of $P < .05$ was considered statistically significant.

3. Results

3.1. Simple linear regression analysis between BMI, FM, TGs, HDL cholesterol, or LPL and IRI, FPG, leptin, or adiponectin in subjects without hyperglycemia

BMI correlated significantly with IRI (men, $r = 0.361$, $P < .0001$; women, $r = 0.262$, $P = .0001$), FPG (men, $r = 0.218$, $P = .0016$; women, $r = 0.310$, $P < .0001$), leptin (men, $r = 0.501$, $P < .0001$; women, $r = 0.667$, $P < .0001$), and adiponectin (men, $r = -0.312$, $P < .0001$; women, $r = -0.319$, $P < .0001$) both in men and in women (Table 2). As for BMI, the highest correlation coefficients were shown with leptin in men and in women. Fat mass correlated significantly with IRI (men, $r = 0.405$, $P < .0001$; women, $r = 0.277$, $P < .0001$), FPG (men, $r = 0.176$, $P = .0117$; women, $r = 0.307$, $P < .0001$), leptin (men, $r = 0.658$; $P < .0001$; women, $r = 0.747$, $P < .0001$), and adiponectin (men, $r = -0.267$, $P = .0001$; women, $r = -0.390$, $P < .0001$) in men and women. As for FM, the highest correlation coefficients were shown with leptin too. TG level correlated significantly with IRI ($r = 0.138$, $P = .0490$), leptin ($r = 0.234$, $P = .0003$), and adiponectin ($r = -0.285$, $P < .001$) in men, and with IRI ($r = 0.203$, $P = .0034$), FPG ($r = 0.196$, $P = .0046$), leptin ($r = 0.299$, $P < .0001$), and adiponectin ($r = -0.181$, $P = .0093$) in women. Regarding TGs, the highest correlation coefficients were shown with adiponectin in men, and leptin in women. HDL cholesterol level correlated significantly with IRI ($r = -0.177$, $P = .0109$) and adiponectin ($r = 0.405$, $P < .0001$) in men and with IRI ($r = -0.144$, $P = .0383$), FPG ($r = -0153$, $P = .0280$), leptin ($r = -0.210$, $P = .0024$), and adiponectin ($r = 0.442$, $P < .0001$) in women. In the case of HDL cholesterol, the highest correlation coefficients were shown with adiponectin in men and in women. LPL level correlated significantly with adiponectin ($r = 0.228$, $P = .001$) in men and with IRI ($r = -0.229$, $P = .0009$) and adiponectin ($r = 0.452$, $P < .0001$) in women. As for LPL, the highest correlation coefficients were shown with adiponectin in men and in women.

In this study, the highest correlation coefficients between each parameter (BMI, FM, TGs, HDL cholesterol, or LPL) and adiponectin, leptin, IRI, or FPG were seen with leptin or adiponectin, but not with either IRI or FPG in men and in women.

3.2. Simple linear regression analysis between BMI, FM, TGs, HDL cholesterol, or LPL and HOMA-R or A/L ratio in subjects without hyperglycemia

BMI correlated significantly with HOMA-R (men, $r = 0.357$, $P < .0001$; women, $r = 0.290$, $P < .0001$) and A/L ratio (men, $r = -0.532$, $P < .0001$; women, $r = -0.506$, $P < .0001$) both in men and in women (Table 3). FM correlated significantly with HOMA-R (men, $r = 0.392$,

Table 2
Simple linear regression analysis between BMI, FM, TGs, HDL cholesterol, or LPL and IRI, FPG, leptin, or adiponectin

	IRI		FPG		Leptin		Adiponectin	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Men								
BMI	0.361	<.0001	0.218	.0016	0.501	<.0001	−0.312	<.0001
FM	0.405	<.0001	0.176	.0117	0.658	<.0001	−0.267	.0001
TGs	0.138	.0490	0.042	.5478	0.234	<.0003	−0.285	<.0001
HDL cholesterol	−0.177	.0109	−0.090	.2017	−0.093	.1554	0.405	<.0001
LPL	−0.137	.0506	−0.037	.5996	−0.216	.0717	0.228	.0010
Women								
BMI	0.262	.0001	0.310	<.0001	0.667	<.0001	−0.319	<.0001
FM	0.277	<.0001	0.307	<.0001	0.747	<.0001	−0.390	<.0001
TGs	0.203	.0034	0.196	.0046	0.299	<.0001	−0.181	.0093
HDL cholesterol	−0.144	.0383	−0.153	.0280	−0.210	.0024	0.442	<.0001
LPL	−0.229	.0009	−0.133	.0574	0.084	.2300	0.452	<.0001

Table 3
Simple linear regression analysis between BMI, FM, TGs, HDL cholesterol, or LPL and HOMA-R or A/L ratio

	Men					Women				
	HOMA-R		A/L ratio			HOMA-R		A/L ratio	
	r	*P*	*r*	*P*		*r*	*P*	*r*	*P*
BMI	0.357	<.0001	−0.532	<.0001	BMI	0.290	<.0001	−0.506	<.0001
FM	0.392	<.0001	−0.562	<.0001	FM	0.305	<.0001	−0.598	<.0001
TGs	0.123	.0798	−0.274	<.0001	TGs	0.216	.0018	−0.232	.0008
HDL cholesterol	−0.165	.0181	0.145	.0379	HDL cholesterol	−0.148	.0342	0.264	.0001
LPL	−0.134	.0553	0.151	.0302	LPL	−0.229	.0009	0.266	.0001

$P < .0001$; women, $r = 0.305$, $P < .0001$) and A/L ratio (men, $r = -0.562$, $P < .0001$; women, $r = -0.598$, $P < .0001$) both in men and in women. TG level correlated significantly with HOMA-R (women, $r = 0.216$, $P = .0018$) and A/L ratio (men, $r = -0.274$, $P < .0001$; women, $r = -0.232$, $P = .0008$). HDL cholesterol level correlated significantly with HOMA-R (men, $r = -0.165$, $P = .0181$; women, $r = -0.148$, $P = .0342$) and A/L ratio (men, $r = 0.145$, $P = .0379$; women, $r = 0.264$, $P = .0001$) both in men and in women. LPL level correlated significantly with HOMA-R (women, $r = -0.229$, $P = .0009$) and A/L ratio (men, $r = 0.151$, $P = .0302$; women, $r = 0.266$, $P = .0001$). The highest correlation coefficients overall were seen with the A/L ratio but not with HOMA-R except HDL cholesterol in men.

3.3. Multiple regression analysis of the association between A/L ratio or HOMA-R and FM, TGs, HDL cholesterol, and LPL simultaneously

We examined simple linear regression analysis to determine correlation coefficients between various parameters (BMI, FM, TGs, HDL cholesterol, or LPL), respectively. Multicollinearity existed with the association between BMI and FM ($r = 0.799$ in men, $r = 0.928$ in women) (data not shown). Therefore, we carried out multiple liner regression to analyze the association between A/L ratio or HOMA-R and FM, TGs, HDL-cholesterol, and LPL excluding BMI, simultaneously.

Multiple linear regression models for the dependent variable A/L ratio or HOMA-R are presented in Table 4. In men, A/L ratio was significantly correlated with FM and TGs, and HOMA-R was significantly correlated with FM. This model explained 34% of the variance in A/L ratio and 17% of the variance in HOMA-R. In women, A/L ratio was significantly correlated with FM and LPL, and HOMA-R was significantly correlated with FM and LPL. This model explained 39% of the variance in A/L ratio and 14% of the variance in HOMA-R.

4. Discussion

Recent research has shown that adipose tissue is not simply an inert storage depot for lipids but that it is also an important endocrine organ that plays a key role in the integration of endocrine functions and metabolic signs for the control of energy homeostasis. In our modern society, changes in lifestyle such as consumption of energy-rich foods and lack of exercise have led to excessive accumulation of body fat, resulting in obesity, which triggers lifestyle-related diseases such as diabetes mellitus, hyperlipidemia, and atherosclerosis [1]. Central obesity is a grouping together of metabolic abnormalities in subjects who often display the metabolic syndrome. The important of central obesity has been gaining much attention because of the relationship between the accumulation of visceral fat and an elevated risk of many diseases such as hypertension

Table 4
Multiple regression analysis for A/L ratio or HOMA-R in men and women

Independent variables	A/L ratio			HOMA-R		
	Coefficient	SE	*P*	Coefficient	SE	*P*
Men						
Intercept	10.692	1.268	<.0001	0.224	0.426	.5996
FM	−0.313	0.036	<.0001	0.066	0.012	<.0001
TGs	−0.010	0.004	.0232	−0.00007	0.001	.9563
HDL cholesterol	0.009	0.013	.4751	−0.007	−0.004	.0856
LPL	−0.003	0.007	.6959	−0.0003	0.002	.8747
Women						
Intercept	8.446	1.452	<.0001	0.499	0.342	.1465
FM	−0.283	0.030	<.0001	0.025	0.007	.0005
TGs	−0.004	0.006	.4309	0.002	0.001	.0755
HDL cholesterol	0.006	0.014	.6543	0.001	0.003	.7766
LPL	0.026	0.009	.0047	−0.005	0.002	.0109

The dependent variable is A/L ratio or HOMA-R. The model R^2 is 0.340 for A/L ratio and 0.168 for HOMA-R in men, and 0.392 for A/L ratio and 0.140 for HOMA-R in women. SE is the standard error for the regression coefficient.

[39,40], type 2 diabetes mellitus [41,42], cardiovascular disease [43,44], and stroke [39]. It has been suggested that insulin resistance is the primary etiologic factor for the metabolic syndrome [45], and a number of factors have been implicated in the etiology of insulin resistance arising from central obesity. It is important to measure insulin resistance because it plays a role in the development of metabolic syndrome. In a clinical setting, many investigators consider the hyperinsulinemic euglycemic clamp [18,19] and steady-state plasma glucose [20] value to be "gold standards" for estimating insulin resistance, but they are the most complicated methods to implement because they require simultaneous infusions of insulin and glucose, besides multiple blood sampling for a period of 3 hours. A simple index of insulin sensitivity based on fasting glucose and insulin levels, such as HOMA-R, is easily obtained and may be a useful tool for large epidemiologic studies [21,22], although some limitations have been reported restricting its clinical use [16,23,24]. Indeed, several investigators have reported that HOMA-R is not useful to accurately evaluate insulin resistance, particularly in individuals with impaired glucose tolerance [46] or elderly patients with poorly controlled type 2 diabetes mellitus [47].

Leptin, adiponectin, and more recently, a number of additional hormones, growth factors, and cytokines [48] have been reported to be secreted by adipocytes and to have paracrine as well as endocrine effects on a variety of target tissues. It is also known that the different fat depots in the body have different metabolic activities and this may relate to their differential effects on insulin sensitivity. Adiponectin secretion is decreased by insulin resistance, and leptin increases as BMI increases. The effects of adiponectin and leptin on energy metabolism differ; adiponectin is thought to increase insulin sensitivity and tissue fat oxidation resulting in reduced circulating fatty acid levels and reduced liver and intramyocellular triglyceride content [49,50]; leptin is thought to provide information about nutritional status and fat mass to neural centers regulating feeding behavior, appetite, and energy expenditure [51]. The level of adiponectin decreases and the level of leptin increases with insulin resistance [52,53]. Moreover, adiponectin and leptin levels tend to correlate with the various parameters (BMI, FM, TGs, HDL cholesterol, and LPL) in an opposite manner. Although the mechanisms and processes of these hormones remain unclear, they supposedly are involved in regulation of energy metabolism and manifestation of insulin resistance.

In a recent study, Yamauchi et al [54] reported that low levels of adiponectin were strongly implicated in the development of insulin resistance in a mouse model of both obesity and lipoatrophy, and the increased insulin resistance improved when adiponectin was administered. Moreover, insulin resistance further improved when a physiologic concentration of leptin was administered. Therefore, we thought that the A/L ratio could reflect insulin resistance more accurately than HOMA-R because both are often considered central components of insulin resistance. Indeed, the ratio of leptin to adiponectin has been recently proposed as a potential index for comprehensively identifying obesity in cynomolgus monkeys [13] and/or as a potential atherogenic index in obese patients with type 2 diabetes mellitus [14,15]. Moreover, we previously reported that the A/L ratio was a more accurate parameter of insulin resistance than adiponectin or leptin alone, and a more sensitive and reliable marker of insulin resistance than HOMA-R as the FPG level elevated in patients with type 2 diabetes mellitus [16]. The A/L ratio has been reported as a potential predictor of cardiovascular risk in HIV-infected patients [17].

In this study, we first investigated the correlation between IRI, FPG, leptin, or adiponectin and BMI, FM, TGs, HDL cholesterol, or LPL as parameters of insulin resistance in subjects without hyperglycemia; significant correlations between the A/L ratio and HOMA-R were shown in this study (men, $r = -0.386$, $P < .0001$; women, $r = -0.299$, $P < .0001$) (data not shown). The analysis of the relationship between IRI, FPG, leptin, or adiponectin and BMI, FM, TGs, HDL cholesterol, or LPL showed that the highest correlation coefficients were seen with leptin and/or adiponectin in both men and women. Next, we examined the relationship between each parameter of insulin resistance and the A/L ratio or HOMA-R. Interestingly, the relationship between each parameter of insulin resistance and the A/L ratio or HOMA-R showed that the highest correlation coefficients were seen with the A/L ratio but not with HOMA-R both in men and in women, except HDL cholesterol in men. Furthermore, by multiple linear regression, we found that the A/L ratio (R^2 = 34% in men, 39% in women) was higher than HOMA-R (R^2 = 17% in men, 14% in women). Multiple linear regression analysis revealed that A/L ratio might be the more accurate surrogate index than HOMA-R for determining insulin resistance in subjects without hyperglycemia. The results of the present study suggested that the A/L ratio might be more useful to accurately assess markers of insulin resistance than HOMA-R not only in patients with type 2 diabetes mellitus [16], but also in subjects without hyperglycemia. Originally, HOMA-R was the index regulated by FPG level and fasting plasma IRI level. It is the method to evaluate effective insulin resistance in the situation where insulin secretion capacity is sustained to some extent. Insulin secretion capacity is inhibited because of aging or glucotoxicity caused by elevated blood glucose level [16,23,24,46,47]. In this situation, it becomes difficult to accurately evaluate insulin resistance by using HOMA-R, whereas A/L ratio may be the index to evaluate effective insulin resistance without being affected by blood glucose level. As to the mechanisms involved, adipocytokines are often considered as central components of insulin resistance. It seems that we have entered an age where insulin resistance may be seen from the viewpoint of a combination of adipocytokines, which are factors that are considered to cause insulin resistance, instead of evaluating insulin resistance by HOMA-R. In this

study, we did not investigate the correlation between A/L ratio and M values, which was evaluated by the hyperinsulinemic euglycemic clamp technique using an artificial pancreas. In the future, it will be necessary to study the correlation between the A/L ratio and M value in patients with type 2 diabetes mellitus or nondiabetic subjects to determine whether it is possible to use the A/L ratio as a marker of insulin resistance.

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