Abstract

Insulin sensitivity has a strong correlation with aging. Little is known about insulin resistance in youths. The purpose of the study was to examine the association of age and metabolic fitness in college students with different levels of anthropometrics. Six hundred and eighty-three normal-weight (NW), 204 overweight (OW) and 274 Obese (OB) subjects aged 18.4±0.87 were enrolled in this study. Blood pressure (BP), triglyceride (TG), plasma insulin, total cholesterol, low density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C) were performed. Insulin resistance (IR) was obtained from fasting insulin levels, metabolic syndrome score (MSS) and triglyceride-high density lipoprotein cholesterol ratio (TG/HDL-C). The results showed we found age had positively correlation with IR in all groups ($p<.001$). The age had a trend of lower correlation with IR in OB group. Older-age youth had significantly higher IR than younger in different body mass index (BMI). Though younger-age of OB subjects were significantly younger than older of NW, the former had higher MSS ($p<.01$). Obesity may deteriorate insulin sensitivity sharply and cause cardiovascular risk factors in youths (range 17-20 yrs). We suggested that weight loss program is important to obese youths for health promotion.

Keywords: aging, insulin sensitivity, obese youth, metabolic syndrome, TG/HDL-C

Introduction

Metabolic syndrome (MetS) has been defined as the clustering of hypertension, dyslipidemia and impaired glucose tolerance in people with fasting hyperinsulinaemia (Reaven, 1988). The prevalence of MetS was 20.4% of the men and 15.3% of the women in Taiwan (Hwang, Bai, Chen, & Chien, 2007). Insulin resistance (IR) was an independent predictor of all clinical events, coronary heart disease, stroke, cancer and type 2 diabetes (Facchini, Hua, Abbasi, & Reaven, 2001). Cerebrovascular disease, heart disease and diabetes mellitus were the most common cause of death, followed by cancer (Tseng, 2004). These add up to a total of 28.4% of deaths (Yuan, 2004).

The triglyceride to high density lipoprotein cholesterol ratio (TG/HDL-C) correlates with LDL-C (low density lipoprotein cholesterol) phenotype B, small HDL particles and insulin resistance (Jia et al., 2006; McLaughlin et al., 2005). Free fatty acids (FFAs) from adipose tissues inhibit insulin-stimulated glucose uptake at the level of glucose transport and/or phosphorylation. When overproduction of glucose, FFAs and insulin was caused, insulin sensitivity was decreased (Han et al., 2008; Kruszynska et al., 2002). Diabetes, dyslipidaemia or hypertension was predicted over an 8-year followup period when the healthy subjects presented hyperinsulinaemia (Haffner et al., 1992). The syndrome is that of signalling a heightened atherogenic risk (Bianchi et al., 1995).

An redcution of insulin sensitivity has a strong correlation with aging (Chuang, S. Y., Chen, & Chou, 2004). Obesity is one of major factors of IR (Kopelman, 2000). The prevalence of obesity in Taiwan was 18.7 % and 22.0% by body mass index (BMI) in women and men (Chen, Lai, Lin, Liu, & Chen, 2003). The epidemiological study indicated the prevalence of MetS increased sharply beyond 50-60 years (Chuang, S. Y. et al., 2004).The odds of having developed MetS are increasingly with the weight gain from 20-70 year-old.(Hwang et al., 2007).

Aging is associated with an increase in bodyweight and fat mass (Ryan, 2000). Both aging and obesity is well correlated with IR. Metabolic fitness test is a sensitive indicator for determining age-difference in health. (Chou et al., 2004). There are various metabolic fitness tests, including fasting insulin and TG/HDL-C. Fasting insulin is usually taken as a surrogate measure of insulin resistance of whole-body glucose disposal (Ferrannini & Balkau, 2002). The ratio of TG/HDL-C has been proposed as an easily obtainable atherogenic maker (Dobiasova & Frohlich, 2001). We found most of past studies, which observed insulin resistance with aging, divided at least greater than 10 years from the different ages. Little is known about the relation between aging, obesity and IR in youths. The purpose of the study was to examine the association of age and metabolic fitness in college students with different levels of anthropometrics.

Materials and Methods

Subjects

Subjects (17-20 yrs-old) consisted of 486 men and 675 women who participated health screening. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and fasting blood sampling were conducted by registered nurses of the authorized hospital. All subjects were asked to avoid vigorous exercise and binges for 3 days before testing. Waist circumference measures were conducted by 5 trained technicians. The procedures of the study were had the approval of the institute authorities. The subject characteristics were presented in Table 1.

Anthropometric indices

Stature and weight were measured by standard stadiometer and scale (JENIX, Seoul, Korea). Subjects exhaled with upright standing and feet together when technicians measured. A BMI was calculated as weight (kg)/ height^2(m^2). Waist circumference measured at end-expiration as the point midway between the iliac crest and lower costal margin. Measurements were recorded to the nearest 0.1 cm, and a minimum of two measures was obtained from each site assuring a difference of no more than 0.2 cm between trials. An average of the two closest for each site was calculated. All subjects were classified as normal weight (BMI=18-23.9), overweight (BMI=24-26.9) and obesity (BMI$\geqq$27).

Blood pressure

Blood Pressure was measured quietly by an automated oscillometric BP monitor (BPVIEW, Seoul, Korea) on left hand, SBP and DBP were recorded.

Blood analysis

Blood samples were obtained after an overnight fasting (~8 hours). Blood glucose (GLU), total cholesterol (TC), TG, HDL-C, and LDL-C were determined by the GMI CX9 analyzer (Beckman coulter, Minnesota, USA). Plasma insulin was determined by enzyme-linked immunosobent assay (ELISA) using GMI access 2 (Beckman coulter, Minnesota, USA).

Insulin resistance

Insulin resistance (IR) was obtained from fasting insulin levels, metabolic syndrome score (MSS) and triglyceride to high density lipoprotein cholesterol ratio (TG/HDL-C). A MSS was calculated (Wing et al. 2007) by adding the quartile ranks from the distribution of TG, HDL-C, LDL-C, fasting blood glucose and insulin level of each subject. Higher levels of TG, LDL-C, GLU, insulin and lower level of HDL-C were corresponded to a higher summary score. TG/HDL-C was calculated by dividing triglyceride by high density lipoprotein cholesterol.

Statistical analysis

All values were expressed as mean ± SE. The one-way analysis of variance (ANOVA) was used to compare all variables among three groups in different BMI. Scheffe method was used for post hoc. The age of 3 groups was calculated by the median. The independent *t* test was used to compare the IR difference between younger and older. The relations between the various variables were analyzed using spearman's rank correlation coefficients. The statistical analysis was performed with SPSS 17.0 for windows. Significance was selected at P values <0.05 for all tests.

Results

Body mass index, WC, SBP, and DBP were significantly difference among 3 groups (Table 1). The obesity group was greater than OW and NW groups. The normal weight group was less than the others.

Table 1 All Subjects characteristics

	NW (n=683)	OW (n=204)	OB (n=274)
Age	18.4±0.76	18.4±0.81	18.5±1.13
Height	162.8±8.09	164.0±8.79	164.0±8.48
Weight	61.5±6.38	68.4±7.66*a	83.8±14.14*#
BMI	21.0±1.53	25.3±0.87*a	31.2±3.80*#
WC	70.9±5.86	80.5±7.02*a	92.6±10.09*#
SBP	116.1±12.40	122.3±12.7*a	126.9±12.7*#
DBP	72.5±8.24	75.2±8.11*a	79.0±10.4*#

* Significantly different from NW group (p< .001)
# Significantly different from OW group (p< .001)
a Significantly different from OB group (p< .001)

NW: normal weight, OW: overweight, OB: Obesity, BMI: body mass index, WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure

There were significant difference among 3 groups in fasting insulin, TG, HDL, LDL, TG/HDL-C ratio and MSS (Table 2). The obesity group was highest than the others. Normal weight group was lowest than the others. There was no difference in GLU among 3 groups. Insulin and TC in OB were higher than the others.

Table 2 The blood biochemical values and IR among 3 groups in different BMI

	NW (n=683)	OW (n=204)	OB (n=274)
Insulin	7.2±7.25	8.6±7.54	12.9±9.46*#
GLU	82.7±9.89	82.2±9.83	84.1±22.52
TC	184.3±28.03	188.6±32.32	194.3±36.54*#
TG	79.7±26.09	90.4±51.64*a	109.3±47.52*#
HDL-C	57.2±10.25	54.2±8.74*a	50.2±8.84*#
LDL-C	111.2±21.88	117.0±25.95*a	123.5±32.23*#
TG/HDL-C	1.4±0.63	1.7±1.28*a	2.27±1.16*#
MSS	11.6±2.64	12.6±2.93*a	14.4±2.78*#

* Significantly different from NW group (p< .05)
# Significantly different from OW group (p< .05)
a Significantly different from OB group (p< .05)
NW: normal weight, OW: overweight, OB: Obesity, TG: triglyceride,
HDL-C: high density lipoprotein cholesterol,
TG/HDL-C: triglyceride-high density lipoprotein cholesterol ratio,
MSS: metabolic syndrome score

We found age had positively lower correlation with IR in all groups (Table 3). The age had a trend of lower correlation with IR in the OB group.

Table 3 Relationship between age and IR in different BMI

	NW (n=683)	OW (n=204)	OB (n=274)
Insulin	0.36**	0.37**	0.25**
TG/HDL-C	0.21**	0.3**	0.25**
MSS	0.28**	0.36**	0.23**

*p<.001

Table 4 showed older-age youths had higher IR than younger in each group. There was higher significantly insulin in older-age of NW than younger of OW. No significant difference existed in TG/HDL-C and MSS. Younger-OB had higher MSS than older-OW. No significant difference existed in TG/HDL-C and Insulin between the groups.

Table 4 The IR difference between younger and older by age of the median in different BMI

	NW		OW		OB	
	younger (n=344)	older (n=339)	younger (n=344)	older (n=344)	younger (n=135)	older (n=137)
Insulin	5.8±6.31	8.5±7.89[#]	7.9±9.95 [a]	10.7±7.86[#]	11.1±9.28	14.7±9.40[#]
TG/HDL-C	1.3±0.53	1.5±0.72[#]	1.5±0.80	2.1±1.73[#]	1.9±0.88	2.5±1.34[*]
MSS	11.1±2.52	12.2±2.64[#]	12.2±3.01	13.3±2.72[#]	14.3±2.85 [b]	14.4± 2.76

[*] Significant difference from young in each group (p< .01)

[#] Significant difference from young in each group (p< .001)

[a] Significant difference from older of NW group (p< .05)

[b] Significant difference from older of OW group (p< .01)

NW: normal weight, OW: overweight, OB: Obesity,

TG/HDL-C: triglyceride-high density lipoprotein cholesterol ratio,

MSS: metabolic syndrome score

Discussion

The principle finding of this study was a significant correlation between aging, obesity and IR in youths ranged 17-20 years. Older-age youths had higher IR than younger as BMI was identical. There was higher significantly insulin in older-age of NW than younger of OW. Younger-OB had significantly higher MSS than older-NW.

A low correlation between age and insulin in youth was not surprising. Elder people with IR are strongly related to sarcopenia (Rasmussen et al., 2006). The youth with IR was caused by adipocytes secreting inflammatory cytokines (IL-6, TNF-α, CRP). Those cytokines not only induces insulin-signaling impaired (Han et al., 2008), but reduce the density of muscle. Muscle protein synthesis increased in the young during hyperinsulinemia (Rasmussen et al., 2006). Reduction attenuation of muscle may be another body composition characteristic important in the development of IR (Benson, Torode, & Fiatarone Singh, 2008).

The TG/HDL-C ratio is a powerful independent predictor of cardiovascular events (Bittner et al., 2009; Gaziano, Hennekens, O'Donnell, Breslow, & Buring, 1997). The LDL-C reduction remains the primary target of intervention for lipid-lowering (Barzi et al., 2005). TG/HDL-C ratio was well correlated with IR. Insulin resistance was significantly and strongly associated with coronary heart disease (CHD) risk. A High TG/HDL cholesterol ratio was also as a lipid predictor of CHD in people with IR (Kannel, Vasan, Keyes, Sullivan, & Robins, 2008). A higher MSS existed significantly in young-OB, but not in TG/HDL-C and insulin with comparing young-OB to older-OW. The age of younger-OB was significantly younger than older-OW ($p<.001$, the data didn't show). The MSS was calculated by quartiles of GLU、fasting insulin、HDL-C、LDL-C and TG. This implied the metabolism of blood glucose and lipid started to degenerated regardless of age.

Obesity is one of major factors of insulin resistance (Kopelman 2000; Tonino 1989). Both BMI and WC have a similar predictability for cardiac events, type 2 diabetes and metabolic syndrome (Chuang, Y. C. et al., 2006). The study showed significant differences among 3 levels of BMI and WC groups in fasting insulin, TG, HDL, LDL, TG/HDL-C ratio and MSS. The body fat accumulation is particularly evident in the abdominal region, with notable increases in both subcutaneous and visceral fat.

BMI is a factor that significantly affects the physical fitness of children, adolescents, and adults (Huang & Malina, 2007).It has been shown that approximately 50% of the variability in insulin-mediated glucose disposal between apparently healthy individuals is related to lifestyle(Bogardus, Lillioja, Mott, Hollenbeck, & Reaven, 1985). The development of MetS was slower in people with normal-weight and exercise habits (Hwang et al., 2007). We suggested early promotion of weight loss program for college students is considered an optimal strategy for preventing these lifelong diseases. Further study is needed to determined the relationship among physical, metabolic fitness and age.

References

Bittner, V., Johnson, B.D., Zineh, I., Rogers, W.J., Vido, D., Marroquin, O.C., et al. (2009). The triglyceride/high-density lipoprotein cholesterol ratio predicts all-cause mortality in women with suspected myocardial ischemia: a report from the Women's Ischemia Syndrome Evaluation (WISE). *Am Heart J*; 157: 548-555.

Facchini, F.S., Hua, N., Abbasi, F.Reaven, G.M. (2001). Insulin resistance as a predictor of age-related diseases. *J Clin Endocrinol Metab*; 86: 3574-3578.

Ferrannini, E.Balkau, B. (2002). Insulin: in search of a syndrome. *Diabet Med*; 19: 724-729.

Kannel, W.B., Vasan, R.S., Keyes, M.J., Sullivan, L.M.Robins, S.J. (2008). Usefulness of the triglyceride-high-density lipoprotein versus the cholesterol-high-density lipoprotein ratio for predicting insulin resistance and cardiometabolic risk (from the Framingham Offspring Cohort). *Am J Cardiol*; 101: 497-501.

Barzi, F., Patel, A., Woodward, M., Lawes, C.M., Ohkubo, T., Gu, D., et al. (2005). A comparison of lipid variables as predictors of cardiovascular disease in the Asia Pacific region. *Ann Epidemiol*; 15: 405-413.

Benson, A.C., Torode, M.E.Fiatarone Singh, M.A. (2008). Effects of resistance training on metabolic fitness in children and adolescents: a systematic review. *Obes Rev*; 9: 43-66.

Bianchi, S., Bigazzi, R., Quinones Galvan, A., Muscelli, E., Baldari, G., Pecori, N., et al. (1995). Insulin resistance in microalbuminuric hypertension. Sites and mechanisms. *Hypertension*; 26: 789-795.

Bogardus, C., Lillioja, S., Mott, D.M., Hollenbeck, C.Reaven, G. (1985). Relationship between degree of obesity and in vivo insulin action in man. *Am J Physiol*; 248: E286-291.

Chen, T.L., Lai, S.W., Lin, W.Y., Liu, C.S.Chen, W.K. (2003). Descriptive analysis of body staus in patients reveving health checkups: A hopistal-based stduy. *Mid Taiwan J Med*; 8: S114-118.

Chou, C.H., Ho, C.F., Hu, Y.W., Wang, J.S., Yang, S.C. (2004). Comparison in Physical Fitness and Metabolic Fitness Between Different Age Groups in College. *Physical Education Journal*; 37: 11-21.

Chuang, S.Y., Chen, C.H.Chou, P. (2004). Prevalence of metabolic syndrome in a large health check-up population in Taiwan. *J Chin Med Assoc*; 67: 611-620.

Chuang, Y.C., Hsu, K.H., Hwang, C.J., Hu, P.M., Lin, T.M.Chiou, W.K. (2006). Waist-to-Thigh Ratio Can also be a Better Indicator Associated with Type 2 Diabetes Than Traditional Anthropometrical Measurements in Taiwan Population. *Annals of Epidemiology*; 16: 321-331.

Dobiasova, M.Frohlich, J. (2001). The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). *Clin Biochem*; 34: 583-588.

Gaziano, J.M., Hennekens, C.H., O'Donnell, C.J., Breslow, J.L.Buring, J.E. (1997). Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. *Circulation*; 96: 2520-2525.

Haffner, S.M., Valdez, R.A., Hazuda, H.P., Mitchell, B.D., Morales, P.A.Stern, M.P. (1992). Prospective analysis of the insulin-resistance syndrome (syndrome X). *Diabetes*; 41: 715-722.

Han, P., Zhang, Y.Y., Lu, Y., He, B., Zhang, W.Xia, F. (2008). Effects of different free fatty acids on insulin resistance in rats. *Hepatobiliary Pancreat Dis Int*; 7: 91-96.

Huang, Y.Malina, R. (2007). BMI and health-related physical fitness in Taiwanese youth 9-18 years. *Medicine and Science in Sports and Exercise*; 39: 701-708.

Hwang, L.C., Bai, C.H., Chen, C.J.Chien, K.L. (2007). Gender different on the development of metabolic syndrome: a population-based study in taiwan. *Eur J Epidemiol*; 22: 899-906.

Jia, L., Long, S., Fu, M., Yan, B., Tian, Y., Xu, Y., et al. (2006). Relationship between total cholesterol/high-density lipoprotein cholesterol ratio, triglyceride/high-density lipoprotein cholesterol ratio, and high-density lipoprotein subclasses. *Metabolism*; 55: 1141-1148.

Kopelman, P.G. (2000). Obesity as a medical problem. *Nature*; 404: 635-643.

Kruszynska, Y.T., Worrall, D.S., Ofrecio, J., Frias, J.P., Macaraeg, G.Olefsky, J.M. (2002). Fatty acid-induced insulin resistance: decreased muscle PI3K activation but unchanged Akt phosphorylation. *J Clin Endocrinol Metab*; 87: 226-234.

McLaughlin, T., Reaven, G., Abbasi, F., Lamendola, C., Saad, M., Waters, D., et al. (2005). Is there a simple way to identify insulin-resistant individuals at increased risk of cardiovascular disease? *Am J Cardiol*; 96: 399-404.

Rasmussen, B.B., Fujita, S., Wolfe, R.R., Mittendorfer, B., Roy, M., Rowe, V.L., et al. (2006). Insulin resistance of muscle protein metabolism in aging. *Faseb J*; 20: 768-769.

Reaven, G.M. (1988). Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*; 37: 1595-1607.

Ryan, A.S. (2000). Insulin resistance with aging: effects of diet and exercise. *Sports Med*; 30: 327-346.

Tseng, C.H. (2004). Mortality and causes of death in a national sample of diabetic patients in Taiwan. *Diabetes Care*; 27: 1605-1609.

Yuan, D.o.H. (2004). *Vital statistics: mortality in Taiwan.* Taipei.