Certain Hormonal Markers in Urban Thai Adults with Metabolic Syndrome

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Background: *The prevalence of metabolic syndrome (MS) accompanied with cardiometabolic complications has progressively increased in Thailand. The roles of insulin resistance, leptin, adiponectin, and free testosterone as prognostic indicators of MS among Thai population were evaluated.*
Material and Method: *Men and women aged 34 to 89 years (n = 308) having 0-5 criteria of MS according to NCEP III with Asian-specific cut-points for waist circumference were enrolled in this cross-sectional study. Blood glucose, lipids, insulin, leptin, adiponectin, and free testosterone were measured.*
Results: *Each component of MS, especially the enlarged waist, adversely affected insulin sensitivity. MS subjects were at higher risk for developing insulin resistance, decreasing of plasma adiponectin, and increasing of leptin and the leptin/adiponectin ratio in comparison to non-MS individuals. The hormonal changes that have been shown to be associated with increased cardiometabolic risk were amplified as more MS criteria have been met. Odds ratios of increased leptin/adiponectin ratio among MS group were highest in comparison to others. Free testosterone levels declined with age and did not discriminate men with MS.*
Conclusion: *The results indicate the benefit of hormonal assessment, particularly the leptin/adiponectin ratio in identifying MS individuals with high cardiometabolic disease risk.*

Keywords: *Leptin adiponectin ratio, Insulin resistance, Free testosterone, Metabolic syndrome, Cardiometabolic disease*

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The metabolic syndrome (MS) is composed of abdominal obesity, dyslipidemia (high triglycerides and low high-density lipoprotein cholesterol, HDLC), elevated fasting blood glucose, and blood pressure. According to the Ministry of Public Health Reports in 2010, the cardiovascular disease is one of the three leading causes of death in Thailand. The hazards ratios for cardiovascular disease events and all-cause mortality between 1983 and 2002 survey among Thais with MS were 2.41 and 1.60 respectively[1].

Several hormonal changes in either their secretion or actions are found in MS. Insulin resistance is the main underlying cause and a predictor of subsequent type 2 diabetes mellitus and cardiovascular diseases in metabolic syndrome[2,3]. Leptin and adiponectin are adipokine hormones affecting insulin actions. Reduced leptin actions, as they occur in a leptin-resistant state, augment food intake, beta cell dysfunction, insulin resistance, and obesity[4]. Leptin increased in MS regardless of overall or central obesity, and hyperleptinemia was a risk factor for coronary heart disease[5,6]. Adiponectin carries insulin-sensitizing action. A reduction of adiponectin caused insulin resistance and subsequently MS development independent of obesity[7]. Moreover, hypoadiponectinemia may indicate the presence of cardiovascular disease in MS patients[8]. In addition, MS is closely related to low testosterone level, their interactions result in insulin resistance and vascular endothelial dysfunction, which are potential causal factors for increased cardiovascular diseases[9].

The prevalence of MS according to the National Cholesterol Education Program III (NCEP III) criteria among Thai adults increased from 10 to 15% in 2005 to 32.6% in 2011[10,11]. The prediction of MS individuals at high risk of developing complicating diseases therefore becomes necessary. This study aimed at evaluating whether insulin resistance, leptin, adiponectin, and free testosterone blood levels are

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useful for detecting persons with MS who are more likely to have cardiometabolic complications among the Thai population.

Material and Method

Subjects

Three hundred eight subjects with zero to five components of MS according to the harmonized criteria of six international expert groups with Asian-specific cut-points for waist circumference[12] were randomly selected from 1,530 volunteers attending another community-based research. All participants resided in Bangkok. With informed consent, history taking and general physical examination were done. Individuals with chronic illness or type 1 diabetes mellitus and steroid or certain drug users were excluded from the study. Fasting venous blood was drawn. Blood samples were immediately analyzed for glucose and lipid concentrations and kept as serum at -70°C until assayed. Maximum storage period was three months. In this cross-sectional study, participants were divided into six groups of each sex by zero to five criteria of MS diagnosis (Table 1). Participants who had zero to two criteria of MS were classified as non-MS and those with three to five MS criteria were classified as MS. The research proposal was approved by the Human Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Measurements

Blood pressure was recorded after a 10 minutes rest. Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. BMI was calculated by divided body weight (kg) by the square of their height (m^2).

Blood glucose and lipids were measured by enzymatic method using Hitachi 917 automatic analyzer. Serum insulin, leptin, and adiponectin were analyzed using the Iodine-125 radioimmunoassay kits for human hormones (Linco Research, Inc.). Free testosterone (the biologically active form) was assessed by solid phase enzyme-linked immunosorbent assay kit (IBL International GMBH). Intra- and inter-assay variability of plasma hormone measurement within our laboratory was less than 10%. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated according to a formula: fasting plasma glucose (mmol/l) x fasting plasma insulin (μU/ml)/22.5. HOMA-IR value more than 3.13, which was mean plus two SD value obtained from subjects who had no MS component[13] was used to identify insulin resistance. The ratios between leptin and adiponectin as well as between adiponectin and HOMA-IR were determined.

Table 1. Criteria for diagnosis of metabolic syndrome (NCEP III)

Criteria	Categorical cut points
Waist circumference	>90 cm in men* >80 cm in women*
Elevated blood pressure	≥130 mmHg systolic and/or ≥85 mmHg diastolic or on antihypertensive drug
Elevated triglycerides	>150 mg/dl or on triglyceride-lowering drug
Abnormal fasting blood glucose	>100 mg/dl or on glucose-lowering drug
Reduced HDLC	<40 mg/dl in men or <50 mg/dl in women

NCEP III = national cholesterol education program III; HDLC = high density lipoprotein cholesterol
*Adapted for Asian population[12]

Statistical analysis

Most data were not normally distributed, thus, Mann-Whitney U test or Kruskal-Wallis test was used for the comparison. Normally distributed variables were compared using student's paired t-test. Spearman Rank Correlation was performed for the association study. Binary logistic regression analysis was used to determine the relationship between component of metabolic syndrome and insulin resistance as well as between an outcome of metabolic syndrome and change of studied hormone. Data analysis was done using SPSS version 13 software for Windows. A $p<0.05$ was considered statistically significant.

Results

The demographic and biochemical characteristics of participants stratified by MS and non-MS groups are shown in Table 2. Age and BMI in the MS group were higher than the non-MS group. The MS group demonstrated significantly higher HOMA-IR, leptin, and leptin/adiponectin ratio but lesser adiponectin, and adiponectin/HOMA-IR ratio in comparison to the non-MS group (Table 3).

As shown in Fig. 1, HOMA-IR tended to increase as numbers of components of MS increased from three to five. The MS group demonstrated higher chance of having insulin resistance (HOMA-IR >3.13) in comparison to their counterpart (age-adjusted OR

Table 2. Demographic and biochemical characteristics of subjects

	Non-MS			MS		
	Men (n = 82)	Women (n = 75)	Total (n = 157)	Men (n = 73)	Women (n = 78)	Total (n = 151)
Age (year)	48.00 (41.00-57.00)[1]	49.00 (43.00-56.00)[1]	48.00 (41.75-56.25)[1]	64.00 (52.00-70.00)[1]	59.00 (50.00 -67.00)[1]	60.00 (51.00-68.00)[1]
BMI (kg/m^2)	23.17±3.40	23.56±3.86	23.36±3.62[1]	26.91±3.88	27.18±4.25	27.05±4.06[1]
Waist (cm)	82.70±8.80	79.89±9.32	81.36±9.13[1]	95.63±9.36[2]	91.01±8.40[2]	93.24±9.15[1]
Systolic BP (mmHg)	114 (110-130)	110 (108-120)	110 (109.5-124.5)[1]	130 (120-141.5)	130 (120-140)	130 (120-140)[1]
Diastolic BP (mmHg)	71 (70-80)	70 (70-80)	70 (70-80)[1]	80 (78-90)	80 (70-90)	80 (78-90)[1]
Triglycerides (mg/dl)	113.00 (85.00-147.00)[2]	93.00 (68.00-129.00)[2]	104.00 (76.00-140.00)[1]	203.00 (147.00-248.75)	180.00 (124.00-241.00)	184.00 (137.00-246.25)[1]
HDL-cholesterol (mg/dl)	55.26±12.08[2]	64.73±13.89[2]	59.78±13.77[1]	45.74±12.31[2]	54.51±15.21[2]	50.27±14.52[1]
FBS (mg/dl)	89.50 (85.00-95.00)	88.00 (83.25-95.00)	89.00 (84.75-95.00)[1]	111.00 (95.75-132.25)[2]	101.50 (88.00-118.00)[2]	107.00 (92.00-123.75)[1]

Values in mean ± SD or median (25th-75th percentile); FBS = fasting blood sugar; BMI = body mass index; MS = metabolic syndrome; BP = blood pressure
Significant differences between non-MS and MS groups at p<0.0001[1]
Significant differences between sex within MS or non-MS group at p<0.05[2]

2.97, 95% CI 1.56-5.66, p<0.001). Positive association between waist circumference and HOMA-IR was found (Spearman's rank correlation, r_s = 0.48, p<0.0001). Enlarged waist had the greatest impact on the occurrence of insulin resistance (Table 4). Significant positive correlation between HOMA-IR and leptin (r_s = 0.47, p<0.0001) and negative correlation between HOMA-IR and adiponectin (r_s = -0.36, p<0.0001) were detected.

MS subjects had higher circulating leptin but lesser adiponectin concentrations than non-MS subjects (Table 3). In addition, as more MS criteria have been met, increasing levels of leptin, decreasing adiponectin, and rising of the leptin/adiponectin ratios were observed (Fig. 1). Moreover, both crude and adjusted OR of increased leptin/adiponectin ratio in MS were highest when compared with a decreased adiponectin/HOMA-IR ratio and sole changes of insulin, leptin, adiponectin, HOMA-IR or free testosterone (Table 5). Leptin/adiponectin ratio was found to directly correlate with HOMA-IR (r_s = 0.55, p<0.0001).

Serum free testosterone (free T) concentrations in male subjects was negatively associated with age (r_s = -0.34, p<0.0001) and systolic blood pressure (r_s = -0.26, p<0.01). Serum free T levels in men with and without MS were not significantly different though men with MS were significantly older than men without MS (Table 2). Likewise, the OR of lowering free T in MS males over non-MS males was statistically insignificant.

Fig. 1 Changes of HOMA-IR values, leptin and adiponectin concentrations and their ratio according to the number of MS components (value in median and 25th-75th percentile).

Table 3. Hormone concentrations in non-MS and MS subjects

	Non-MS (n = 157) median (25^{th}-75^{th} percentiles)	MS (n = 151) median (25^{th}-75^{th} percentiles)
Insulin (mU/ml)	12.08 (8.56-18.16)	13.44 (9.57-19.10)
HOMA-IR	2.59 (1.88-4.19)[1]	3.80 (2.53-5.32)[1]
Leptin (ng/ml)	6.35 (3.23-12.70)[1]	12.85 (6.85-22.07)[1]
Adiponectin (mg/ml)	6.75 (4.48-9.84)[1]	5.25 (3.77-7.47)[1]
Leptin/ADP ratio	0.95 (0.47-2.23)[1]	2.48 (1.18-4.74)[1]
ADP/HOMA-IR ratio	2.41 (1.17-4.90)[1]	1.40 (0.73-2.70)[1]
Free T (pg/ml)*	4.98 (3.58-6.81)*	4.74 (2.70-6.01)*

HOMA-IR = homeostasis model assessment of insulin resistance; ADP = adiponectin; Free T = free testosterone
* Free testosterone was measured only in male subjects (n = 78 for non-MS, n = 67 for MS)
Significant differences between non-MS and MS groups at $p<0.0001$[1]

Table 4. Association between component of metabolic syndrome and insulin resistance

MS components	Crude OR (95% CI)	Adjusted OR (95% CI)
Large waist circumference (>90 cm in men, >80 cm in women)	4.97 (3.03-8.15)[1]	3.19 (1.74-5.84)[1]
High blood pressure (≥130 mmHg systolic and/or 85 diastolic mmHg or on antihypertensive drug)	2.10 (1.33-3.31)[2]	1.40 (0.82-2.41)
High triglyceride levels (>150 mg/dl or on triglyceride-lowering drug)	2.49 (1.56-3.97)[1]	1.33 (0.74-2.38)
Abnormal fasting blood glucose (>100 mg/dl or on glucose-lowering drug)	4.58 (2.74-7.64)[1]	3.39 (1.84-6.24)[1]
Low HDLC levels (<40 mg/dl in men or <50 mg/dl in women)	1.94 (1.13-3.32)[2]	0.77 (0.43-1.39)

n = 308; OR = odds ratio for MS group; Adjusted odds ratio for age, sex and other 4 MS components
Significance of OR at $p<0.0001$[1] and $p<0.05$[2]; Insulin resistance = HOMA-IR >3.13

Table 5. Odds ratios of changes in studied hormones due to metabolic syndrome

Hormonal alterations	Crude OR (95% CI)	Adjusted OR (95% CI)
Increased insulin	1.54 (0.89-2.66)	0.52 (0.22-1.25)
Increased HOMA-IR	3.30 (1.86-5.85)[1]	1.42 (0.63-3.19)
Increased leptin	4.76 (2.64-8.59)[1]	2.39 (0.75-7.59)
Decreased adiponectin	2.45 (1.39-4.29)[2]	2.68 (1.26-5.68)[2]
Increased leptin/adiponectin ratio	6.52 (3.55-11.97)[1]	5.58 (2.31-13.48)[1]
Decreased adiponectin/HOMA-IR ratio	3.48 (1.96-6.18)[1]	2.80 (1.37-5.75)[2]
Decreased free testosterone	1.39 (0.62-3.11)	0.96 (0.26-3.54)

n of free testosterone = 145 (from running out of some samples) and n = 308 for other hormones
OR = odds ratio for MS group; Adjusted odds ratio for age, sex and other hormones
Significance of OR at $p<0.0001$[1], $p<0.05$[2]

Discussion

Consistent with other previous studies, increased prevalence of insulin resistance in MS subjects and its direct association with increasing number of MS components were found in this study[3,14]. Though insulin resistance may not always occur together with MS, it is inseparably involved in the MS pathogenesis. Impaired fasting glucose is a result of insulin resistance in the liver and peripheral tissues as well as from a defective β-cell glucose sensitivity[15]. Accumulation of visceral adipose tissue can cause insulin resistance by producing inflammatory cytokines and metabolically toxic products that impair insulin signaling[16]. Insulin resistance enhances free fatty acid (FFA) production from fat cells and impairs FFA oxidation by endothelial lipoprotein lipase.

Increased circulating and hepatic influx of FFA augment the hepatic synthesis, release triglyceride-rich very-low-density lipoprotein into blood, and lower HDLC formation[17]. In addition, impairment of nitric oxide production and vascular-endothelial cell functions from high circulating FFA and insulin resistant status can induce blood pressure increment[18]. In the present study, waist circumference most directly associated with HOMA-IR. This signifies that abdominal obesity may be the most important risk factor for insulin resistance among Thai MS patients which is similar to finding in other Asian population[19].

Leptin and adiponectin changed in the opposite direction in MS subjects. Alterations of these two adipokines and their ratio (leptin/adiponectin ratio), which have been amplified by increasing MS components in Thai population, are consistent with the data reported in other nationalities[5,7,20]. Leptin decreases insulin secretion while enhances insulin sensitivity; thus, leptin resistant status as marked by hyperleptinemia could result in the development of insulin resistance[4,5]. Adiponectin exerts a direct insulin-sensitizing effect in human; hence, an insulin resistance would occur in the hypoadiponectinemic condition[21]. However, a possibility that low adiponectin levels may be a consequence of insulin resistance with compensatory hyperinsulinemia is also suggested[22]. Significant linear relationships between HOMA-IR and serum levels of leptin and adiponectin as well as their ratio found in the present study emphasize the links of these two adipokines with insulin resistance in pathophysiology of MS as previously described by other investigators[20,22,23].

The metabolic disruption in adipoinsular axis and its consequences including insulin resistance, tissue inflammation, endothelial dysfunction, and disorder of lipid metabolism, as occur in MS subjects are the risk factors of cardiovascular diseases[2,4]. Likewise, the leptin/adiponectin ratio has been shown to be a good marker of intima media thickness in healthy subjects with or without MS[24]. Since the leptin/adiponectin ratio had the strongest association with MS, it may be a better predictor of the cardiometabolic risk in MS patients. Besides, therapeutic means for reduction of leptin and/or stimulation of adiponectin synthesis may be helpful for management of MS and its related complications. However, our study is limited by a cross-sectional in design; further study using longitudinal design is needed to investigate the relationships between these hormonal markers and the cardiometabolic complications. Besides, effects of confounding variables such as drug-induced hormonal changes should be controlled in further studies.

The present study showed an age-related decline in serum free T among Thais similar to those reported in other populations[25,26]. Testosterone reduction was shown to increase visceral fat and was identified as a risk factor for the development of MS in men[27]. Alternatively, it may be possible that synthesis of testosterone is suppressed by MS. However, in the present study, free T concentrations as well as its adjusted OR calculated between MS and non-MS males was not statistically different. This relationship is inconclusive as previous studies reporting conflicting results[28-30]. Additionally, sex hormone binding globulin but not testosterone was shown to be associated with the risk of MS in the Framingham's heart study[31]. The relationship between testosterone and MS has not yet been fully understood and needs further investigation. Nevertheless, either age-related or MS-related decreased free T are hazardous to health among men, as prospective cohort studies point to the effect of low free T in increasing all-cause mortality and cardiovascular disease[32,33].

In conclusion, hormonal changes in either their secretion or actions in MS have been shown from previous literature review. In comparison to non-MS individuals, the present study shows that Thai individuals with MS have higher chance of promoting harmful changes in hormones that may lead to increased risk of cardiovascular diseases. Leptin/adiponectin ratio was found to have the strongest association with MS among Thais, and thus, may be a useful prognostic marker of the syndrome.

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What is already known on this topic?

Increasing of MS prevalence has been reported in several epidemiological studies in Thai population. Additionally, the risk for cardiovascular diseases and all-cause mortality among Thais with MS are higher than non-MS. The pathophysiological basis for the relationship between MS and cardiovascular diseases has been associated with hormones, especially adipokines and insulin resistance. However,

relationships between changes in these crucial hormones and MS diagnostic criteria have never been studied in Thais.

What this study adds?

The present study demonstrates higher chance for undesirable changes in hormones that may lead to increased risk of cardiovascular diseases among Thais with MS in comparison to the non-MS. Measurements of these hormones and adequate manipulations to normalize their blood levels should be considered when managing MS patients to reduce the risks of cardiovascular complications.

Potential conflicts of interest

None.

References

1. Tanomsup S, Aekplakorn W, Sritara P, Woodward M, Yamwong S, Tunlayadechanont S, et al. A comparison of components of two definitions of the metabolic syndrome related to cardiovascular disease and all-cause mortality in a cohort study in Thailand. Diabetes Care 2007; 30: 2138-40.
2. Jeppesen J, Hansen TW, Rasmussen S, Ibsen H, Torp-Pedersen C, Madsbad S. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease: a population-based study. J Am Coll Cardiol 2007; 49: 2112-9.
3. Verhagen SN, Wassink AM, van der Graaf Y, Gorter PM, Visseren FL. Insulin resistance increases the occurrence of new cardiovascular events in patients with manifest arterial disease without known diabetes. the SMART study. Cardiovasc Diabetol 2011; 10: 100. doi: 10.1186/1475-2840-10-100.
4. Martin SS, Qasim A, Reilly MP. Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. J Am Coll Cardiol 2008; 52: 1201-10.
5. Esteghamati A, Noshad S, Khalilzadeh O, Morteza A, Nazeri A, Meysamie A, et al. Contribution of serum leptin to metabolic syndrome in obese and nonobese subjects. Arch Med Res 2011; 42: 244-51.
6. Wallace AM, McMahon AD, Packard CJ, Kelly A, Shepherd J, Gaw A, et al. Plasma leptin and the risk of cardiovascular disease in the west of Scotland coronary prevention study (WOSCOPS). Circulation 2001; 104: 3052-6.
7. Hung J, McQuillan BM, Thompson PL, Beilby JP. Circulating adiponectin levels associate with inflammatory markers, insulin resistance and metabolic syndrome independent of obesity. Int J Obes (Lond) 2008; 32: 772-9.
8. Selcuk MT, Selcuk H, Temizhan A, Maden O, Saydam GS, Dogan M, et al. Impact of plasma adiponectin levels to the presence and severity of coronary artery disease in patients with metabolic syndrome. Coron Artery Dis 2008; 19: 79-84.
9. Wang C, Jackson G, Jones TH, Matsumoto AM, Nehra A, Perelman MA, et al. Low testosterone associated with obesity and the metabolic syndrome contributes to sexual dysfunction and cardiovascular disease risk in men with type 2 diabetes. Diabetes Care 2011; 34: 1669-75.
10. Aekplakorn W, Chongsuvivatwong V, Tatsanavivat P, Suriyawongpaisal P. Prevalence of metabolic syndrome defined by the International Diabetes Federation and National Cholesterol Education Program criteria among Thai adults. Asia Pac J Public Health 2011; 23: 792-800.
11. Pan WH, Yeh WT, Weng LC. Epidemiology of metabolic syndrome in Asia. Asia Pac J Clin Nutr 2008; 17 (Suppl 1): 37-42.
12. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120: 1640-5.
13. Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG. Prevalence and determinants of insulin resistance among U.S. adolescents: a population-based study. Diabetes Care 2006; 29: 2427-32.
14. Medeiros CC, Ramos AT, Cardoso MA, Franca IS, Cardoso AS, Gonzaga NC. Insulin resistance and its association with metabolic syndrome components. Arq Bras Cardiol 2011; 97: 380-9.
15. Ferrannini E, Gastaldelli A, Iozzo P. Pathophysiology of prediabetes. Med Clin North Am 2011; 95: 327-39, vii-viii.
16. Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity? Curr Opin Endocrinol Diabetes Obes 2012; 19: 81-7.
17. Gallagher EJ, Leroith D, Karnieli E. Insulin resistance in obesity as the underlying cause for the metabolic syndrome. Mt Sinai J Med 2010;

77: 511-23.
18. Cersosimo E, DeFronzo RA. Insulin resistance and endothelial dysfunction: the road map to cardiovascular diseases. Diabetes Metab Res Rev 2006; 22: 423-36.
19. Kamezaki F, Sonoda S, Nakata S, Kashiyama K, Muraoka Y, Okazaki M, et al. Proposed cutoff level of waist circumference in Japanese men: evaluation by homeostasis model assessment of insulin resistance levels. Intern Med 2012; 51: 2119-24.
20. Kotani K, Sakane N. Leptin:adiponectin ratio and metabolic syndrome in the general Japanese population. Korean J Lab Med 2011; 31: 162-6.
21. Cook JR, Semple RK. Hypoadiponectinemia—cause or consequence of human "insulin resistance"? J Clin Endocrinol Metab 2010; 95: 1544-54.
22. Di Chiara T, Argano C, Corrao S, Scaglione R, Licata G. Hypoadiponectinemia: A Link between Visceral Obesity and Metabolic Syndrome. J Nutr Metab 2012; 2012: 175245. doi: 10.1155/2012/175245.
23. Gupta A, Gupta V, Agrawal S, Natu SM, Agrawal CG, Negi MP, et al. Association between circulating leptin and insulin resistance, the lipid profile, and metabolic risk factors in North Indian adult women. Biosci Trends 2010; 4: 325-32.
24. Norata GD, Raselli S, Grigore L, Garlaschelli K, Dozio E, Magni P, et al. Leptin:adiponectin ratio is an independent predictor of intima media thickness of the common carotid artery. Stroke 2007; 38: 2844-6.
25. Gray A, Feldman HA, McKinlay JB, Longcope C. Age, disease, and changing sex hormone levels in middle-aged men: results of the Massachusetts Male Aging Study. J Clin Endocrinol Metab 1991; 73: 1016-25.
26. Iwamoto T, Yanase T, Koh E, Horie H, Baba K, Namiki M, et al. [Reference ranges of total serum and free testosterone in Japanese male adults]. Nihon Hinyokika Gakkai Zasshi 2004; 95: 751-60.
27. Saad F, Aversa A, Isidori AM, Gooren LJ. Testosterone as potential effective therapy in treatment of obesity in men with testosterone deficiency: a review. Curr Diabetes Rev 2012; 8: 131-43.
28. Katabami T, Kato H, Asahina T, Hinohara S, Shin T, Kawata T, et al. Serum free testosterone and metabolic syndrome in Japanese men. Endocr J 2010; 57: 533-9.
29. Hong D, Kim YS, Son ES, Kim KN, Kim BT, Lee DJ, et al. Total testosterone and sex hormone-binding globulin are associated with metabolic syndrome independent of age and body mass index in Korean men. Maturitas 2013; 74: 148-53.
30. Li C, Ford ES, Li B, Giles WH, Liu S. Association of testosterone and sex hormone-binding globulin with metabolic syndrome and insulin resistance in men. Diabetes Care 2010; 33: 1618-24.
31. Bhasin S, Jasjua GK, Pencina M, D'Agostino R Sr, Coviello AD, Vasan RS, et al. Sex hormone-binding globulin, but not testosterone, is associated prospectively and independently with incident metabolic syndrome in men: the framingham heart study. Diabetes Care 2011; 34: 2464-70.
32. Hyde Z, Norman PE, Flicker L, Hankey GJ, Almeida OP, McCaul KA, et al. Low free testosterone predicts mortality from cardiovascular disease but not other causes: the Health in Men Study. J Clin Endocrinol Metab 2012; 97: 179-89.
33. Vikan T, Schirmer H, Njolstad I, Svartberg J. Endogenous sex hormones and the prospective association with cardiovascular disease and mortality in men: the Tromso Study. Eur J Endocrinol 2009; 161: 435-42.

ฮอร์โมนบ่งชี้ความเสี่ยงทางหัวใจและเมตาบอลิซึมในคนไทยที่เป็นโรคอ้วนลงพุง

สุพรพิมพ์ เจียสกุล, มยุรี หอมสนิท, กมล อุดล, สุวัฒณี คุปติวุฒิ, มาลิกา ชุรินทรพรรณ, น้ำอ้อย เสมประเสริฐ, สมาน อ่อนเรียบร้อย

ภูมิหลัง: *ความชุกของโรคอ้วนลงพุงร่วมกับภาวะแทรกซ้อนทางหัวใจและเมตาบอลิซึมในประเทศไทยเพิ่มขึ้นเป็นลำดับ จึงทำการศึกษาภาวะดื้ออินซูลิน ระดับเลปติน อะดิโพเนกติน และเทสโทสเตอโรนอิสระในเลือดผู้เป็นโรคอ้วนลงพุง เพื่อประเมินความเสี่ยงในการเกิดภาวะแทรกซ้อนของโรค*

วัสดุและวิธีการ: *ทำการศึกษาแบบตัดขวางในชายและหญิงไทยอายุ 34-89 ปี จำนวน 308 ราย ที่มีองค์ประกอบของการวินิจฉัยโรคอ้วนลงพุงตามเกณฑ์ NCEP III จำนวน 0-5 เกณฑ์ และใช้ขนาดรอบเอวชาวเอเชีย วัดระดับกลูโคส อินซูลิน เลปติน อะดิโพแนกติน และเทสโทสเตอโรนอิสระในเลือด*

ผลการศึกษา: *องค์ประกอบของโรคอ้วนลงพุงโดยเฉพาะรอบเอวที่ใหญ่ขึ้นทำให้ความไวของอินซูลินลดลง เมื่อเทียบกับผู้ที่ไม่เป็นโรคอ้วนลงพุง ผู้เป็นโรคอ้วนลงพุงมีความเสี่ยงสูงกว่าที่จะเกิดภาวะดื้ออินซูลินมีระดับอะดิโพเนกตินลดลงขณะที่ระดับเลปตินและอัตราส่วนระหว่างเลปตินและอะดิโพเนกตินสูงขึ้น การเปลี่ยนแปลงทางฮอร์โมนซึ่งสัมพันธ์กับความเสี่ยงด้านหัวใจและเมตาบอลิซึมเหล่านี้มากขึ้นตามจำนวนเกณฑ์ของโรคอ้วนลงพุง โอกาสเปลี่ยนแปลงของอัตราส่วนระหว่างเลปตินและอะดิโพเนกตินในโรคอ้วนลงพุงมากกว่าของฮอร์โมนอื่นที่ศึกษา เทสโทสเตอโรนอิสระในเลือดลดลงตามอายุที่เพิ่มขึ้นและไม่แตกต่างกันระหว่างผู้ที่เป็นและไม่เป็นโรคอ้วนลงพุง*

สรุป: *การวัดระดับฮอร์โมนโดยเฉพาะอัตราส่วนระหว่างเลปตินและอะดิโพเนกตินอาจมีประโยชน์เพื่อแยกแยะผู้ป่วยโรคอ้วนลงพุงซึ่งมีความเสี่ยงสูงที่โรคจะลุกลามและเกิดภาวะแทรกซ้อนด้านหัวใจและเมตาบอลิซึม*