J Korean Med Sci. 2018 Jul 16;33(29):e197
https://doi.org/10.3346/jkms.2018.33.e197
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Endocrinology, Nutrition & Metabolism

The Cut-off Values of Surrogate Measures for Insulin Sensitivity in a Healthy Population in Korea according to the Korean National Health and Nutrition Examination Survey (KNHANES) 2007–2010

Shinje Moon [1*], **Jung Hwan Park** [2*], **Eun-Jung Jang** [3], **Yoo-Kyung Park** [1], **Jae Myung Yu** [1], **Joon-Sung Park** [2], **Youhern Ahn** [2], **Sung-Hee Choi** [4], and **Hyung Joon Yoo** [1]

[1]Department of Internal Medicine, Hallym University College of Medicine, Seoul, Korea
[2]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea
[3]Korea Centers for Disease Control and Prevention, Osong, Korea
[4]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

Received: Nov 20, 2017
Accepted: May 10, 2018

Address for Correspondence:
Sung-Hee Choi, MD, PhD
Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82 Gumi-ro 173-beon-gil, Bundang-gu, Seongnam 13620, Republic of Korea.
E-mail: shchoimd@gmail.com

Hyung Joon Yoo, MD, PhD
Division of Endocrinology and Metabolism, Department of Internal Medicine, Hallym University College of Medicine, 1 Singil-ro, Yeongdeungpo-gu, Seoul 07440, Republic of Korea.
E-mail: hjoonyoo@gmail.com

*Shinje Moon and Jung Hwan Park contributed equally to this work.

ABSTRACT

Background: This study aimed to identify the gender-specific characteristics of the surrogate measures of insulin resistance and to establish valid cut-off values for metabolic abnormalities in a representative sample in Korea.
Methods: Data were collected from the datasets of the Korean National Health and Nutrition Examination Survey between 2007 and 2010. The total number of eligible participants was 10,997. We used three measures of insulin resistance: the homeostasis model assessment-insulin resistance (HOMA-IR), McAuley index, and triglyceride and glucose (TyG) index. The estimated cut-off values were determined using the highest score of the Youden index.
Results: The area under the curve (AUC) of the HOMA-IR, McAuley index, and TyG index were 0.737 (95% confidence interval [CI], 0.725–0.750), 0.861 (95% CI, 0.853–0.870), and 0.877 (95% CI, 0.868–0.885), respectively. The cut-off values of the HOMA-IR were 2.20 in men, 2.55 in premenopausal women, and 2.03 in postmenopausal women, and those of the McAuley index were 6.4 in men and 6.6 in premenopausal and postmenopausal women. For the TyG index, the cut-off values were 4.76 in men and 4.71 in premenopausal and postmenopausal women.
Conclusion: In conclusion, the present study provides the valid cut-off values of the indirect surrogate measures of insulin sensitivity. These values may be used as reference for insulin sensitivity in a clinical setting and may provide a simple and supplementary method for identifying populations at risk of insulin resistance.

Keywords: Homeostasis Model Assessment; McAuley Index; Triglyceride and Glucose Index; Insulin Resistance; Metabolic Syndrome

ORCID iDs
Shinje Moon
https://orcid.org/0000-0003-3298-3630
Jung Hwan Park
https://orcid.org/0000-0003-3941-4836
Eun-Jung Jang
https://orcid.org/0000-0001-8381-3901
Yoo-Kyung Park
https://orcid.org/0000-0003-0545-3562
Jae Myung Yu
https://orcid.org/0000-0001-9179-1554
Joon-Sung Park
https://orcid.org/0000-0003-4740-3061
Youhern Ahn
https://orcid.org/0000-0002-4357-1730
Sung-Hee Choi
https://orcid.org/0000-0003-0740-8116
Hyung Joon Yoo
https://orcid.org/0000-0002-7755-9246

Disclosure
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Moon S, Choi S, Yoo HJ. Data curation: Moon S, Park JH, Jang EJ, Park YK, Yu JM, Park JS. Formal analysis: Moon S, Park JH, Jang EJ, Park YK, Yu JM, Park JS, Ahn Y, Choi SH, Yoo HJ. Methodology: Moon S, Park JH, Jang EJ, Park YK, Yu JM, Park JS, Ahn Y, Yoo HJ. Writing - original draft: Moon S, Park JH.

INTRODUCTION

Insulin resistance is a pathological condition that is characterized by a reduced physiological response of the peripheral tissues to normal insulin levels.[1,2] It is considered as an independent risk factor for cardiovascular and cerebrovascular diseases and can result in metabolic syndrome.[3-8]

Insulin resistance can be measured using the pancreatic suppression test, hyperinsulinemic-euglycemic clamp technique (HIEG clamp), or minimal model approximation of the metabolism of glucose (MMAMG).[9-11] However, these tests are complicated, invasive, and costly, and they are only suitable for small-scale studies. For epidemiological and clinical studies, simple indirect methods have been proposed. Such methods include the homeostasis model assessment-insulin resistance (HOMA-IR) and McAuley index that use fasting insulin level.[12-14] However, because the measurement of fasting insulin level is cumbersome with no standard assay available, an insulin-free equation for estimating insulin resistance was investigated and developed. In 2010, the product of fasting triglyceride and glucose (TyG) levels, which is referred to as the TyG index, was proposed as a useful surrogate measure of insulin resistance in healthy adults.[15] However, the sex-specific cut-off values of these measures have not been established.

Thus, this study aimed to evaluate the sex-specific characteristics of the surrogate measures of insulin resistance in a representative sample in Korea. Moreover, the valid cut-off values for metabolic abnormalities were identified.

METHODS

Study population

Data were collected from the Korean National Health and Nutrition Examination Survey (KNHANES) between 2007 and 2010. KNHANES was a cross-sectional and nationally representative survey with a multistage and stratified sample design. The total number of participants from each source was 33,552. The following participants were excluded from this study: those with missing data (anthropometric or laboratory data), those below 20 years of age, those with a past history of cardiovascular diseases, stroke, liver cirrhosis, and hepatitis B and C infections, as well as individuals with diabetes, rheumatic arthritis, asthma, chronic obstructive pulmonary disease, or chronic kidney disease with an estimated glomerular filtration rate lower than 60 or those who were receiving medications for dyslipidemia. The total number of eligible participants was 10,997.

Clinical and laboratory measurements

Blood pressure (BP) was measured three times in sitting position after at least 5 minutes of rest. The average of three recorded systolic and diastolic BP values was used in the present study. Waist circumference (WC) was measured using a flexible tape at the narrowest point between the uppermost lateral border of the iliac crest and the lowest border of the rib cage at the end of normal expiration. Venous blood sampling was performed, and the samples were transported daily to the central laboratory (Seoul Medical Science Institute, Seoul, Korea, in 2007; Neodin Medical Institute, Seoul, Korea between 2008 and 2010). After 8 hours of overnight fasting, the fasting plasma concentrations of glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol were determined according to standard procedures using the Advia 1650 (Siemens, Washington, DC, USA) in 2007 and the Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan) between 2008 and 2010. For the accuracy and consistency of each survey, we used the revised HDL cholesterol values between 2007 and 2010 based on the Korea Centers for Disease Control and Prevention guidelines.[16,17] Insulin concentrations were measured with an immunoradiometric assay (INS-IRMA; BioSource, Nivelles, Belgium) using the 1470 WIZARD automatic gamma counter (PerkinElmer, Turku, Finland).

Definition

Based on the revised National Cholesterol Education Program criteria, metabolic syndrome is defined as the presence of three or more of the following[18]: 1) BP ≥ 130/85 mmHg or use of antihypertensive medications, 2) WC > 90 cm and > 80 cm using the International Obesity Task Force criteria for an Asian Pacific population for WC,[19] 3) fasting glucose ≥ 100 mg/dL or use of anti-diabetic medications, 4) HDL cholesterol level < 40 mg/dL in men and < 50 mg/dL in women or use of cholesterol-lowering medications, and 5) triglyceride level ≥ 150 mg/dL or use of triglyceride-lowering medications.

Insulin sensitivity was evaluated using the HOMA-IR, McAuley index, and TyG index. The standard formulas were as follows:

$$\text{HOMA} - \text{IR} = \text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glucose (mmol/L)}/22.5$$

$$\text{McAuley index} = \exp\{2.63 - 0.28 \text{ Ln fasting insulin } (\mu\text{IU/mL}) - 0.31 \text{ Ln triglycerides (mmol/L)}\}$$

$$\text{TyG index} = \text{Ln}\{\text{fasting glucose (mg/dL)} \times \text{triglycerides (mg/dL)}\}/2$$

Statistical analysis

Data, including socio-demographic information, medical condition, anthropometric data, and laboratory measures, were presented as mean or percentage (%) with 95% confidence interval (CI). The prevalence rate of metabolic syndrome and its components was calculated, and Pearson's χ^2 test was used to compare the proportions of individuals according to sex and menstrual status. The values of each surrogate measure of insulin sensitivity were presented as the 10th, 25th, 50th, 75th, and 90th percentiles in terms of age and sex. Data were analyzed with sampling weights for multistage and stratified sampling.

In the present study, we analyzed the surrogate measures of insulin sensitivity using the receiver operating characteristic (ROC) curve for metabolic syndrome to estimate the valid cut-off values. Because several studies have reported that several surrogate measures differed according to sex,[20] in the present study, analyses were performed independently in men and women. In addition, we also divided the female participants into two subgroups according to menstrual status. The estimated cut-off values were determined using the highest score of the Youden index (YI). Analyses were performed using the SPSS software version 21.0 (IBM, Armonk, NY, USA).

RESULTS

Baseline characteristics of the participants

Overall, data from 10,997 participants were assessed (4,577 men and 6,420 women). The anthropometric, clinical, and biochemical characteristics of the participants are summarized in **Table 1**. The prevalence of metabolic syndrome was significantly higher in men than in women. Low HDL cholesterol level was one of the predominant metabolic syndrome components in both men and women. Hypertriglyceridemia was one of the main components in men, whereas central obesity was frequently reported in women.

Distribution of the surrogate measures of insulin sensitivity

The distributions of surrogate measures according to sex and menstrual status are summarized in **Table 2**. We selected the 75th percentile values of the HOMA-IR and TyG index and the 25th percentile values of the McAuley index as the cut-off values for insulin

Table 1. Weighted clinical characteristics of the participants in KNHANES

Characteristics	Total (n = 10,997)	Men (n = 4,577)	Women (n = 6,420)	*P* value
Age, yr	40.9 (40.4–41.3)	40.7 (40.2–41.3)	41.0 (40.5–41.5)	0.314
Waist circumference, cm	79.6 (79.3–79.9)	83.1 (82.8–83.4)	76.2 (75.9–76.6)	< 0.001
Body mass index, kg/m²	23.3 (23.2–23.4)	23.9 (23.7–24)	22.7 (22.6–22.8)	< 0.001
Systolic blood pressure, mmHg	112.8 (112.3–113.2)	116.2 (115.6–116.7)	109.6 (109–110.1)	< 0.001
Diastolic blood pressure, mmHg	74.3 (74.0–74.7)	77.3 (76.9–77.7)	71.5 (71.1–71.8)	< 0.001
Fasting serum glucose, mg/dL	91.1 (90.8–91.3)	92.3 (91.9–92.6)	89.9 (89.6–90.2)	< 0.001
Fasting insulin, μIU/mL	9.53 (9.39–9.66)	9.52 (9.35–9.69)	9.54 (9.36–9.71)	0.882
HDL-cholesterol, mg/dL	49.0 (48.7–49.3)	46.3 (45.9–46.7)	51.6 (51.2–51.9)	< 0.001
Triglyceride, mg/dL	123.6 (121.1–126)	148.4 (144–152.7)	100.0 (97.9–102.1)	< 0.001
Metabolic syndrome (%)	16.0 (15.2–16.9)	18.2 (16.9–19.6)	14.0 (13–15.1)	< 0.001
Increased waist circumference	26.6 (25.6–27.7)	20.8 (19.5–22.3)	32.1 (30.6–33.6)	< 0.001
High blood pressure	19.6 (18.6–20.7)	26.7 (25.2–28.4)	12.8 (11.8–13.9)	< 0.001
High fasting serum glucose	15.5 (14.6–16.4)	19.5 (18.1–20.9)	11.7 (10.7–12.7)	< 0.001
High triglyceride	24.3 (23.4–25.2)	34.0 (32.4–35.7)	15.1 (14.1–16.1)	< 0.001
Low HDL-cholesterol	38.8 (37.6–40.1)	30.0 (28.3–31.8)	47.2 (45.7–48.7)	< 0.001

Data are expressed as means (95% CI) or percentage (95% CI).
KNHANES = Korean National Health and Nutrition Examination Survey, CI = confidence interval.

Table 2. Distribution of surrogate measures for insulin sensitivity

Characteristics	Percentile				
	10th	25th	50th	75th	90th
HOMA-IR					
Total	1.20	1.50	1.94	2.53	3.26
Men	1.19	1.51	1.96	2.57	3.32
Women	1.20	1.49	1.92	2.49	3.20
Premenopausal women	1.23	1.51	1.93	2.50	3.24
Postmenopausal women	1.17	1.47	1.89	2.45	3.10
TyG index					
Total	4.18	4.34	4.54	4.76	4.97
Men	4.28	4.44	4.64	4.86	5.06
Women	4.12	4.28	4.45	4.65	4.85
Premenopausal women	4.11	4.25	4.41	4.60	4.78
Postmenopausal women	4.24	4.40	4.59	4.79	4.95
McAuley Index					
Total	5.2	6.2	7.3	8.4	9.6
Men	5.0	5.8	6.9	8.0	9.1
Women	5.8	6.6	7.7	8.8	9.9
Premenopausal women	5.8	6.8	7.8	8.9	9.9
Postmenopausal women	5.4	6.2	7.2	8.3	9.4

HOMA-IR = homeostasis model assessment-insulin resistance, TyG = triglyceride and glucose.

Table 3. The cut-off values of each surrogate measures by percentile criteria and modified YI criteria

Indirect index	Percentile criteria (75th percentile)			YI criteria		
	Cut-off	Sensitivity (%)	Specificity (%)	Cut-off	Sensitivity (%)	Specificity (%)
For insulin resistance						
HOMA-IR						
Total	2.53	51	81	2.20	65	70
Men	2.57	50	82	2.20	66	70
Women	2.49	52	81	2.20	64	71
Premenopausal women	2.50	67	80	2.55	66	81
Postmenopausal women	2.45	42	83	2.03	63	66
TyG index						
Total	4.76	76	87	4.72	80	83
Men	4.86	71	86	4.76	86	77
Women	4.65	79	83	4.71	75	89
Premenopausal women	4.60	80	81	4.71	70	91
Postmenopausal women	4.79	64	91	4.71	77	83
For insulin sensitivity						
McAuley index						
Total	6.2	70	85	6.6	77	81
Men	5.8	66	86	6.4	74	82
Women	6.6	83	75	6.6	83	75
Premenopausal women	6.8	83	80	6.6	84	79
Postmenopausal women	6.2	59	88	6.6	79	73

YI = Youden index, HOMA-IR = homeostasis model assessment-insulin resistance, TyG = triglyceride and glucose.

resistance. This point corresponded to the HOMA-IR value of 2.53, McAuley index score of 6.2, and TyG index score of 4.76. **Table 3** depicts the sensitivity and specificity of the metabolic syndrome of each point according to sex and menstrual status.

ROC curves of the surrogate measures for insulin sensitivity

The ROC curve of each marker according to sex and menstrual status is shown in **Fig. 1**. The area under the curves (AUCs) of the HOMA-IR were 0.747 (95% CI, 0.730–0.765) in men and 0.804 (95% CI, 0.779–0.828) and 0.692 (95% CI, 0.665–0.718) in premenopausal and postmenopausal women, respectively. The AUCs of the McAuley index were 0.856 (95% CI, 0.844–0.869) in men and 0.894 (95% CI, 0.877–0.911) and 0.823 (95% CI, 0.802–0.845) in premenopausal and postmenopausal women, respectively, and the cut-off values of the TyG index were 0.872 (95% CI, 0.860–0.884) in men, 0.893 (95% CI, 0.875–0.91) in premenopausal women, and 0.853 (95% CI, 0.833–0.874) in postmenopausal women. The

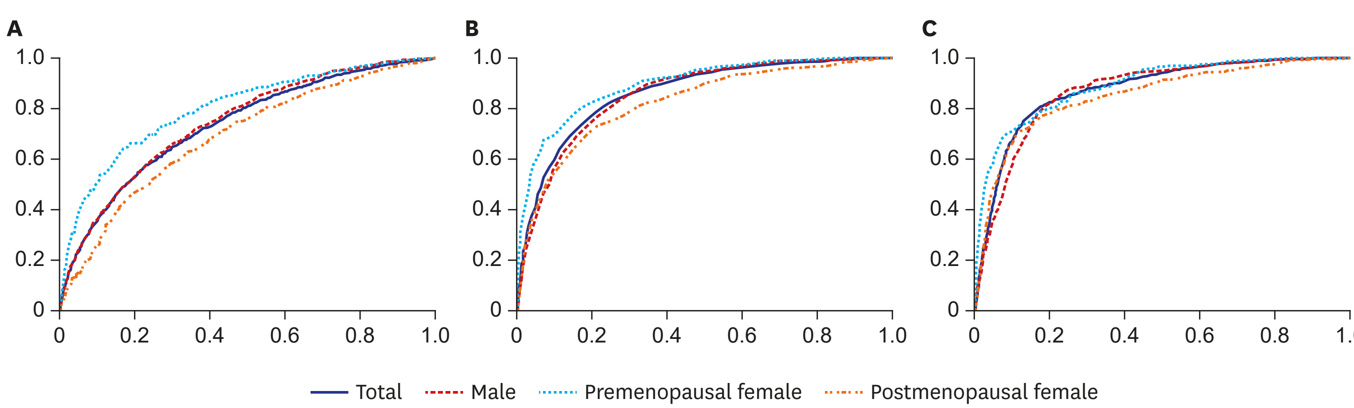

Fig. 1. The ROC curve of each surrogate measure by sex and menstrual status. (**A**) HOMA-IR. (**B**) McAuley index. (**C**) TyG index.
ROC = receiver operating characteristic, HOMA-IR = homeostasis model assessment-insulin resistance, TyG = triglyceride and glucose.

 https://doi.org/10.3346/jkms.2018.33.e197

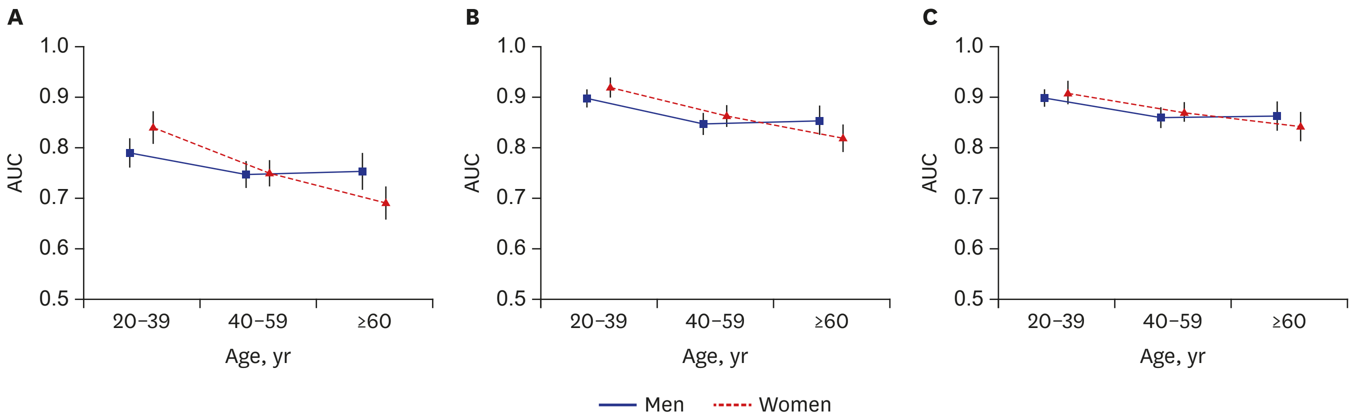

Fig. 2. AUC of each surrogate measure by sex and age. (**A**) AUC of HOMA-IR. (**B**) AUC of McAuley index. (**C**) AUC of TyG index.
AUC = area under the curve, HOMA-IR = homeostasis model assessment-insulin resistance, TyG = triglyceride and glucose.

AUC of each marker according to sex and age is shown in **Fig. 2**. The cut-off values of the HOMA-IR were 2.20 in men, 2.55 in premenopausal women, and 2.03 in postmenopausal women, and those of the McAuley index were 6.4 in men and 6.6 in premenopausal and postmenopausal women. For the TyG index, the cut-off values were 4.76 in men and 4.71 in premenopausal and postmenopausal women. The cut-off values with their corresponding sensitivity and specificity for each subgroup are summarized in **Table 3**.

DISCUSSION

The present study aimed to evaluate the sex-specific characteristics of the surrogate measures of insulin sensitivity. Moreover, their valid cut-off values were established to identify individuals at risk of insulin resistance.

Several previous studies have determined the cut-off values of the surrogate measures as the value with a specific percentile criterion, such as the 75th, 80th, or 90th percentile.[21-25] However, how the proposed cut-off values could identify the risk of clinically relevant outcomes was not fully elucidated. Therefore, to determine a valid cut-off value, we used the ROC curve of each surrogate measure of metabolic syndrome that could accurately reflect pathologic conditions due to insulin reaction. In the present study, the McAuley and TyG indexes had a higher sensitivity and specificity for metabolic syndrome than the HOMA-IR. These results were due to the McAuley and TyG indexes that included triglyceride in their equations, which was the main component of metabolic syndrome. In addition, the AUC of the surrogate measures differed according to sex and menstrual status. Insulin resistance is often associated with alterations in sex hormone.[26] Ovarian estrogens promote peripheral fat storage, whereas androgens promote the accumulation of visceral abdominal fat. Significant decrease in estrogen concentrations and relative hyperandrogenism are considered as the important factors associated with weight gain and hyperinsulinemia in postmenopausal women.[26,27] In addition, a decreased level of sex hormone-binding globulin (SHBG) is considered as a strong indicator of insulin resistance in postmenopausal women.[28,29] Interestingly, SHBG was more significantly associated with the indices of insulin resistance in postmenopausal women than in premenopausal women.[26,28,29] Therefore, alterations in sex hormone in menopausal women had a confounding effect on the surrogate measures of insulin resistance. Gayoso-Diz et al.[20] have revealed a significant decline in the AUC of the

HOMA-IR in women older than 50 years. These results might reflect the effect of alterations in sex hormones. As shown in **Fig. 2**, the present study also revealed similar results.

Interestingly, the AUC of the HOMA-IR decreased more significantly than those of the McAuley and TyG indexes. Considering the significant decline in the AUC of the HOMA-IR in postmenopausal women, the McAuley and TyG indexes may be used as supplementary methods.

HOMA-IR is a robust tool for the surrogate assessment of insulin resistance. The current study showed that the optimal cut-off value was 2.20 (sensitivity: 65% and specificity: 70%). This result was slightly lower than those previously reported in other studies in Korea. Ryu et al.[30] have suggested that the cut-off value of the HOMA-IR was 2.43 (sensitivity: 73.7% and specificity: 73.7%), and Lee et al.[31] have reported that the cut-off value of the HOMA-IR was 2.34 (sensitivity: 62.8% and specificity: 66.8%).

Moreover, several studies have suggested that the McAuley index was a good surrogate measure of insulin sensitivity, which had a significantly higher sensitivity than the HOMA-IR compared to the HIEG clamp and MMAMG method in the group without diabetes.[1,14] However, these studies were performed using a small number of participants. Thus, this study showed the clinical relevance of the McAuley index. Moreover, the cut-off values in a population-based study were proposed.

The TyG index has been proposed as a good surrogate measure of insulin sensitivity. The TyG index is a more simple and inexpensive method than the surrogate measures that use insulin, considering the absence of a standard assay for insulin measurement and the cumbersome nature of the direct estimation of insulin level. In addition, the TyG index value was associated with the gold standard methods for insulin resistance. Guerrero-Romero et al.[15] have reported a correlation between the TyG index and the HIEG clamp results in a study on a Mexican population. Vasques et al.[32] have also found this correlation in a Brazilian population. Bastard et al.[33] have reported that the TyG index had a relatively modest correlation to the HIEG clamp results. Abbasi and Reaven[34] have also reported a modest correlation between the TyG index and insulin-stimulated glucose uptake during insulin suppression testing. Several population-based studies have demonstrated the clinical usefulness of the TyG index as a surrogate measure.[35,36] The present study supports the clinical relevance of the TyG index in a large Korean population as well. In addition, it is important to propose the valid cut-off value of the TyG index that can be used as a reference in clinical settings for identifying groups at risk for insulin resistance.

The present study has key strengths. This was a large population-based study, and different surrogate measures of insulin resistance were included in the analysis. To the best of our knowledge, this is the first study that evaluated the sex- and age-specific characteristics of the McAuley and TyG indexes. However, the present study has several potential limitations. First, this is a cross-sectional study. To validate the relationship between each surrogate measure and cardiovascular risk factors, further prospective studies must be conducted. Second, because the present study involved a population of healthy Korean adults, these results are applicable only in Korea. Third, we cannot compare the surrogate measures with the gold standard methods for insulin resistance.

In conclusion, the present study presented the valid cut-off values of the indirect surrogate measures of metabolic syndrome. These values may serve as the reference for insulin sensitivity in a clinical setting and may provide a simple and supplementary method for identifying individuals at risk of insulin resistance. However, to establish more valid cut-off values, further studies, including correlational studies on these surrogate measures and the gold standard methods for insulin resistance, must be conducted.

REFERENCES

1. Ascaso JF, Pardo S, Real JT, Lorente RI, Priego A, Carmena R. Diagnosing insulin resistance by simple quantitative methods in subjects with normal glucose metabolism. *Diabetes Care* 2003;26(12):3320-5.
PUBMED | CROSSREF
2. Hanefeld M. The metabolic syndrome: roots, myths, and facts. In: Hanefeld M, Leonhardt W, editors. *The Metabolic Syndrome*. Jena: Gustav Fischer; 1997, 13-24.
3. Després JP, Lamarche B, Mauriège P, Cantin B, Dagenais GR, Moorjani S, et al. Hyperinsulinemia as an independent risk factor for ischemic heart disease. *N Engl J Med* 1996;334(15):952-7.
PUBMED | CROSSREF
4. Folsom AR, Rasmussen ML, Chambless LE, Howard G, Cooper LS, Schmidt MI, et al. Prospective associations of fasting insulin, body fat distribution, and diabetes with risk of ischemic stroke. *Diabetes Care* 1999;22(7):1077-83.
PUBMED | CROSSREF
5. Kuusisto J, Mykkänen L, Pyörälä K, Laakso M. Hyperinsulinemic microalbuminuria. A new risk indicator for coronary heart disease. *Circulation* 1995;91(3):831-7.
PUBMED | CROSSREF
6. Shinozaki K, Naritomi H, Shimizu T, Suzuki M, Ikebuchi M, Sawada T, et al. Role of insulin resistance associated with compensatory hyperinsulinemia in ischemic stroke. *Stroke* 1996;27(1):37-43.
PUBMED | CROSSREF
7. Pollare T, Lithell H, Berne C. Insulin resistance is a characteristic feature of primary hypertension independent of obesity. *Metabolism* 1990;39(2):167-74.
PUBMED | CROSSREF
8. Goodarzi MO, Erickson S, Port SC, Jennrich RI, Korenman SG. Relative impact of insulin resistance and obesity on cardiovascular risk factors in polycystic ovary syndrome. *Metabolism* 2003;52(6):713-9.
PUBMED | CROSSREF
9. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol* 1979;237(3):E214-23.
PUBMED
10. Bergman RN, Prager R, Volund A, Olefsky JM. Equivalence of the insulin sensitivity index in man derived by the minimal model method and the euglycemic glucose clamp. *J Clin Invest* 1987;79(3):790-800.
PUBMED | CROSSREF
11. Greenfield MS, Doberne L, Kraemer F, Tobey T, Reaven G. Assessment of insulin resistance with the insulin suppression test and the euglycemic clamp. *Diabetes* 1981;30(5):387-92.
PUBMED | CROSSREF
12. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28(7):412-9.
PUBMED | CROSSREF
13. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 2000;85(7):2402-10.
PUBMED | CROSSREF
14. McAuley KA, Williams SM, Mann JI, Walker RJ, Lewis-Barned NJ, Temple LA, et al. Diagnosing insulin resistance in the general population. *Diabetes Care* 2001;24(3):460-4.
PUBMED | CROSSREF
15. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab* 2010;95(7):3347-51.
PUBMED | CROSSREF
16. Korea Centers for Disease Control and Prevention. *The Guideline of the Forth Korea National Health and Nutrition Examination Survey (KNHANES-IV).* Cheongwon: Centers for Disease Control and Prevention; 2009.

17. Korea Centers for Disease Control and Prevention. *The Guideline of the Fifth Korea National Health and Nutrition Examination Survey (KNHANES-V-1).* Cheongwon: Centers for Disease Control and Prevention; 2010.

18. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112(17):2735-52.
PUBMED | CROSSREF

19. World Health Organization, International Association for the Study of Obesity, International Obesity Task Force. *The Asia-Pacific Perspective: Redefining Obesity and Its Treatment.* Sydney: Health Communications; 2000, 15-21.

20. Gayoso-Diz P, Otero-González A, Rodriguez-Alvarez MX, Gude F, García F, De Francisco A, et al. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. *BMC Endocr Disord* 2013;13(1):47.
PUBMED | CROSSREF

21. Hedblad B, Nilsson P, Janzon L, Berglund G. Relation between insulin resistance and carotid intima-media thickness and stenosis in non-diabetic subjects. Results from a cross-sectional study in Malmö, Sweden. *Diabet Med* 2000;17(4):299-307.
PUBMED | CROSSREF

22. Geloneze B, Repetto EM, Geloneze SR, Tambascia MA, Ermetice MN. The threshold value for insulin resistance (HOMA-IR) in an admixtured population IR in the Brazilian Metabolic Syndrome Study. *Diabetes Res Clin Pract* 2006;72(2):219-20.
PUBMED | CROSSREF

23. Marques-Vidal P, Mazoyer E, Bongard V, Gourdy P, Ruidavets JB, Drouet L, et al. Prevalence of insulin resistance syndrome in southwestern France and its relationship with inflammatory and hemostatic markers. *Diabetes Care* 2002;25(8):1371-7.
PUBMED | CROSSREF

24. Do HD, Lohsoonthorn V, Jiamjarasrangsi W, Lertmaharit S, Williams MA. Prevalence of insulin resistance and its relationship with cardiovascular disease risk factors among Thai adults over 35 years old. *Diabetes Res Clin Pract* 2010;89(3):303-8.
PUBMED | CROSSREF

25. Nakai Y, Nakaishi S, Kishimoto H, Seino Y, Nagasaka S, Sakai M, et al. The threshold value for insulin resistance on homeostasis model assessment of insulin sensitivity. *Diabet Med* 2002;19(4):346-7.
PUBMED | CROSSREF

26. Stefanska A, Bergmann K, Sypniewska G. Metabolic syndrome and menopause: pathophysiology, clinical and diagnostic significance. *Adv Clin Chem* 2015;72:1-75.
PUBMED | CROSSREF

27. Golden SH, Ding J, Szklo M, Schmidt MI, Duncan BB, Dobs A. Glucose and insulin components of the metabolic syndrome are associated with hyperandrogenism in postmenopausal women: the atherosclerosis risk in communities study. *Am J Epidemiol* 2004;160(6):540-8.
PUBMED | CROSSREF

28. Akin F, Bastemir M, Alkiş E, Kaptanoglu B. SHBG levels correlate with insulin resistance in postmenopausal women. *Eur J Intern Med* 2009;20(2):162-7.
PUBMED | CROSSREF

29. Davis SR, Robinson PJ, Moufarege A, Bell RJ. The contribution of SHBG to the variation in HOMA-IR is not dependent on endogenous oestrogen or androgen levels in postmenopausal women. *Clin Endocrinol (Oxf)* 2012;77(4):541-7.
PUBMED | CROSSREF

30. Ryu S, Sung KC, Chang Y, Lee WY, Rhee EJ. Spectrum of insulin sensitivity in the Korean population. *Metabolism* 2005;54(12):1644-51.
PUBMED | CROSSREF

31. Lee S, Choi S, Kim HJ, Chung YS, Lee KW, Lee HC, et al. Cutoff values of surrogate measures of insulin resistance for metabolic syndrome in Korean non-diabetic adults. *J Korean Med Sci* 2006;21(4):695-700.
PUBMED | CROSSREF

32. Vasques AC, Novaes FS, de Oliveira MS, Souza JR, Yamanaka A, Pareja JC, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. *Diabetes Res Clin Pract* 2011;93(3):e98-100.
PUBMED | CROSSREF

33. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R. Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. *Diabetes Metab* 2012;38(3):258-63.
PUBMED | CROSSREF

34. Abbasi F, Reaven GM. Comparison of two methods using plasma triglyceride concentration as a surrogate estimate of insulin action in nondiabetic subjects: triglycerides × glucose versus triglyceride/high-density lipoprotein cholesterol. *Metabolism* 2011;60(12):1673-6.
PUBMED | CROSSREF

35. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord* 2008;6(4):299-304.
PUBMED | CROSSREF

36. Lee SH, Kwon HS, Park YM, Ha HS, Jeong SH, Yang HK, et al. Predicting the development of diabetes using the product of triglycerides and glucose: the Chungju Metabolic Disease Cohort (CMC) study. *PLoS One* 2014;9(2):e90430.
PUBMED | CROSSREF