Insulin Resistance and Heart Disease

Subjects: Others

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Insulin resistance is defined as an impaired biological response to insulin actions in the insulin-responsive tissues and is considered key to metabolic syndrome. The prevalence of insulin resistance has increased globally, and it is known to be from 15.5 to 46.5% of adults. Previous studies have suggested that insulin resistance is significantly related to the development and progression of coronary atherosclerosis and adverse plaque characteristics and is a major risk factor for cardiovascular diseases via pathophysiological mechanisms. Insulin resistance is also the common pathophysiology of prehypertension and prediabetes.

metabolic score for insulin resistance | cardiometabolic risk | longitudinal study | ischemic heart disease

1. Overview

The metabolic score for insulin resistance (METS-IR) is a novel noninsulin-based marker for assessing the risk of insulin resistance and cardiometabolic risk. However, whether METS-IR is associated with incident ischemic heart disease (IHD) risk is unknown. Therefore, we aimed to investigate the longitudinal effect of METS-IR on incident IHD risk in a large cohort of Korean adults without diabetes. We assessed 17,943 participants without diabetes from the Health Risk Assessment Study (HERAS) and Korea Health Insurance Review and Assessment (HIRA) data. The participants were divided into four groups according to METS-IR index quartiles: (ln ((2 × fasting plasma glucose) + triglyceride) × body mass index)/(ln (HDL-cholesterol)). We prospectively assessed hazard ratios (HRs) with 95% confidence intervals (CIs) for IHD using multivariate Cox proportional hazard regression models over a 50-month period. During the follow-up period, 332 participants (1.9%) developed IHD. HRs of IHD for METS-IR quartiles 1–4 were 1.00, were 1.62 (95% CI 1.04–2.53), 1.87 (95% CI 1.20–2.91), and 2.11 (95% CI 1.35–3.30), respectively, after adjusting for potential confounding variables. A higher METS-IR precedes future IHD among Koreans without diabetes. Moreover, compared with metabolic syndrome, METS-IR had a better predictive value for IHD.

2. Insulin Resistance

Cardiovascular diseases (CVDs) are the leading cause of death worldwide in 2019, and the majority of deaths from CVD are caused by ischemic heart disease (IHD), with most deaths occurring between the ages of 30 and 70 [1][2]. IHD is a major cause of rising medical expenses. The early onset of IHD in the aging population is important because it lowers the quality of life and increases the burden of social, medical expenses [3].

Insulin resistance is defined as an impaired biological response to insulin actions in the insulin-responsive tissues and is considered key to the mechanism of metabolic syndrome [4]. The prevalence of insulin resistance has increased globally, and it is known to be from 15.5 to 46.5% of adults [5]. Previous studies have suggested that insulin resistance is significantly related to the development and progression of coronary atherosclerosis and adverse plaque characteristics and is a major risk factor for cardiovascular diseases via pathophysiological mechanisms [4]. Insulin resistance is also the common pathophysiology of prehypertension and prediabetes [6]. Moreover, some studies have found that nondiabetic individuals with IHD tend to exhibit a poorer prognosis than diabetic patients without IHD [7][8]. Thus, early detection of insulin resistance in the early stages of IHD is necessary in, for example, non-diabetes patients with metabolic risks and a high risk of IHD, preventing other diseases and reducing the socioeconomic burden for IHD.

Recently, the metabolic score for insulin resistance (METS-IR), a higher concordance with the hyperinsulinemic-euglycemic clamp, has been developed. It has been reported that METS-IR is strongly associated with hypertension and predictive abilities for type 2 diabetes [9][10]. However, to our knowledge, information is limited to the longitudinal association between METS-IR and incident IHD. Therefore, we prospectively investigated the association between METS-IR and IHD incidence in a large-scale, community-dwelling Korean population without diabetes using the Health Risk Assessment Study (HERAS) and Korea Health Insurance Review and Assessment Service (HIRA) database.

3. Conclusions

Among a community-based population of Korean adults without diabetes, we found that elevated METS-IR was positively and independently associated with IHD incidence in this longitudinal cohort study that included a 50-month follow-up. We also found that METS-IR outperformed the prediction for IHD compared to metabolic syndrome.

Insulin resistance is a low response to insulin action in adipose tissue, skeletal muscles, and the liver. Only compensatory hyperinsulinemia appears in the early stage of insulin resistance, and then, in the late stage, insulin resistance can cause the development of dyslipidemia, hypertension, CVDs, etc. [4]. According to pathophysiological mechanisms, insulin is known as the headstream of metabolic syndrome [4]. Insulin resistance is involved in atherosclerosis, and hyperglycemia plays an important role in the early stages of atherosclerosis, which is the main risk factor for developing IHD [11]. Previous studies also revealed that insulin resistance is associated with an increased risk of CVD in nondiabetic patients [12][13]. Thus, early detection of insulin resistance in adults at risk for future IHD is important for prevention and slowing the progression of IHD. HOMA-IR is the most widely used method to evaluate the degree of insulin resistance [14]. However, it is likely to cause bias depending on the use of insulin assay, including calibration setup in the kit and conversions between units [15][16]. Recently, METS-IR, a non-insulin-based insulin resistance, has been reported to have strong predictive abilities for CVD risk [9][10][17][18]. To date, there has been no research on the correlation between METS-IR and IHD.

Metabolic syndrome consists of a cluster of heart disease risk factors, including low HDL-C, high triglyceride, impaired carbohydrate metabolism, central obesity, and high blood pressure [19]. An important feature of metabolic syndrome is insulin resistance, characterized in nondiabetics by increased serum insulin levels, and it has been suggested that insulin itself is atherogenic [20]. Many epidemiological studies have indicated that metabolic syndrome is associated with IHD and used to predict the risk of IHD in the clinical field [21][22]. Our results are consistent with the findings of previous prospective studies showing that metabolic syndrome was associated with an increased incidence of IHD or CVDs [23][24]. However, the findings of our study showed that the METS-IR had higher predictive power than MetS as a dichotomous classification for IHD. Some possible explanations for this observed association deserve consideration. First, the diagnostic criteria for metabolic syndrome are inconsistent across countries. For example, some studies reported that metabolic syndrome based on Japanese criteria had a weak association with the risk of IHD and predicted IHD less effectively because of the difference in the cutoff values of waist circumference of Japanese metabolic syndrome diagnosis criteria [22]. Second, recent studies have shown that the prognostic role of metabolic syndrome does not increase more than the sum of its components [23][25]. Metabolic syndrome increases cardiovascular risk, and each of its components is associated with an increased risk of CVD [24][26][27][28]. Some studies found that an increased FPG level is a less competent indicator of cardiovascular outcomes [29]. Moreover, the role of BMI in CVDs remains debatable because different studies have presented conflicting results [30][31]. However, studies have demonstrated that triglyceride, HDL-C, glucose intolerance, and insulin levels expectedly correlate best with insulin resistance [32]. In Korea, obesity is strongly associated with insulin resistance. A combination of the triglyceride glucose (TyG) index and BMI was superior to other modified TyG indices for predicting insulin resistance in adults [33]. Previous studies have reported that the TyG index may be a useful predictive marker of CVD [34][35]. In addition, triglycerides and HDL-C have been more predictive of CVD than total cholesterol in the Asia Pacific region [36]. Thus, METS-IR may be regarded as a more favorable predictor of IHD than metabolic syndrome because the combination of triglyceride, BMI, FPG, and HDL-C may lead to a better explanation of the cardiometabolic risk for CVD outcome. Third, some studies have suggested that the risk of cardiovascular disease increases with an increase in the number of metabolic syndrome components [37][38]. Previous studies have suggested that the incidence of coronary heart disease and incident CVD risk shows a progressive increase from one to five metabolic syndrome components [39][40]. Some studies found that the risk of developing CVD increased significantly with an increasing number of metabolic syndrome components, and this trend persisted even after adjusting for sex, drinking status, and family history of hypertension, diabetes, and CVD; participants with ≥3 metabolic syndrome components were at three times higher risk of developing CVD than those without any components [37][38]. We also found that the number of components of metabolic syndrome was more highly predictive of IHD than metabolic syndrome as a dichotomous classification among individuals without diabetes. Thus, consideration of the number of risk components of metabolic syndrome may be more informative than metabolic syndrome as a dichotomous classification when determining the risk of IHD.

A significant strength of the work was that we conducted a cohort study using many Korean individuals linked to HIRA data from the universal coverage system in Korea. However, the HERAS-HIRA dataset assessed only newly developed IHD, not coronary angioplasty, myocardial resuscitation, or sudden death. Additionally, the study

population may have included some individuals with diabetes because hemoglobin A1c and 2-h postprandial glucose tests were not available at the baseline.

References

1. Roth, G.A.; Mensah, G.A.; Johnson, C.O.; Addolorato, G.; Ammirati, E.; Baddour, L.M.; Barengo, N.C.; Beaton, A.Z.; Benjamin, E.J.; Benziger, C.P.; et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update from the GBD 2019 Study. J. Am. Coll. Cardiol. 2020, 76, 2982–3021.
2. Naghavi, M.; Abajobir, A.A.; Abbafati, C.; Abbas, K.M.; Abd-Allah, F.; Abera, S.F.; Aboyans, V.; Adetokunboh, O.; Afshin, A.; Agrawal, A. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: A systematic analysis for the global burden of disease study 2016. Lancet 2017, 390, 1151–1210.
3. Yusuf, S.; Reddy, S.; Ôunpuu, S.; Anand, S. Global burden of cardiovascular diseases: Part i: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001, 104, 2746–2753.
4. Ormazabal, V.; Nair, S.; Elfeky, O.; Aguayo, C.; Salomon, C.; Zuñiga, F.A. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc. Diabetol. 2018, 17, 122.
5. Fahed, M.; Jaoudeh, M.G.A.; Merhi, S.; Mosleh, J.M.B.; Ghadieh, R.; Al Hayek, S.; Fares, J.E.E.H. Evaluation of risk factors for insulin resistance: A cross sectional study among employees at a private university in Lebanon. BMC Endocr. Disord. 2020, 20, 1–14.
6. Vafaeimanesh, J.; Parham, M.; Norouzi, S.; Hamednasimi, P.; Bagherzadeh, M. Insulin resistance and coronary artery disease in non-diabetic patients: Is there any correlation? Casp. J. Intern. Med. 2018, 9, 121–126.
7. Evans, J.M.M.; Wang, J.; Morris, A.D. Comparison of cardiovascular risk between patients with type 2 diabetes and those who had had a myocardial infarction: Cross sectional and cohort studies. BMJ 2002, 324, 939.
8. Lee, C.D.; Folsom, A.R.; Pankow, J.S.; Brancati, F.L. Cardiovascular events in diabetic and nondiabetic adults with or without history of myocardial infarction. Circulation 2004, 109, 855–860.
9. Bello-Chavolla, O.Y.; Almeda-Valdes, P.; Gómez-Velasco, D.; Viveros-Ruiz, T.; Cruz-Bautista, I.; Romo-Romo, A.; Sánchez-Lázaro, D.; Meza-Oviedo, D.; Vargas-Vazquez, A.; Campos, O.A.; et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur. J. Endocrinol. 2018, 178, 533–544.

10. Liu, X.Z.; Fan, J.; Pan, S.J. METS-IR, a novel simple insulin resistance indexes, is associated with hypertension in normal-weight Chinese adults. J. Clin. Hypertens. 2019, 21, 1075–1081.
11. Bornfeldt, K.E.; Tabas, I. Insulin Resistance, Hyperglycemia, and Atherosclerosis. Cell Metabol. 2011, 14, 575–585.
12. Yanase, M.; Takatsu, F.; Tagawa, T.; Kato, T.; Arai, K.; Koyasu, M.; Horibe, H.; Nomoto, S.; Takemoto, K.; Shimizu, S.; et al. Insulin Resistance and Fasting Hyperinsulinemia Are Risk Factors for New Cardiovascular Events in Patients with Prior Coronary Artery Disease and Normal Glucose Tolerance. Circ. J. 2004, 68, 47–52.
13. Karrowni, W.; Li, Y.; Jones, P.G.; Cresci, S.; Abdallah, M.S.; Lanfear, D.E.; Maddox, T.M.; McGuire, D.K.; Spertus, J.A.; Horwitz, P.A. Insulin resistance is associated with significant clinical atherosclerosis in nondiabetic patients with acute myocardial infarction. Arter. Thromb. Vasc. Biol. 2013, 33, 2245–2251.
14. Wallace, T.M.; Matthews, D.R. The assessment of insulin resistance in man. Diabet. Med. 2002, 19, 527–534.
15. Rudvik, A.; Månsson, M. Evaluation of surrogate measures of insulin sensitivity—correlation with gold standard is not enough. BMC Med. Res. Methodol. 2018, 18, 64.
16. Manley, S.E.; Stratton, I.; Clark, P.M.; Luzio, S. Comparison of 11 Human Insulin Assays: Implications for Clinical Investigation and Research. Clin. Chem. 2007, 53, 922–932.
17. Eeg-Olofsson, K.; Gudbjörnsdottir, S.; Eliasson, B.; Zethelius, B.; Cederholm, J. The triglycerides-to-HDL-cholesterol ratio and cardiovascular disease risk in obese patients with type 2 diabetes: An observational study from the Swedish National Diabetes Register (NDR). Diabetes Res. Clin. Pract. 2014, 106, 136–144.
18. Tatsumi, Y.; Morimoto, A.; Asayama, K.; Sonoda, N.; Miyamatsu, N.; Ohno, Y.; Miyamoto, Y.; Izawa, S.; Ohkubo, T. Fasting Blood Glucose Predicts Incidence of Hypertension Independent of HbA1c Levels and Insulin Resistance in Middle-Aged Japanese: The Saku Study. Am. J. Hypertens. 2019, 32, 1178–1185.
19. Reaven, G.M. Role of insulin resistance in human disease. Diabetes 1988, 37, 1595–1607.
20. Stout, R.W. Insulin and Atheroma: 20-Yr Perspective. Diabetes Care 1990, 13, 631–654.
21. Bonora, E.; Targher, G.; Formentini, G.; Calcaterra, F.; Lombardi, S.; Marini, F.; Zenari, L.; Saggiani, F.; Poli, M.; Perbellini, S.; et al. The Metabolic Syndrome is an independent predictor of cardiovascular disease in Type 2 diabetic subjects. Prospective data from the Verona Diabetes Complications Study. Diabet. Med. 2004, 21, 52–58.
22. Ninomiya, T.; Kubo, M.; Doi, Y.; Yonemoto, K.; Tanizaki, Y.; Rahman, M.; Arima, H.; Tsuryuya, K.; Iida, M.; Kiyohara, Y. Impact of metabolic syndrome on the development of cardiovascular

disease in a general japanese population: The hisayama study. Stroke 2007, 38, 2063–2069.

23. McNeill, A.M.; Rosamond, W.D.; Girman, C.J.; Golden, S.H.; Schmidt, M.I.; East, H.E.; Ballantyne, C.M.; Heiss, G. The Metabolic Syndrome and 11-Year Risk of Incident Cardiovascular Disease in the Atherosclerosis Risk in Communities Study. Diabetes Care 2005, 28, 385–390.
24. Ford, E.S. The metabolic syndrome and mortality from cardiovascular disease and all-causes: Findings from the national health and nutrition examination survey ii mortality study. Atherosclerosis 2004, 173, 307–312.
25. Mente, A.; Yusuf, S.; Islam, S.; McQueen, M.J.; Tanomsup, S.; Onen, C.L.; Rangarajan, S.; Gerstein, H.; Anand, S.S. Metabolic Syndrome and Risk of Acute Myocardial Infarction: A Case-Control Study of 26,903 Subjects From 52 Countries. J. Am. Coll. Cardiol. 2010, 55, 2390–2398.
26. Lakka, H.-M.; Laaksonen, D.E.; Lakka, T.; Niskanen, L.K.; Kumpusalo, E.; Tuomilehto, J.; Salonen, J.T. The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-aged Men. JAMA 2002, 288, 2709–2716.
27. Sattar, N.; Gaw, A.; Scherbakova, O.; Ford, I.; O'Reilly, D.S.; Haffner, S.M.; Isles, C.; Macfarlane, P.W.; Packard, C.J.; Cobbe, S.M.; et al. Metabolic Syndrome with and Without C-Reactive Protein as a Predictor of Coronary Heart Disease and Diabetes in the West of Scotland Coronary Prevention Study. Circulation 2003, 108, 414–419.
28. Malik, S.; Wong, N.D.; Franklin, S.S.; Kamath, T.V.; L'Italien, G.J.; Pio, J.R.; Williams, G.R. Impact of the Metabolic Syndrome on Mortality from Coronary Heart Disease, Cardiovascular Disease, and All Causes in United States Adults. Circulation 2004, 110, 1245–1250.
29. Borg, R.; Kuenen, J.C.; Carstensen, B.; Zheng, H.; Nathan, D.M.; Heine, R.J.; Nerup, J.; Borchjohnsen, K.; Witte, D. HbA1c and mean blood glucose show stronger associations with cardiovascular disease risk factors than do postprandial glycaemia or glucose variability in persons with diabetes: The A1C-Derived Average Glucose (ADAG) study. Diabetology 2010, 54, 69–72.
30. Meigs, J.B.; Wilson, P.W.F.; Fox, C.S.; Vasan, R.S.; Nathan, D.M.; Sullivan, L.; D'Agostino, R.B. Body Mass Index, Metabolic Syndrome, and Risk of Type 2 Diabetes or Cardiovascular Disease. J. Clin. Endocrinol. Metab. 2006, 91, 2906–2912.
31. St-Pierre, A.C.; Cantin, B.; Mauriège, P.; Bergeron, J.; Dagenais, G.R.; Després, J.-P.; Lamarche, B. Insulin resistance syndrome, body mass index and the risk of ischemic heart disease. Can. Med. Assoc. J. 2005, 172, 1301–1305.
32. Chopra, A.K. Metabolic Syndrome or Insulin Resistance: Evolution, Controversies and Association with Cardiovascular Disease Risk. Indian J. Clin. Cardiol. 2020, 1, 77–85.
33. Lim, J.; Kim, J.; Koo, S.H.; Kwon, G.C. Comparison of triglyceride glucose index, and related parameters to predict insulin resistance in Korean adults: An analysis of the 2007-2010 Korean

National Health and Nutrition Examination Survey. PLoS ONE 2019, 14, e0212963.

34. Park, B.; Lee, Y.-J.; Lee, H.S.; Jung, D.-H. The triglyceride-glucose index predicts ischemic heart disease risk in Koreans: A prospective study using National Health Insurance Service data. Cardiovasc. Diabetol. 2020, 19, 1–8.
35. Jin, J.-L.; Cao, Y.-X.; Wu, L.-G.; You, X.-D.; Guo, Y.-L.; Wu, N.-Q.; Zhu, C.-G.; Gao, Y.; Dong, Q.-T.; Zhang, H.-W.; et al. Triglyceride glucose index for predicting cardiovascular outcomes in patients with coronary artery disease. J. Thorac. Dis. 2018, 10, 6137–6146.
36. Collaboration, A.P.C.S. A comparison of lipid variables as predictors of cardiovascular disease in the asia pacific region. Ann. Epidemiol. 2005, 15, 405–413.
37. Yang, W.; Ma, R.; Zhang, X.; Guo, H.; He, J.; Mao, L.; Mu, L.; Hu, Y.; Yan, Y.; Liu, J.; et al. Comparison Between Metabolic Syndrome and the Framingham Risk Score as Predictors of Cardiovascular Diseases Among Kazakhs in Xinjiang. Sci. Rep. 2018, 8, 16474.
38. Liu, J.; Zhao, N.; Wang, W.; Sun, J.-Y.; Liu, J.; Wang, M.; Qin, L.-P.; Wu, Z.-S. Incidence risk of cardiovascular diseases associated with specific combinations regarding the metabolic syndrome components. Zhonghua Liu Xing Bing Xue Za Zhi 2008, 29, 652–655.
39. Woodward, M.; Tunstall-Pedoe, H. The metabolic syndrome is not a sensible tool for predicting the risk of coronary heart disease. Eur. J. Cardiovasc. Prev. Rehabil. 2009, 16, 210–214.
40. Knuiman, M.W.; Hung, J.; Divitini, M.L.; Davis, T.M.; Beilby, J. Utility of the metabolic syndrome and its components in the prediction of incident cardiovascular disease: A prospective cohort study. Eur. J. Cardiovasc. Prev. Rehabil. 2009, 16, 235–241.

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