

A Risk Prediction Model of Atherosclerotic Cardiovascular Disease in Japan

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European and US guidelines use a lipid management approach based on absolute risk to prevent atherosclerotic cardiovascular disease (ASCVD), i.e., the probability of developing or dying from ASCVD. The 2018 US ACC/AHA guidelines pooled five major US cohorts, including the Framingham and Atherosclerosis Risk in Community studies¹⁾. The studies were pooled to create a Pooled Cohort Equation that accounts for differences in the frequency of ASCVD by gender and race, and the value of the absolute risk of ASCVD in 10 years was incorporated into the guideline flow.

The Japan Atherosclerosis Society Guidelines for prevention of ASCVD 2012 used the NIPPON DATA80 risk chart²⁾, and the 2017 guidelines used the Suita score to estimate the absolute risk of death or development of coronary artery disease (CAD) over 10 years³⁾, and set targets for lipid management. However, the Suita score adopted in the 2017 edition of the guidelines is based on the absolute risk of developing CAD, including myocardial infarction, as an outcome, and does not cover the entire ASCVD, including cerebrovascular disease, as indicated by Western risk scores.

Honda T, *et al.*⁴⁾ developed a prediction model to estimate the absolute risk of ASCVD, which includes CAD and atherothrombotic stroke in the Hisayama study. The risk factors consisted of eight items: gender, systolic blood pressure (<120, 120–129, 130–139, 140–159, and ≥ 160 mmHg), diabetes mellitus (presence or absence), high-density lipoprotein cholesterol (HDL-C) (<40, 40–59, and ≥ 60 mg/dl), low-density lipoprotein cholesterol (LDL-C) (<120, 120–139, 140–159, and ≥ 160 mg/dl), urinary protein (presence or absence), smoking

(presence or absence), and regular exercise (presence or absence). Similar results were obtained when non-HDL-C was used instead of LDL-C. All items are used in general health examinations in communities and occupational areas and are easy to use. The presence or absence of diabetes mellitus was determined in those who were undergoing treatment or who had been assessed by a 75-g glucose tolerance test, which may lead to an underestimation when assessed by HbA1c or a single blood glucose level. Since an exercise habit was included in the items, it can be expected to be used as a motivator for exercise.

Strokes can be broadly classified into a subarachnoid hemorrhage, intracerebral hemorrhage, and cerebral infarction based on the type of stroke. Cerebral infarction is further classified into penetrating artery infarction (lacunar infarction) and large-artery occlusive infarction in epidemiological studies, and the latter into thrombotic and embolic types. Hypertension is a major risk for any type of stroke, while serum total cholesterol is negatively associated with cerebral hemorrhage, not associated with penetrating artery infarction and positively associated with atherothrombotic cerebral infarction⁵⁾. This fact was supported by pathological epidemiological findings⁶⁾. Recent cohort studies in Japan have shown that elevated LDL-C and non-HDL-C were risk factors for atherothrombotic cerebral infarction, the etiology of which is atherosclerosis^{7, 8)}. As with CAD, lipid management is considered to be important in stroke treatment guidelines for primary prevention. Furthermore, although cerebral hemorrhage and penetrating artery infarction have been the most common types of strokes in Japan, over the past 40 years, the incidence of penetrating artery infarction has decreased by 72.0% in men and 37.8% in women⁹⁾. As a result, atherothrombotic cerebral infarction tends to account

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for a higher percentage of cerebral infarctions. In light of this situation, atherothrombotic stroke has an impact in the form of an atherosclerotic disease for lipid management.

It has been pointed out that there are differences in the incidence of cardiovascular diseases due to regional differences and social factors. Therefore, it is necessary to take such factors into account when assessing absolute risk. It was reported that there are differences between urban and rural areas and that the risk of cardiovascular disease mortality was higher among workers in small businesses than among workers in large businesses or civil servants. The US study also pointed out the association with socioeconomic factors, showing that the actual absolute risk in groups with higher socioeconomic poverty was higher than predicted¹⁰⁾. In the future, it will be necessary to test the external validity of this model to see how well it applies to other regions. It is hoped that the absolute risk for ASCVD prevention, developed in Japan, will be utilized, given that absolute risk can vary depending on regional and social factors.

Conflicts of Interest

None.

References

- 1) Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tomasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith SC, Jr., Sperling L, Virani SS, Yeboah J. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*, 2019; 139: e1082-e1143
- 2) Nippon Data80 Research Group. Risk Assessment Chart for Death From Cardiovascular Disease Based on a 19-Year Follow-up Study of a Japanese Representative Population: NIPPON DATA80. *Circ J*, 2006; 70: 1249-1255
- 3) Nishimura K, Okamura T, Watanabe M, Nakai M, Takegami M, Higashiyama A, Kokubo Y, Okayama A, Miyamoto Y. Predicting coronary heart disease using risk factor categories for a Japanese urban population, and comparison with the Framingham risk score: the Suita study. *J Atheroscler Thromb*, 2014; 21: 784-798
- 4) Honda T, Chen S, Hata J, Yoshida D, Hirakawa Y, Furuta Y, Shibata M, Sakata S, Kitazono T, Ninomiya T. Development and Validation of a Risk Prediction Model for Atherosclerotic Cardiovascular Disease in Japanese Adults: The Hisayama Study. *J Atheroscler Thromb*, 2022; 29: 345-361
- 5) Cui R, Iso H, Yamagishi K, Saito I, Kokubo Y, Inoue M, Tsugane S. High serum total cholesterol levels is a risk factor of ischemic stroke for general Japanese population: the JPHC study. *Atherosclerosis*, 2012; 221: 565-569
- 6) Konishi M, Iso H, Komachi Y, Iida M, Shimamoto T, Jacobs DR, Jr., Terao A, Baba S, Sankai T, Ito M. Associations of serum total cholesterol, different types of stroke, and stenosis distribution of cerebral arteries. The Akita Pathology Study. *Stroke*, 1993; 24: 954-964
- 7) Imamura T, Doi Y, Arima H, Yonemoto K, Hata J, Kubo M, Tanizaki Y, Ibayashi S, Iida M, Kiyohara Y. LDL cholesterol and the development of stroke subtypes and coronary heart disease in a general Japanese population: the Hisayama study. *Stroke*, 2009; 40: 382-388
- 8) Saito I, Yamagishi K, Kokubo Y, Yatsuya H, Iso H, Sawada N, Inoue M, Tsugane S. Non-High-Density Lipoprotein Cholesterol and Risk of Stroke Subtypes and Coronary Heart Disease: The Japan Public Health Center-Based Prospective (JPHC) Study. *J Atheroscler Thromb*, 2020; 27: 363-374
- 9) Kubo M, Hata J, Doi Y, Tanizaki Y, Iida M, Kiyohara Y. Secular trends in the incidence of and risk factors for ischemic stroke and its subtypes in Japanese population. *Circulation*, 2008; 118: 2672-2678
- 10) Dalton JE, Perzynski AT, Zidar DA, Rothberg MB, Coulton CJ, Milinovich AT, Einstadter D, Karichu JK, Dawson NV. Accuracy of Cardiovascular Risk Prediction Varies by Neighborhood Socioeconomic Position: A Retrospective Cohort Study. *Ann Intern Med*, 2017; 167: 456-464