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COMMENTARY

The impact of pulse wave velocity in a Japanese population with metabolic syndrome

Akihiro Hirashiki and Toyoaki Murohara

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Both childhood and adult obesity are serious public health concerns in Japan and in the United States. Metabolic syndrome (MetS) has been closely associated with mortality in both men and women.[1,2] In particular, cardiovascular disease (CVD) is more common in patients with MetS, even in the absence of baseline CVD and diabetes.[1] Atherosclerotic changes in large arteries are considered to be an important contributor to the pathogenesis of CVD.

Current evidence supports a central role for inflammation in all phases of the atherosclerotic process in MetS.[3] Circulating markers of inflammation, such as C-reactive protein, tumor necrosis factor-α and some interleukins (that is, interleukin-6 and interleukin-18), correlate with the propensity to develop ischemic events; moreover, circulating phase reactants elicited by inflammation may not only contribute to the pathogenesis of atherosclerosis but may also increase the risk of vascular events.[4,5]

Recent research has shown that inflammation has a key role in coronary artery disease and in other manifestations of atherosclerosis. Evidence suggests that atherosclerosis, the main cause of coronary artery disease, is an inflammatory disease in which immune mechanisms interact with metabolic risk factors to initiate, propagate and activate lesions in the arterial tree.[6]

The mechanisms responsible for the process of high pulse wave velocity (PWV) seem to have an important role in arteriosclerosis, increased cardiac pressure, decreased coronary flow due to decreased diastolic pressure, direct effects of progression in arteriosclerosis and left ventricular abnormality. Figure 1 shows the association between MetS and PWV and the processes involved in the development of cardiovascular events.

Arterial stiffness has also been elucidated as an independent risk marker for the occurrence of CVD and its mortality. Increased arterial stiffness is associated with hypertension, renal disease and atherosclerosis. Arterial stiffness assessed by PWV has been established for nearly 10 years as an independent prognostic factor for CVD. PWV is a noninvasive method for measuring arterial stiffness in the assessment of atherosclerosis. The brachial-ankle PWV (baPWV) measurements are very simple and can be performed even in large study populations. Yamashina *et al.*[7] demonstrated that baPWV has considerably high validity and reproducibility and correlates well with aortic PWV, which can be obtained using a catheter-tip manometer. Therefore, despite its limitations, baPWV has been widely used to screen for vascular damage. Recent studies have demonstrated that PWV is not only a risk marker for CVD but also a prognostic predictor. In other words, an increase in a patient's PWV may reflect a worsening prognosis. Many reports have commented on the relationship between PWV and the development of atherosclerotic disease.[8–10]

Because aortic stiffness has been identified as an independent predictor of cardiovascular mortality in the specific setting of essential hypertension, changes in arterial stiffness may, in part, mediate the association between MetS and cardiovascular risk. Several studies have reported the association between MetS and arterial stiffness. For example, Scillaci *et al.*[11] reported that MetS represents a strong, independent risk factor for future CVD in hypertensive patients. Over and above the prognostic information provided by all other traditional cardiovascular risk markers, the simple, inexpensive assessment of MetS may help to further refine cardiovascular risk stratification in hypertension.

Many studies reporting an association between MetS and arterial stiffness were carried out in Caucasian populations. Modified NCEP and WHO definitions are often used as diagnostic criteria of MetS for Caucasians. Recently, the diagnostic criteria for MetS in Japanese patients were proposed by Matsuzawa.[12] Because patients' average height, body weight, body mass index and diet vary by ethnic group or country, the diagnostic criteria of MetS should differ among races. As Japanese, we aimed to evaluate the association between MetS and arterial stiffness in an Asian population.

Recently, Choi *et al.*[13] demonstrated that baPWV significantly correlates with features of MetS in Korean women. This study was limited by its small size and inclusion of only women. In addition, the authors applied the WHO Asia-Pacific obesity criteria as a definition of abdominal obesity. Yamashina *et al.*[7] reported that baPWV in patients with coronary artery disease is significantly higher than in non-coronary artery disease patients. These results suggested that baPWV measured by this simple noninvasive method is appropriate for screening early atherosclerotic changes of the vascular system in a large population.[7]

In this study, Satoh and Tsutsui[14] have identified MetS as a significant and independent risk factor for increased arterial stiffness in both male and female patients in the Japanese general population. The study used diagnostic criteria for MetS defined for Japanese patients in 2005. This study has very important implications for Japanese people.

A phased increase in baPWV in the presence of an increasing number of patients

Dr A Hirashiki and T Murohara are at the Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan.
E-mail: hirasiki@med.nagoya-u.ac.jp

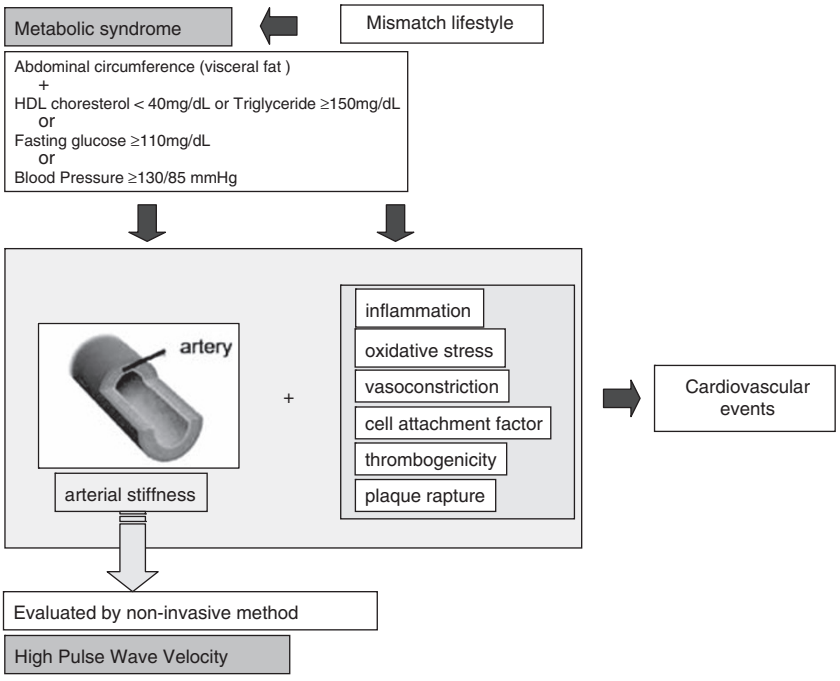

Figure 1 The association between metabolic syndrome and pulse wave velocity and the processes that contribute to the development of cardiovascular events.

with MetS is consistent with the well-known marked increase in the risk of atherosclerotic CVD in patients with MetS. Therefore, increased arterial stiffness may serve as a marker for the pathophysiological basis for increased risk of cardiovascular events in patients with MetS.

A WHO expert consultation has addressed the debate about the interpretation of recommended body mass index cutoff points for determining overweight and obesity in Asian populations. The consultation also considered whether population-specific cutoff points for body mass index are necessary. Revisions may be warranted for body mass index cutoff points to define obesity among South Asians, Chinese and Aboriginals. Using the putative revised cutoff points would greatly increase the estimated burden of obesity-related metabolic disorders among non-European populations.[15] No attempt was made, therefore, to redefine cutoff points for each population separately.

Although Japan has diagnostic criteria for both childhood and adult obesity and MetS, the appropriateness of the proposed criteria has been questioned. The data accumulated in these studies should be useful for further research into determining appropriate screening cutoff points in Japanese patients.

Finally, early identification, treatment and prevention of MetS present a major challenge for health-care professionals facing an epidemic of overweight and a sedentary lifestyle. The assessment of baPWV may stratify patients with MetS at risk for developing CVD.

1 Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002; **288**: 2709–2716.
2 Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, Williams GR. 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.
3 Ridker PM, Brown NJ, Vaughan DE, Harrison DG, Mehta JL. Established and emerging plasma biomarkers in the prediction of first atherothrombotic events. *Circulation* 2004; **109**: IV6–I19.
4 Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atheroslcerosis. *Am J Physiol Heart Circ Physiol* 2005; **288**: H2031–H2041.
5 Giugliano D, Ceriello A, Esposito K. The effects of diet on inflammation: emphasis on the metabolic syndrome. *J Am Coll Cardiol* 2006; **48**: 677–685.
6 Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 2005; **352**: 1685–1695.
7 Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, Koji Y, Hori S, Yamamoto Y. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res* 2002; **25**: 359–364.
8 Tomiyama H, Koji Y, Yambe M, Motobe K, Shiina K, Gulnisa Z, Yamamoto Y, Yamashina A. Elevated C-reactive protein augments increased arterial stiffness in subjects with the metabolic syndrome. *Hypertension* 2005; **45**: 997–1003.
9 Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; **37**: 1236–1241.
10 Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, Eber B. Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation* 2004; **109**: 184–189.
11 Schillaci G, Pirro M, Vaudo G, Gemelli F, Marchesi S, Porcellati C, Mannarino E. Prognostic value of the metabolic syndrome in essential hypertension. *J Am Coll Cardiol* 2004; **43**: 1817–1822.
12 Matsuzawa Y. Metabolic syndrome—definition and diagnostic criteria in Japan. *J Atheroscler Thromb* 2005; **12**: 301.
13 Choi KM, Lee KW, Seo JA, Oh JH, Kim SG, Kim NH, Choi DS, Baik SH. Relationship between brachial-ankle pulse wave velocity and cardiovascular risk factors of the metabolic syndrome. *Diabetes Res Clin Pract* 2004; **66**: 57–61.
14 Satoh H, Kishi R, Tsutsui H. Metabolic syndrome is a significant and independent risk for increased arterial stiffness in Japanese subjects *Hypertension Res* 2009; **32**: 1067–1071.
15 Razak F, Anand SS, Shannon H, Vuksan V, Davis B, Jacobs R, Teo KK, McQueen M, Yusuf S. Defining obesity cut points in a multiethnic population. *Circulation* 2007; **115**: 2111–2118.