

Is the Carotid Intima-Media Thickness a Reliable Predictor of Future Cardiovascular Events?

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See article vol. 27: 38-46

With a large number of subjects in the population being at a high risk for cardiovascular diseases (CVDs), simple markers are needed for assessing the risk for future CVDs. Several risk assessment models based on data obtained from general health checkups are available, such as the Framingham risk score and Suita score. The Japan Atherosclerosis Society guidelines for the prevention of atherosclerotic diseases recommend the use of the Suita score for assessing the risk of CVDs¹⁾. However, a reasonable estimate is that the major established risk factors explain only approximately 75% of the occurrences of coronary heart disease events within populations²⁾. To overcome this limitation, the multiple marker approach (i.e., the use of risk prediction model in combination with other markers) has been proposed³⁾. While the usefulness of several markers in combination with the conventional risk prediction models for the evaluation of CVD risk has been examined, none has been established as being useful so far³⁾. As mentioned above, because of the large population that needs CVD risk assessment, the availability of marker(s) that are simple to measure is important. The carotid intima-media thickness (IMT) is a simple-to-measure marker to assess the severity of carotid atherosclerosis⁴⁾. Atherosclerosis is characterized by focal rather than diffuse lesions in the arterial wall. However, to satisfy the criteria of simplicity of measurement and applicability to large populations as a marker to assess the risk of CVD, carotid IMT is measured as a fixed-point observation. This could underestimate the severity of carotid atherosclerosis in some cases. Meta-analyses conducted to examine whether carotid IMT is an independent predictor of future CVD events have reported inconsistent results^{5,6)}.

In this issue, Tada *et al.* reported that the plaque

score rather than carotid IMT may be a more reliable independent predictor of future CVD events in subjects with a history of CVDs (i.e., a marker for secondary prevention)⁷⁾. Plaque score may also be a more reliable marker for the severity of carotid atherosclerosis than carotid IMT because the plaque score reflects the severity of atherosclerosis in focal lesions. Plaque score is based on ultrasound examination, which provides two-dimensional images of a three-dimensional lesion. Therefore, in Tada's study, trained sonographers assessed the carotid plaque score with acceptable reproducibility and generalizability⁷⁾. Recently, however, ultrasound techniques that provide three-dimensional images have become available in clinical practice, which may improve the reproducibility and generalizability of the assessment of carotid plaques in general practice. Most of Tada's study subjects presented a history of CVD and may therefore have had advanced atherosclerosis. Furthermore, in Tada's study, the prevalence of heart disease was higher than that of stroke. Therefore, they speculated that the carotid plaque score reflects the total atherosclerotic burden in the systemic arterial tree, which might contribute to CVD events. On the other hand, Zureik *et al.* reported that carotid plaques, but not the common carotid IMT, was independently associated with the aortic stiffness, an independent risk factor for future CVD events⁸⁾. Apart from the total atherosclerotic burden, increased arterial stiffness is thought to mediate CVD events via inducing hemodynamic abnormalities⁹⁾. In addition, van Sloten *et al.* reported from their meta-analysis of studies conducted in the general population (i.e., subjects with less advanced atherosclerosis) that the carotid arterial stiffness, assessed as stiffness index beta, is a predictor of future stroke but not of coronary heart diseases¹⁰⁾. They speculated that high blood pulsatility rather than the severity of atherosclerosis causes stroke. Thus, the next logical step is

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Received: May 14, 2019 Accepted for publication: May 20, 2019

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to clarify whether the carotid plaque score rather than carotid IMT is a more reliable predictor of stroke as well as coronary heart disease in subjects without a past history of cardiovascular disease.

Disclosure

Reserch funding: Teijin Pharma; Courses endowed by Omron Health Care company and Asahi Calpis wellness company

References

- 1) Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S, Umemoto S, Egusa G, Ohmura H, Okamura T, Kihara S, Koba S, Saito I, Shoji T, Daida H, Tsukamoto K, Deguchi J, Dohi S, Dobashi K, Hamaguchi H, Hara M, Hiro T, Biro S, Fujioka Y, Maruyama C, Miyamoto Y, Murakami Y, Yokode M, Yoshida H, Rakugi H, Wakatsuki A, Yamashita S; Committee for Epidemiology and Clinical Management of Atherosclerosis. Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017. *J Atheroscler Thromb*, 2018; 25: 846-984
- 2) Magnus P, Beaglehole R. The real contribution of the major risk factors to the coronary epidemics: time to end the “only-50%” myth. *Arch Intern Med*, 2001; 161: 2657-2660
- 3) Wang TJ. Assessing the role of circulating, genetic, and imaging biomarkers in cardiovascular risk prediction. *Circulation*, 2011; 123: 551-565
- 4) Wada S, Koga M, Toyoda K, Minematsu K, Yasaka M, Nagai Y, Aoki S, Nezu T, Hosomi N, Kagimura T, Origasa H, Kamiyama K, Suzuki R, Ohtsuki T, Maruyama H, Kitagawa K, Uchiyama S, Matsumoto M; Japan Statin Treatment Against Recurrent Stroke (J-STARS) Echo Study Collaborators. Factors Associated with Intima-Media Complex Thickness of the Common Carotid Artery in Japanese Noncardioembolic Stroke Patients with Hyperlipidemia: The J-STARS Echo Study. *J Atheroscler Thromb*, 2018; 25: 359-373
- 5) Eikendal AL, Groenewegen KA, Anderson TJ, Britton AR, Engström G, Evans GW, de Graaf J, Grobbee DE, Hedblad B, Holewijn S, Ikeda A, Kitagawa K, Kitamura A, Lonn EM, Lorenz MW, Mathiesen EB, Nijpels G, Dekker JM, Okazaki S, O’Leary DH, Polak JF, Price JF, Robertson C, Rembold CM, Rosvall M, Rundek T, Salonen JT, Sitzer M, Stehouwer CD, Hoefer IE, Peters SA, Bots ML, den Ruijter HM; USE-IMT Project Group. Common carotid intima-media thickness relates to cardiovascular events in adults aged <45 years. *Hypertension*, 2015; 65: 707-713
- 6) Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Völzke H, Tuomainen TP, Sander D, Plichart M, Catapano AL, Robertson CM, Kiechl S, Rundek T, Desvarieux M, Lind L, Schmid C, DasMahapatra P, Gao L, Ziegelbauer K, Bots ML, Thompson SG; PROG-IMT Study Group. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. *Lancet*, 2012; 379: 2053-2062
- 7) Tada H, Nakagawa T, Okada H, Nakahashi T, Mori M, Sakata K, Nohara A, Takamura M, Kawashiri M. Clinical Impact of Carotid Plaque Score rather than Carotid Intima-Media Thickness on Recurrence of Atherosclerotic Cardiovascular Disease Events. *J Atheroscler Thromb*, 2020; 27: 38-46
- 8) Zureik M, Temmar M, Adamopoulos C, Bureau JM, Courbon D, Thomas F, Bean K, Touboul PJ, Ducimetière P, Benetos A. Carotid plaques, but not common carotid intima-media thickness, are independently associated with aortic stiffness. *J Hypertens*, 2002; 20: 85-93
- 9) Tomiyama H, Matsumoto C, Shiina K, Yamashina A. Brachial-Ankle PWV: Current Status and Future Directions as a Useful Marker in the Management of Cardiovascular Disease and/or Cardiovascular Risk Factors. *J Atheroscler Thromb*, 2016; 23: 128-146
- 10) van Sloten TT, Sedaghat S, Laurent S, London GM, Pannier B, Ikram MA, Kavousi M, Mattace-Raso F, Franco OH, Boutouyrie P, Stehouwer CDA. Carotid stiffness is associated with incident stroke: a systematic review and individual participant data meta-analysis. *J Am Coll Cardiol*, 2015; 66: 2116-2125