

# There are Doubtless Many Different Languages in the World, and None is without Meaning (1 Corinthians 14:10)

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See article vol. 29: 654-666

Latest decade, diversity and inclusion became common words for our future society. It is also applicable in science, biology, and medicine, not only in career making or opportunity for youth but the concepts of pathophysiology. It has been well accepted that atherosclerosis is a major risk for cardiovascular event and high glucose, hyperinsulinemia or insulin resistance state are the risk for atherosclerosis. Based upon those well-accepted ideas, many laboratory exams had been developed to evaluate atherosclerosis by noninvasive methods, such as carotid ultrasound (**Fig. 1**) for morphological change, pulse wave velocity, cardio ankle vascular index, and flow mediated vasodilation (FMD) for functional tests. As for carotid ultrasound intima-media thickness (IMT), carotid artery diameter (CAD), resistance index (RI) or pulsatility index (PI) have been developed and widely used clinically. The clinical implications of those parameters diverse, IMT is regarded as a general marker for atherosclerosis; on the other hand, CAD is a marker for vascular remodeling. RI indicates the vascular resistance of interest portion of vessel and PI reflects vascular resistance of distal portion of the vessel. The risk for stroke or cardiac events associated with IMT in nonlinear fashion<sup>1)</sup>, and in the recent guideline of the Japanese societies<sup>2, 3)</sup> besides Diabetes Association recommend IMT to screen for atherosclerosis in hypertensives. On the contrary European or the US guidelines do not recommend the routine use of IMT for the evaluation of atherosclerosis<sup>4)</sup>. It is because the lack of standardization regarding the measurement of IMT and its high variability and low reproducibility raised concerns and addition of IMT to classical risk score failed to show advantages in predicting future cardiovascular disease<sup>5)</sup>. Why not in diabetic patients

who are very high in risks for atherosclerosis?

The recent study by Sasaki N *et al*<sup>6)</sup> examined the impact of glucose metabolism in IMT, CAD, RI, and PI. Their cross-sectional large scale observational study revealed after adjustment for the confounding factors, CAD, RI, and PI but not IMT correlates with glucose metabolism parameters, such as HOMA-IR or insulin level, after glucose tolerance test. This study is a cross-sectional study, and cause and relationships are not discussed, however, this study implies ultrasound findings of vasculature is so diverse and should not be unified in one category of risk evaluation. In clinical setting, when we evaluate diabetic patients, we should recognize and appreciate their limitation of exams and benefit, and interpret the data with careful consideration of the physiological meaning of the tests.

The therapy for diabetes does not necessarily prevent cardiovascular event although the targeted blood glucose levels were equivalent. Formerly most prominent benefit were obtained in the class of drug that can reverse insulin resistance state, but recently SGLT2 inhibitors and GLP-1 agonists also showed cardioprotective effects but their mechanisms are not fully elucidated. This article raised several clinical and basic questions if those agents alter each atherosclerotic marker differently.

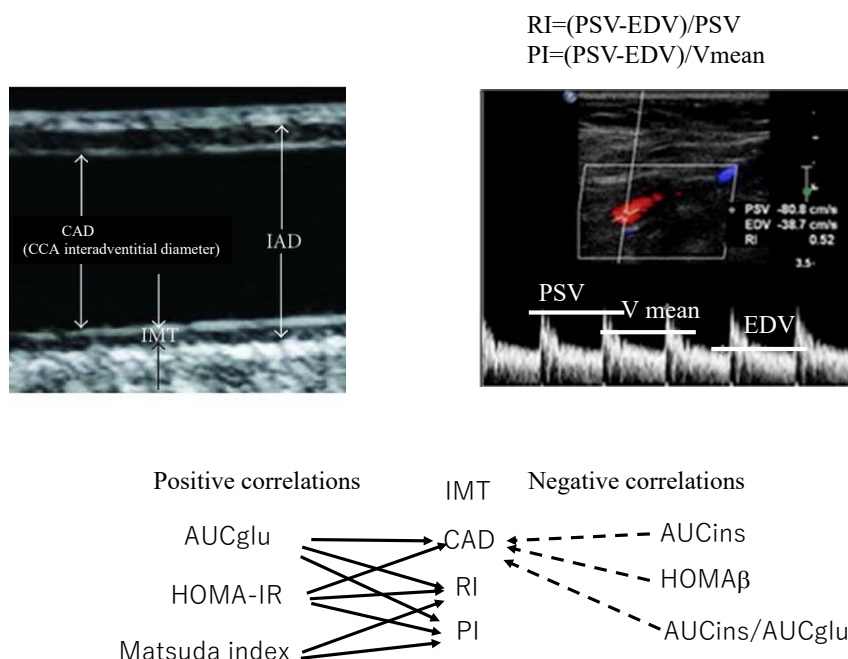
Laboratory exams have their own distinct characters and no two are the same. We appreciate wide variety of tools to evaluate patients.

## Conflicts of Interest

None.

## References

- 1) O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media



**Fig. 1.** Representative trace of carotid artery ultrasound and measure method for atherosclerotic parameters

Sasaki N *et al* reported positive and negative correlations after adjusting confounding factors with glucose and insulin level after oral glucose tolerance test and insulin resistance index (HOMA-IR, Matsuda index), and insulin secretion index (HOMA $\beta$ )<sup>6</sup>. Each parameter has distinct correlations with glucose metabolism and diverse pathophysiological meanings.

- thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med*, 1999; 340: 14-22
- 2) Committee for Epidemiology and Clinical management of Atherosclerosis, Japan Atherosclerosis Society Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017. *J Atheroscler Thromb*, 2018; 25: 846-984
  - 3) Umemura, S., Arima, H., Arima, S. et al. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2019). *Hypertens Res*, 2019; 42, 1235-1481
  - 4) Raggi P. Screening for atherosclerotic cardiovascular disease in patients with type 2 diabetes mellitus: controversies and guidelines. *Canad J Diabetes*, 2020; 44: 86-92
  - 5) Den Ruijter HM, Peters SA, Anderson TJ, Britton AR, Dekker JM, Eijkemans MJ, Engstrom G, Evans GW, de Graaf J, Grobbee DE, Hedblad B, Hofman A, Holewijn S, Ikeda A, Kavousi M, Kitagawa K, Kitamura A, Koffijberg H, Lonn EM, Lorenz MW, Mathiesen EB, Nijpels G, Okazaki S, O'Leary DH, Polak JF, Price JF, Robertson C, Rembold CM, Rosvall M, Rundek T, Salonen JT, Sitzer M, Stehouwer CD, Witteman JC, Moons KG, Bots ML. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. *JAMA*, 2012; 308: 796-803
  - 6) Sasaki N, Maeda R, Ozono R, Nakano Y, Higashi Y. Association of flow parameters and diameter in common carotid artery with impaired glucose metabolism. *J Atheroscler Thromb*, 2022; 29: 654-666