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Coronary calcium is not all we need: Carotid plaque burden measured by ultrasound is better

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To the Editor,

In a paper from the Multi-Ethnic Study of Atherosclerosis, Zhao et al. [1] reported that coronary calcium scores predicted most of the risk of cardiovascular events, with little contribution of carotid intima-media thickness (IMT) and ankle-brachial index. In the accompanying editorial, Paolo Raggi stated "*Coronary calcium is all we need for risk assessment, yet we do not use it often enough*" [2]. He is right that assessing burden of atherosclerosis is much better for predicting risk than calculations from panels of risk factors, and that coronary calcium is much better than IMT and ankle-brachial index. However, omitted was mention of ultrasound measurement of carotid plaque burden, which is much less costly, and avoids the risk of radiation. Although the radiation exposure from a single coronary calcium score may be small, patients with coronary artery disease tend to have repeated exposure to radiation, during angiograms and percutaneous revascularization procedures, and the risk of radiation is cumulative.

In 2002, carotid total plaque area (TPA) was reported to be a very strong predictor of the 5-year risk of stroke, myocardial infarction or vascular mortality [3]. Among patients attending vascular prevention clinics, the quartiles of TPA were 0.00–0.11 cm^2, 0.12–0.45 cm^2, 0.46–1.18 cm^2, and 1.19–6.73 cm^2. By quartile of TPA, the 5-year risk of those events was 5.6%, 10.7%, 13.9%, and 19.5% respectively, *after adjustment for age, sex, blood pressure, smoking, diabetes, serum cholesterol, plasma total homocysteine and treatment of blood pressure and cholesterol.* In the Tromsø study, TPA was a much stronger predictor of myocardial infarction or stroke [4] than IMT.

More recently, 3-dimensional (3D) measurement of carotid plaque burden, in contrast to IMT, has been shown to be highly correlated with coronary calcium scores [5], and as predictive of cardiovascular events [6]. An important advantage of measuring carotid plaque burden is that it can be repeated at low cost and no risk, and in contrast to coronary calcium score, carotid plaque burden changes very quickly with treatment [7,8], so the success of preventive therapy can be followed. Fig. 1 shows change in carotid plaque burden and composition in just 13 weeks. In a randomized trial in patients with severe carotid atherosclerosis, there was significant progression of plaque with placebo (16.81 ± 74.10 mm^3) versus regression on atorvastatin 80 mg ($-90.25 + 85.12$ mm^3) in just 3 months [8]. Carotid plaques are focal, and can therefore change in length, thickness and circumferential extent, whereas coronary plaques, being continuous throughout the length of the pullback, can change only in average thickness. Therefore, change in total plaque volume is the most sensitive way to assess effects of therapy on atherosclerosis [7].

In the 2002 study mentioned above, half the patients had progression of plaque during the first year of follow-up despite usual therapy, and those with progression of plaque had twice the risk of stroke/MI/Vascular mortality, compared with patients whose plaque regressed or remained stable [3]. The recognition that usual care was failing half our patients led to a paradigm change in management of atherosclerosis: treating arteries instead of treating risk factors. Among patients with asymptomatic carotid stenosis, that approach, implemented in our clinics in 2003, was associated with a reduction of carotid microemboli detected by transcranial Doppler from 12.6% to 3.7% of patients, suggesting stabilization of plaque. It was also associated with a > 80% reduction in the 2-year risk of stroke and myocardial infarction [9].

Because coronary calcium scores change very little with therapy, they cannot be used to guide preventive therapy. It is to be hoped that automated measurement of 3D plaque volume, which is on the horizon [10], will enable randomized trials of "treating arteries". Coronary calcium is not all we need. Measurement of carotid plaque burden is not only safer and as predictive of risk, but better for assessing effects of

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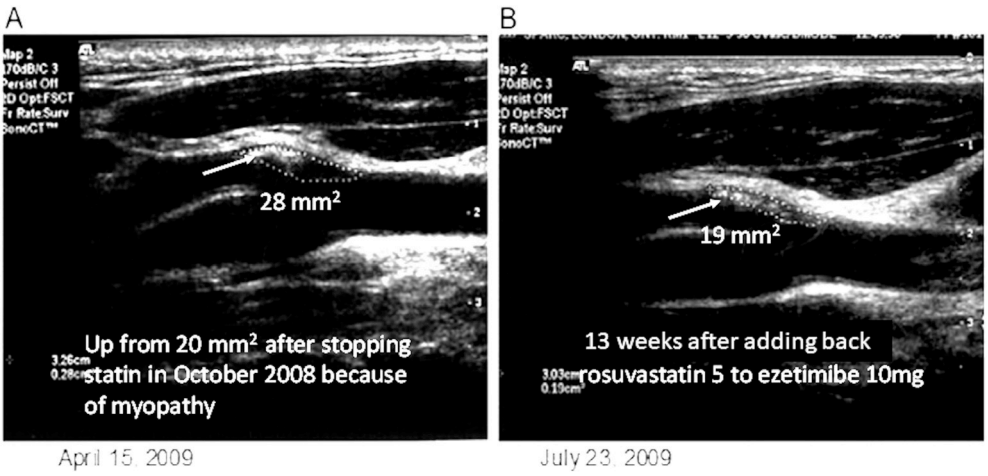

Fig. 1. Plaque regression is much faster than most would expect.
(A) Soft plaque at the origin of the left external carotid in a 64-year-old man using ezetimibe alone because of myalgia and cramps with statins. His plaque (white arrow) had progressed from 20 mm^2 6 months earlier, to 28 mm^2 after stopping rosuvastatin and taking ezetimibe alone. After restarting rosuvastatin 5 mg daily with ezetimibe 10 mg daily, and CoQ10 200 mg daily to prevent myalgia, the plaque area regressed to 19 mm^2 over 13 weeks (B). The plaque had also become denser, with regression of the echolucent plaque. (Reproduced with permission of Wolters Kluver from: Spence JD, Hackam DG. Treating Arteries Instead of Risk Factors. A Paradigm Change in Management of Atherosclerosis. 2010; 41 (6):1193–9. Notations were added.).

preventive therapy.

Conflict of interest

The author shares in a patent on 3D ultrasound measurement of carotid plaque, he is an officer of Vascularis Inc, and is collaborating with Philips on improvement of their 3D ultrasound method for automated measurement of 3D plaque volume. He is also an advisory board member for Amgen and a consultant to Orphan Technologies, and has received lecture fees from Pfizer and Bristol-Meyers Squibb.

References

[1] Y. Zhao, M.A. Evans, M.A. Allison, et al., Multisite atherosclerosis in subjects with metabolic syndrome and diabetes and relation to cardiovascular events: the Multi-Ethnic Study of Atherosclerosis, Atherosclerosis 282 (2019) 202–209.
[2] P. Raggi, Coronary calcium is all we need for risk assessment, yet we do not use it often enough, Atherosclerosis 282 (2019) 167–168.
[3] J.D. Spence, M. Eliasziw, M. DiCicco, et al., Carotid plaque area: a tool for targeting and evaluating vascular preventive therapy, Stroke 33 (2002) 2916–2922.
[4] E.B. Mathiesen, S.H. Johnsen, T. Wilsgaard, et al., Carotid plaque area and intima-media thickness in prediction of first-ever ischemic stroke: a 10-year follow-up of 6584 men and women: the tromso study, Stroke 42 (2011) 972–978.
[5] H. Sillesen, P. Muntendam, A. Adourian, et al., Carotid plaque burden as a measure of subclinical atherosclerosis: comparison with other tests for subclinical arterial disease in the high risk plaque BioImage study, JACC. Cardiovasc. Imaging 5 (2012) 681–689.
[6] U. Baber, R. Mehran, S. Sartori, et al., Prevalence, impact, and predictive value of detecting subclinical coronary and carotid atherosclerosis in asymptomatic adults: the BioImage study, J. Am. Coll. Cardiol. 65 (2015) 1065–1074.
[7] J.D. Spence, Time course of atherosclerosis regression, Atherosclerosis 235 (2014) 347–348.
[8] C.D. Ainsworth, C.C. Blake, A. Tamayo, et al., 3D ultrasound measurement of change in carotid plaque volume: a tool for rapid evaluation of new therapies, Stroke 36 (2005) 1904–1909.
[9] J.D. Spence, V. Coates, H. Li, et al., Effects of Intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis, Arch. Neurol. 67 (2010) 180–186.
[10] J.D. Spence, Approaching automated 3-dimensional measurement of atherosclerotic plaque volume, J. Am. Coll. Cardiol. 70 (2017) 314–317.

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