In this issue of Atherosclerosis, Inaba et al. [1] provide further evidence, in form of a meta-analysis, that measurement of carotid plaque is more strongly predictive of cardiovascular events than is measurement of carotid intima-media thickness (IMT). This was previously noted by Johnsen and Mathiesen [2]. The most important studies to show this are those from the Tromsø study, a prospective population-based study in over 6000 participants who were healthy at baseline. The Tromsø study is the only large prospective study in which both total plaque area (TPA) and IMT were measured. In their report after 6 years of followup [3], they found that baseline IMT in the distal common carotid did not predict myocardial infarction (MI), whereas IMT in the bulb was predictive, and TPA was more strongly predictive. In the report after 10 years of followup [4], they found that IMT did not predict stroke, whereas TPA was strongly predictive.

An important issue raised by their 2007 paper [3] was the difference between IMT in the common carotid at sites deliberately not containing plaque, versus IMT in the carotid bulb, including plaque thickness in patients with plaque at that location. The former is the method recommended in the Mannheim consensus; the latter is that recommended by Bots and others. The meta-analysis by Inaba et al. [1] is important because the authors distinguished between these two approaches to measurement of IMT. They confirmed the finding from the Tromsø study, that IMT including plaque thickness in the bulb was more strongly predictive of cardiovascular events than was IMT in the common carotid where there is no plaque, and that measurement of carotid plaque was more predictive than either IMT phenotype. In their meta-analysis, Inaba et al. found that in 77% of papers it was not clearly stated which approach was used to measurement of IMT.

It is a widespread misconception that IMT represents “preclinical atherosclerosis”. IMT should be regarded as a form of end-organ disease that is a precursor of atherosclerosis. Furthermore, there is a great deal of confusion that arises from lumping together studies in which IMT was measured by these two different approaches. IMT where there is no plaque is not atherosclerosis [5]; it is a different phenotype that represents mainly hypertensive medial hypertrophy. IMT including plaque thickness could be called plaque thickness, which has been shown by Rundek et al. [6] to predict cardiovascular risk, but most or all IMT studies using that method of measurement lump together participants with and without plaque, so the phenotype is mixed. For this reason, neither approach to IMT measurement should be called “atherosclerosis”: they should be called, IMT, and it should be clearly stated which method was used.

A further important advantage of measuring TPA, or 3-dimensional phenotypes such as plaque volume and vessel wall volume, is dynamic scale range. Pollex et al. [7] found in a study of aboriginal Canadians (Ojii-Cree), in which IMT was compared to total plaque volume (TPV), that ~90% of the IMT measurements fall within a relatively narrow 0.55–1.0 mm range, whereas ~60% of TPV values fall within a range of 5–500 mm³. Thus, the dynamic range of measurements varied by ~100-fold for TPV compared to ~2-fold for the IMT.

An equally important, or perhaps more important issue, is the ability to follow patients and assess effects of therapy. The resolution of carotid ultrasound is ~0.3 mm, whereas the annual change of IMT is ~0.15 mm, so change cannot be measured within individuals in clinically meaningful time frames. Carotid TPA, on the other hand, changes on average by ~10 mm², so progression or regression can easily be measured within months [8]. We have reported that a new paradigm, “treating arteries instead of treating risk factors” [8], reversed the proportion of patients with plaque progression vs. regression (from 50:25% to 25:50%), and markedly reduced cardiovascular events among patients with asymptomatic carotid stenosis [9]. This approach is not possible using measurement of IMT. Plaque measurement is also much superior to IMT for assessing novel anti-atherosclerotic therapies. Studies based on IMT require hundreds of patients per group followed for two years; for assessing novel anti-atherosclerotic therapies, Studies based on IMT require hundreds of patients per group followed for two years; with 3D plaque volume or vessel wall volume, significant regression can be measured in 3 months with ~20 patients per study group [10].

It is a great mystery why most investigators persist in measuring only IMT. Anyone who can measure IMT can measure TPA reliably without any additional equipment. An Argentinian group (Blossom Health Care) have applied this approach for the past several years in over 25,000 patients in several large health maintenance organizations. They are reclassifying risk by measuring TPA among the cases with intermediate Framingham risk scores, and basing treatment on TPA (Personal communication of Dr. Luis Armando, June 2011). Their online tool for measurement of TPA and...

Trying to treat arteries without measuring plaque would be like treating hypertension without measuring blood pressure.

Disclosure

The author has received grants for research from HSF, NIH, CIHR for research from Pfizer, Merck, Pan American Labs, lecture fees from Pfizer, AstraZeneca, Merck, Novartis, Boehringer-Ingelheim and consulting fees from Novartis, Boehringer-Ingelheim. The author has an interest in www.vascularis.com.

References


