

# The relationship between carotid intima-media thickness and coronary atherosclerosis revisited

Alain Simon\* and Gilles Chironi

AP-HP, Hôpital Européen Georges Pompidou, Centre de Médecine Préventive Cardiovasculaire, 75015 Paris, France; and Faculté de Médecine Paris Descartes, 75270 Paris, France

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**This editorial refers to 'Carotid intima-media thickness by B-mode ultrasound as surrogate of coronary atherosclerosis: correlation with quantitative coronary angiography and coronary intravascular ultrasound findings' by M. Amato *et al.*, on page 2094**

Many clinical studies support the opinion that carotid intima-media thickness (IMT) assessed by B-mode ultrasound in extracranial carotid arteries, either in a single segment (common carotid) or in multiple segments (aggregate of measures in common carotids, bifurcations, and internal carotids), is a valuable mirror of coronary risk status and a worthwhile predictor of subsequent coronary heart disease (CHD), the leading source of cardiovascular death.<sup>1–3</sup> Indeed, traditional and emerging risk factors for CHD have been found mostly to be closely correlated with increased carotid IMT.<sup>1</sup> Also, increased carotid IMT is associated with substantially increased risk of a future CHD event in primary and secondary prevention populations.<sup>1</sup> Thus, by analysing the proportion of subjects developing a CHD event according to the carotid IMT level at the onset of the follow-up in two pioneering prospective population-based studies,<sup>4,5</sup> it has been shown that markedly increased IMT above ~1 mm was associated with a 12–16% 10-year CHD incidence depending on age, sex, and carotid segment(s) measured, whereas the lowest percentiles of IMT distribution were associated with a CHD incidence of consistently <0.5%.<sup>6</sup> Despite this body of evidence, the widespread application of carotid IMT measurement for assessing CHD risk in the clinical setting has been seriously questioned on the basis of several reports suggesting that increased carotid IMT was not a good indicator of co-existing coronary atherosclerosis.<sup>7</sup> These reports point to a weak relationship between carotid IMT and angiographically assessed coronary atherosclerosis, with correlation coefficients mostly between 0.30 and 0.40, and even insignificant in some cases.<sup>7</sup> Such a weak relationship was

attributed to variability in atherosclerosis development between both vascular beds suggested by scarce post-mortem studies.<sup>7</sup> Another explanation was that IMT, as a combined measure of intima and media thickness, is not a specific marker of atherosclerosis burden because the atherosclerotic process affects mainly the intimal layer while medial hypertrophy is a non-atherosclerotic alteration.<sup>1,7</sup> This explanation may be relevant when IMT is measured exclusively in the common carotid segment free of atherosclerosis and therefore does reflect predominant medial hypertrophy, but it is unlikely when the measurement of carotid IMT, such as performed in most studies,<sup>7</sup> includes multiple carotid segments and frequently incorporates thickness of plaques in carotid bifurcations and internal carotid arteries. In this context, the work by Amato *et al.*<sup>8</sup> is of great interest because it provides a novel and contradictory addition to the debate that carotid IMT and coronary atherosclerosis are weakly correlated.<sup>7</sup> Selecting 48 patients with suspected or proven CHD, this study reports for the first time that carotid IMT was closely related to coronary IMT assessed by intravascular ultrasound (IVUS) via a mathematical equation incorporating both external and lumen cross-sectional areas measured in the more atherosclerotic vessel on coronary angiogram or in the left anterior descending artery in the absence of atherosclerosis. Correlation coefficients of carotid and coronary IMT relationships ranged from 0.49 to 0.55, depending on the segment(s) used for carotid measurement, and became maximal when mean carotid IMT, i.e. the average of measures in the three carotid segments, was used. This work also shows that whatever the carotid segment(s) measured, the relationship of carotid IMT to coronary IMT was much stronger than that of carotid IMT to coronary atherosclerosis burden determined by quantitative angiographic analysis.<sup>8</sup> This last noteworthy finding indicates that patients with markedly increased mean carotid IMT above 1 mm, and showing absent or intermediate atherosclerosis burden on coronary angiogram, had seven times more risk of having IVUS flow-limiting coronary stenosis,<sup>8</sup> suggesting that testing carotid IMT at an early stage of coronary atherosclerosis may have a better performance than quantitative coronary angiography for detecting patients with a positive IVUS test. However, the

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\* Corresponding author. Tel: +33 1 43 95 93 91; fax: 33 1 45 39 11 93.

E-mail address: alain.simon@brs.aphp.fr

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study of Amato *et al.* was performed in a very small number of high-risk patients,<sup>8</sup> and its results need to be confirmed and cannot be extrapolated to subjects with moderately high or intermediate cardiovascular risk. Nevertheless, this study strongly supports the clinically relevant idea that the carotid artery is a 'sentinel vessel' as regards coronary atherosclerotic status. It also suggests that the modest relationship between carotid IMT and angiographically assessed coronary atherosclerosis may reflect the incapacity of angiography to assess atherosclerotic change of the coronary wall accurately because of the phenomenon of compensatory enlargement.<sup>9</sup> Indeed, arterial remodelling inherent to development of atherosclerosis aims at counteracting the development of lumen compromise of the large artery by mutual adaptation of the diameter to wall thickening.<sup>9</sup> Even at the early stage of atherosclerosis characterized by slightly intrusive wall thickening, the lumen size of the artery increases, inducing a compensatory enlargement<sup>10</sup> that may mask arterial wall thickening on angiogram. High-resolution ultrasound overcomes such angiographic limitations by offering the possibility of assessing concomitantly artery wall thickness and lumen diameter. Finally, the next challenge of future studies assessing carotid and coronary IMT concomitantly by ultrasound should be to determine whether changes over time in coronary IMT are parallel to those in carotid IMT during active reduction risk therapy, such as the reduced progression of carotid IMT reported with most blood pressure-lowering drugs, and the reduced progression or sometimes the regression of carotid IMT consistently found with low-density lipoprotein (LDL) cholesterol-lowering drugs.<sup>1</sup>

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