EDITORIAL

Association of carotid intima–media thickness and plaques with diabetic microvascular complications: still much to learn

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Carotid intima–media thickness (IMT) is considered a marker of subclinical atherosclerosis and also of subclinical organ damage. Individuals with diabetes have progressively greater carotid IMT than those with impaired or normal glucose tolerance.[1] This increase seems to be more accentuated in internal than in common carotid artery IMT.[1] Baseline measurement of carotid IMT has been shown to constitute an independent predictor of future cardiovascular events in population-based studies.[2] However, in patients with diabetes, associations between increased carotid IMT and its progression and future cardiovascular morbidity and mortality have not been established yet.[3,4]

Several previous cross-sectional studies in type 2 diabetes investigated associations between early carotid atherosclerosis (IMT and nonobstructive plaques) and the presence of microvascular complications.[5-12] Most of them,[5,6,8-10,12] but not all,[7,11] showed positive associations. Hence, this subject is still under debate. In the current issue of the *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Bartman et al[13] further examined these relationships. They evaluated 73 patients with long-standing type 2 diabetes (mean duration, 12 years) and either microvascular or macrovascular complications (44% and 58% of the patients, respectively). The authors showed that a cumulative plaque score, defined as the summation of the thickness of all carotid plaques, but not carotid IMT, was associated with the presence of microvascular complications independently of potential confounders (age, sex, hypertension, dyslipidemia, smoking, diabetes duration, and presence of macrovascular disease). The finding that diabetic microvascular complications may be more strongly associated with carotid plaques than with carotid IMT has already been reported,[8,12] and suggests that this relationship may be stronger in more advanced stages of carotid atherosclerosis (presence of plaques) than in very early carotid atherosclerosis (with increased IMT but without plaques). Also, there are segment-specific differences in the associations between cardiovascular risk factors and carotid IMT,[14,15] which was also demonstrated in the present study.[13] Additionally, there is no agreement in the literature on which carotid site best correlates with cardiovascular risk factors,[14,15] and whether these differences translate into different cardiovascular prognosis. A recent meta-analysis has suggested that the carotid plaque score may be a better cardiovascular risk predictor than carotid IMT.[16]

The major limitation of the study[13] is its small sample size, which precluded an analysis evaluating which microvascular complication was mainly associated with carotid atherosclerosis. Previous studies suggested that diabetic retinopathy might be the microvascular complication most strongly associated with carotid atherosclerosis,[5,6,8,12] followed possibly by nephropathy,[9,12] whereas the association with diabetic neuropathy is more controversial.[10,11] On the other hand, the pivotal clinical importance of establishing associations between diabetic microvascular complications and initial preclinical cardiovascular disease, beyond suggesting potential common physiopathological pathways (the so called "common soil" hypothesis), lies in the fact that, in general, microvascular complications are established risk markers for future cardiovascular morbidity and mortality both in type 1 and type 2 diabetes patients.[17,18]

From a physiopathological standpoint, a marked difference, although interrelated, between anatomical (increased IMT and plaques) and functional (increased stiffness, reduced compliance/distensibility) carotid abnormalities should be noted. It has been consistently demonstrated that patients with type 2 diabetes have increased arterial stiffness and that this is strongly associated with the presence of all

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microvascular complications.[19] Moreover, ambulatory pulse pressure, a well-known surrogate marker for increased arterial stiffness, was the main determinant of carotid IMT in a cross-sectional study in patients with type 2 diabetes.[8] In this investigation, ambulatory pulse pressure was the covariate that most attenuated the correlations between carotid atherosclerosis and microvascular complications,[8] suggesting that at least part of the associations between early anatomical carotid atherosclerosis markers and microvascular complications may be indeed mediated by its correlated functional alterations. Even more relevant, it was demonstrated that the presence of diabetic retinopathy was independently associated with arterial stiffness progression during follow-up.[20]

The above findings suggest that functional large artery stiffening may have more physiopathological importance in microvascular disease development than anatomical large artery wall thickening. These 2 parameters may possibly reflect different aspects of the atherosclerotic process. Overall, these data reinforce the hypothesis that there may be common or interacting pathogenetic mechanisms in the onset or progression of diabetic microvascular and macrovascular complications. Future large prospective studies on the predictive value of increased carotid IMT or plaques for the development and progression of degenerative microvascular complications, as well as its comparison with the predictive power of increased arterial stiffness, may help elucidate the importance of anatomical carotid abnormalities and their relations with functional alterations in the physiopathological mechanisms involved in the development of diabetic microvascular complications.

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