Association of Increased Plasma Cardiotrophin-1 With Left Ventricular Mass Indexes in Normotensive Morbid Obesity

To the Editor:

We read with great interest the article by López et al, who hypothesize that cardiotrophin-1 (CT-1), a cytokine that induces cardiomyocyte growth, may be abnormally upregulated in hypertensive patients with inappropriate left ventricular mass (LVM), suggesting that an excess of CT-1 may contribute to inappropriate left ventricular growth. This possibility is supported by the finding of a correlation between CT-1 levels and the observed LVM/predicted LVM ratio, independent from concentric left ventricular hypertrophy (LVH).

De Simone et al suggested that, other than hemodynamic load, the process that yields to inappropriate LVH can also depend on the protracted activity over time of cytokines, among other nonhemodynamic factors. The observation by López et al that CT-1 levels were high in treated patients in whom inappropriate LVM persisted despite normalization of blood pressure with treatment, adds further support.

It has long been accepted that the mechanical stimuli of pressure versus volume overload produces distinct cardiac muscle phenotypes, the former resulting in a concentric pattern of hypertrophy, with an increase in cell diameter and the addition of new sarcomeric units in parallel, and the latter promoting an eccentric form of hypertrophy with an increase in cell length, reflecting the addition of new sarcomeric units in series. The signaling pathways mediating these distinct cardiac phenotypes of hypertrophy are still not completely clear.

CT-1, a member of the interleukin-6 superfamily of cytokines, was originally identified as a factor that induces longitudinal hypertrophy of cardiac myocytes by directing sarcomere assembly in series.

This cardiac phenotype (eccentric hypertrophy) may possibly account for the marked increase in LVM in obesity, which is considered an independent stimulus to myocardial cardiomyocyte growth, may be abnormally upregulated in hypertrophic patients with an increase in cell length, reflecting the addition of new sarcomeric units in series. The signaling pathways mediating these distinct cardiac phenotypes of hypertrophy are still not completely clear.

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We recently suggested that, in uncomplicated morbid obesity, the activation of proinflammatory-related cytokine pathways within the myocardium could be responsible for a correlative and causative relationship between the amount of abdominal visceral adipose tissue and subclinical echocardiographic abnormalities.

This was suggested by the association of both echocardiographic parameters and visceral adipose tissue area, with the levels of bioactive proteins involved in ventricular remodeling (eg, soluble interleukin-6 receptor/interleukin-6 complex, monocyte chemoattractant protein-1, and C-reactive protein).

Thus, it is reasonable to consider a role for cytokines and other nonhemodynamic factors in ventricular remodeling, starting before cardiovascular complications arise (eg, hypertension).

We would like to add some information on the association between plasma CT-1 levels and LVM indexes (by echocardiography) in obese patients with eccentric LVH and normal blood pressure. We measured plasma CT-1 levels (ELISA) in 24 normotensive women (resting systolic and diastolic blood pressure <130 and <80 mm Hg) with severe obesity (mean body mass index: 43.4 ± 5.1) and with LVM indexed for height:7 (LVM index: >46.7 g/m²; mean LVM index: 61.3 ± 9.7 g/m²; relative wall thickness: <0.44) and 15 normal-weight normotensive women without LVH (control subjects). Plasma CT-1 was higher in the obese patients than in control subjects (67.36 ± 10.20 versus 27.27 ± 4.11 fmol/mL; P < 0.0001) but was normalized by logarithmic transformation for the correlation analysis. A direct correlation was found between CT-1 and LVM index (r = 0.61; P < 0.0001), LVM (r = 0.41; P < 0.001), end-diastolic septum thickness (r = 0.70; P < 0.0001), ad-diastolic posterior wall thickness (r = 0.67; P < 0.0001), even after correction for visceral adipose tissue (measured by computed tomography) and fat-free mass (measured by bioelectrical impedance). This preliminary result may support the hypothesis that increased CT-1 may be associated with LVM indexes in a situation of chronic volume overload–induced hypertrophy, even in the absence of pressure overload (eg, hypertension).

Thus, the study by López et al opens new insights into a possible pathophysiological role for this cytokine in left ventricular growth and as an additional useful tool in the initial cardiac assessment of patients with LVH.

Disclosures

None.

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