Sympathetic Activity, Heart Failure, Obesity, and Metabolic Syndrome: Is There Any Role for Obstructive Sleep Apnea?

To the Editor:

We read with interest the article by Grassi et al1 regarding the sympathetic activity in patients with heart failure with and without metabolic syndrome. The authors found that the coexistence of metabolic syndrome and heart failure was associated with additive effects on sympathetic activity over and above heart failure alone. Furthermore, waist circumference and body mass index were the variables most related to sympathetic activation. Although this study provided important mechanistic information about sympathetic activation in heart failure, one important factor was not adequately explored and should be taken into account: obstructive sleep apnea (OSA).

OSA is now recognized as an important public health problem that increases cardiovascular morbidity and mortality.2 OSA directly promotes increases on sympathetic activity and is highly prevalent in both heart failure and metabolic syndrome. Obesity is an important risk factor for OSA, which, in turn, is a potent trigger of sympathetic activity. Unfortunately, the study by Grassi et al1 did not perform any investigation for OSA, and the authors recognized this limitation. Now, there is compelling evidence that OSA is not only a local phenomenon characterized by recurrent obstruction of the pharynx during sleep. In fact, OSA is associated with all of the components of metabolic syndrome, including hypertension (OSA is recognized as a secondary cause of hypertension), lipid abnormalities, and insulin resistance. Treatment of OSA with continuous positive airway pressure is able to virtually abolish all adverse respiratory events during sleep and promotes significant improvements not only of 24-hour blood pressure but also of markers of insulin resistance.3,4 It is important to stress that all of the improvements were independent of changes on body mass index.

Several potentially harmful pathways to the metabolic and cardiovascular system are independently associated with OSA, including systemic inflammation, endothelial dysfunction, increased oxidative stress, adhesion molecule expression, lipid lowering in macrophages, vascular smooth cell activation, lipid peroxidation, and high-density lipoprotein dysfunction.5,4 On the other hand, metabolic syndrome has been associated with several of these mechanisms.4 Unfortunately, the great majority of the studies exploring the possible cardiovascular complications of metabolic syndrome did not consider OSA as a potential confounding factor. This fact suggests that the cardiovascular community still underestimates the relative role of OSA on cardiovascular disease. For instance, the last American Heart Association Scientific Statement on Metabolic Syndrome6 quoted OSA as of interest of “other fields of medicine.” OSA received the same attention given to conditions such as cholesterol gallstones and lipodystrophies and received only 1 of 188 references.5

In conclusion, OSA and metabolic syndrome are tightly linked, and both conditions should be considered as potential and independent risk factors to provide additive sympathetic activation in heart failure patients. We strongly believe that it is important to take into account OSA in any future study to make significant progress in our understanding of the link between metabolic syndrome and cardiovascular disease.

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