Resistin: A New Marker of Cardiorenal Risk?

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Resistin is a cysteine-rich protein that was discovered in 2001 and was initially proposed as a potential link between obesity and type 2 diabetes. Sources of resistin differ across species. In rodents, resistin is mainly located and secreted from adipocytes. However, in humans resistin is expressed primarily by macrophages, both inside and outside adipose tissue, and seems to be involved in the secretion of pro-inflammatory factors and in the promotion of endothelial cell activation, although its role in insulin resistance remains a matter of debate. It has been observed in humans that atherosclerotic atherosclerotic vessel wall macrophages secrete resistin. It was also shown that circulating resistin correlates positively with carotid intima media thickness and with coronary artery calcification. For these reasons a potential role of resistin in early atherogenesis and its late complications has been suggested. More recently, elevated serum resistin concentrations were independently and strongly associated with the risk for new onset of heart failure.2

The value of microalbuminuria (MAU) as predictor of cardiovascular events in diabetic and nondiabetic subjects and in patients with essential hypertension is firmly established. The article by Tsioufis et al. published in this issue of the Journal, intriguingly shows that MAU, that is now regarded as an early renal manifestation of a widespread vascular dysfunction, is closely associated with resistin in untreated nondiabetic hypertensive subjects, supporting the notion that this protein may be considered as a new candidate marker of cardiorenal risk. The finding of this study, that is in agreement with previous results obtained in diabetic patients, raises interesting questions about potential mechanistic links.

Insulin resistance is known to be associated with increased urinary albumin excretion and could potentially explain the association between resistin and MAU. Insulin resistance was not directly assessed in the study of Tsioufis et al. However, after adjustment for surrogate markers of insulin sensitivity, such as serum glucose levels, body mass index, waist circumference, triglycerides, high-density lipoprotein cholesterol, the association of plasma resistin with MAU was not altered, suggesting that insulin resistance may not be a major mediator of the link between resistin and albuminuria.

Several investigations documented that MAU is related to various inflammatory markers. Unfortunately, sensitive markers of subclinical inflammation, such as C-reactive protein, were not evaluated in the present study. Therefore, it was not possible to assess the potential influence of subclinical inflammation on the relation between resistin and albumin to creatinine ratio.

On the other hand, the cross-sectional design of the present investigation precludes the assessment of the temporality of the observed associations and thus determination of causality.

MAU has been repeatedly shown to be accompanied by abnormalities in various markers of endothelial cell function. More recently, it has been observed that resistin may induce endothelin-1 release and upregulate adhesion molecules. Thus, it is conceivable, but not demonstrated, that endothelial dysfunction may be a common link between MAU and resistin. Therefore, additional research is required to better explain the interesting findings of Tsioufis et al., that need to be confirmed and extended by further studies before resistin may be accepted as an independent marker of cardiorenal risk.

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