The Tumor Marker CA125 and Heart Failure

To the Editor,

We read with great interest the editorial by Richards,[1] in which a wide range of biomarkers heart failure were reviewed. Although brain natriuretic peptides (BNP)[2,3] are the only ones applied in clinical practice, it is worth noting the role of the carbohydrate antigen 125 (CA125) tumor marker as a biomarker which was not described in the editorial.[1]

D'Aloia et al[4] described a significant correlation between elevated serum CA125 and advanced functional class, and other hemodynamic parameters related to severity, in 286 patients with chronic heart failure. The biomarker was also associated with a poorer short-term prognosis. Other groups have since confirmed this association in both acute[5] and chronic heart failure.[6,7] We recently observed that determination of CA125 added prognostic information to that provided by BNP in 1111 unselected patients with acute heart failure: indeed, the combination of the two biomarkers led to improved risk stratification at 6 to 8 months.[8]

Several studies have shown consistent correlations between levels of CA125 and the presence of serous effusions[5,9]; in our experience, the most important predictors associated with CA125 values were the presence of pleural effusion and peripheral edema.[5] The degree of inflammatory activity has been proposed as another mechanism related to elevated concentrations of CA125. For example, Kosar et al[10] observed strong positive correlations between CA125 values and plasma levels of tumor necrosis factor alpha and interleukin-6 and 10 in 35 patients with systolic dysfunction who were hospitalized for heart failure.

Another remarkable property of CA125 is that it changes over time according to the clinical situation.[4,9] Moreover, unlike the natriuretic peptides, which have a lifespan of minutes, the CA125 has a half-life of over 1 week. This gives it potential clinical utility, for example in monitoring progress and possibly even as a tool to guide treatment.

In summary, this glycoprotein meets a number of the requirements for a bio-marker to be considered of potential clinical utility, ie: *a)* it is widely available for standardized analysis at an acceptable cost; *b)* it is related to processes which are crucial to the pathophysiological progression of the disease; *c)* its relation to prognosis is continuous and it provides additional information beyond the established,

classical variables, including brain natriuretic peptide; *d)* variations in its concentration according to the clinical situation are constant; and *e)* it potentially has therapeutic implications.

Obviously, further studies are required to provide more information on the pathophysiological mechanisms involved in the elevation of this biomarker and to explore its potential usefulness in guiding treatment.

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