Antigen carbohydrate 125 in heart failure: Not just a surrogate for serosal effusions?

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Dear editor,

We have read with interest the letter CA-125 and heart failure: Déjà vu or “still to be seen” by Topatan B and Basaran A [1] where the authors concisely reviewed the current pathophysiological knowledge of CA125 in heart failure (HF). As discussed by these authors, the pathogenesis of this biomarker’s elevation in HF is complex and multifactorial, with apparently different driven forces. For instances, a proinflammatory stimulus (IL-1, tumor necrosis factor-α, lipopolysaccharide) and mesothelial-induced stress appear the key mechanisms related to the increase of this biomarker in HF [1–5]. However, no clear evidence exists in regard to how these two mechanisms differentially participate in CA125 elevation in individual patients with HF. Therefore, despite the fact that the presence of peritoneal effusion has shown to be importantly correlated to higher CA125 values [1], considering this biomarker just a simple surrogate for serosal effusion seems quite unfair. Along this line, we have new evidence pointing-out against the fact that CA125 elevation represents just merely a surrogate for mesothelial irritation. Since July 2008 to the end of July 2010 we included in an ambulatory continuous peritoneal dialysis program 17 patients with advanced congestive HF that meet the following criteria: a) NYHA III/IV in an ambulatory continuous peritoneal dialysis program; b) CA125 serum values within normal ranges at the moment of peritoneal dialysis onset, 70.6% (n = 12) and 82.3% (n = 14) of the patients displayed CA125 < 35 U/ml at 45 and 120 days, respectively (p = 0.05 for both comparisons). Paralleling to this decrease in CA125 values, an improvement in the NYHA functional class and an increase of the relative lymphocyte count (as a marker of improvement of the inflammatory state) were observed (Fig. 1b and c). With this data, we aim to stress the concept that CA125 is more than a simple surrogate for the presence of serosal effusions and mesothelial irritation, under the assumption that peritoneal dialysate is a well known irritator of the peritoneum [6,7]. Nevertheless, why most of the studies assessing the role of CA125 in HF have shown a close relationship with the presence of serosal effusions? Obviously, this question is still unsolved, although we hypothesize that CA125 is synthesized by mesothelial cells in response to certain mechanisms activated in the congestive states, and supported by recent evidence showing a pathogenic role of venous congestion in triggering a proinflammatory state [8,9], which at the end, would activate the mesothelial cells to synthesize CA125. In this framework, CA125 increase and serosal effusion are parallel processes caused by the similar pathophysiological mechanisms although not necessarily a cause–effect phenomenon.

No matter which pathophysiological mechanism is behind the kinetic of this biomarker, there are certain properties that make CA125 serum determination a promising tool for HF risk stratification: a) wide availability, b) additional prognostic utility beyond clinical and biochemical markers (including natriuretic peptides) [5] and; c) in contrast of cytokines and other inflammatory markers that exhibit high variability [10], CA125 changes over time are sustained (half-life higher than 1 week) and correlated with clinical status and prognosis [11,12].

Finally, we believe there is still much to be seen regarding this biomarker, and encourage researchers in HF field to focus into the pathophysiology, biological role and the clinical utility of this glycoprotein for monitoring and guiding therapy in HF setting.

The following is the supplementary material related to this article.

Table 1. Baseline characteristics of the study sample.

Supplementary materials related to this article can be found online at doi:10.1016/j.ijcard.2010.12.027.

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Fig. 1. CA125 serum values, NYHA functional class and relative lymphocyte count pre and 45 and 120 days following peritoneal dialysis onset. a. CA125 serum levels; b. NYHA functional class; c. relative lymphocyte count. Values are expressed as median (interquartile range). CA125: antigen carbohydrate 125; NYHA: New York Heart Association.