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Title: Advanced glycation end products and its soluble receptor (sRAGE) are increased in chronic heart failure but not in chronic obstructive pulmonary disease

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Body: The binding of the receptor for advanced glycation end products (RAGE) with its ligands begins a cellular activation and an inflammatory signal amplification in different diseases. We determined the plasma levels of N(epsilon)-carboxymethyllysine (CML) and soluble RAGE (sRAGE) in chronic heart failure (CHF) patients, in cases with chronic obstructive pulmonary disease (COPD) and in healthy controls. We also investigated the associations between these biomarkers and the clinical and functional characteristics of the study populations. The CML and sRAGE plasma levels were measured by using a sandwich enzyme-linked immunosorbent assay (ELISA) in 146 subjects, aged ≥ 65 years, divided into five groups: 58 with CHF, 23 with COPD, 29 with CHF and COPD and 36 controls (18 current or former smokers, and 18 never smokers). Individuals with diabetes were excluded from this study. The CML and sRAGE levels were higher in CHF patients than in controls [CML: 1.9 (1.5-2.4) vs 1.6 (1.4-2.0) ng/mL; sRAGE: 0.51 (0.3-0.8) vs 0.41 (0.3-0.5) ng/mL; $p=0.01$]. By contrast, both CML and sRAGE were not different when the group with COPD and that with CHF/COPD were compared with controls ($p>0.05$). sRAGE positively correlated with N-terminal proBNP (Nt-Pro BNP) in the three patient groups: CHF ($r=0.43$, $p<0.01$), COPD ($r=0.77$, $p<0.001$) and in CHF/COPD ($r=0.60$, $p<0.01$). In conclusion, subjects with CHF have high plasma levels of CML and sRAGE. The robust association between sRAGE and NT-proBNP concentrations might suggest a potential diagnostic and prognostic significance of this receptor in heart failure. Supported by the Italian Ministry of Health.