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Title: Regulation of ghrelin on appetite in patients with acute exacerbations of chronic obstructive pulmonary disease

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Body: Background: Patients with COPD are usually complicated with malnutrition, which is partly caused by reductions of appetite and food intake, especially in acute exacerbations. Recent studies reported the key roles of ghrelin in appetite stimulation and energy homeostasis. However, the association between the orexigenic function of ghrelin and appetite reduction in AECOPD remains unclear. Objectives: To investigate the secretion, acylation of ghrelin, and its association with appetite reduction in patients with AECOPD. Methods: Thirty-six patients with AECOPD and 23 healthy adults were enrolled. Total and acylated ghrelin, obestatin, simplified nutritional appetite questionnaire (SNAQ) scoring, and calorie intake were compared in patients between in exacerbations and in remissions. Further more, the same indexes were also compared between AECOPD patients and healthy controls. Results: Total ghrelin level in patients was significantly higher in exacerbations than remissions (627.2 ± 234.9 vs. 500.8 ± 181.0 pg/ml, $p=0.001$), while the SNAQ score and calorie intake were significantly lower (10.8 ± 2.3 vs. 14.3 ± 1.8 , $p<0.001$; 663.5 ± 188.3 vs. 1031.4 ± 188.9 kcal, $p<0.001$, respectively). The proportion of acylated ghrelin, the SNAQ score, and calorie intake of patients were significantly lower than controls ($10.6 \pm 6.7\%$ vs. $15.0 \pm 5.9\%$, $p=0.003$; 10.7 ± 2.1 vs. 15.4 ± 1.2 , $p<0.001$; 647.1 ± 164.4 vs. 1257.7 ± 228.0 kcal, $p<0.001$, respectively). Conclusions: A higher ghrelin level in AECOPD indicated increased secretion of ghrelin, but its role in stimulating appetite was compromised. Moreover, the decreased acylation of ghrelin was noted in patients, which might be a cause for appetite reduction in AECOPD.