Title: Osteoporosis and adipose tissue expression of adipokines and osteoprotegerin in severe chronic obstructive pulmonary disease

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Body: Aim: to evaluate the adiponectin, leptin and osteoprotegerin (OPG) levels and its expressions in the adipose tissue, and their relationships with bone metabolism in severe COPD. Methods: serum leptin, adiponectin, OPG, the receptor activator of nuclear factor-kB ligand (RANKL), osteocalcin and type 1 collagen C-telopeptide (CTx) were determined in 43 COPD patients and 42 healthy control. Bone mineral density (BMD) was assessed at the lumbar spine (LS) and left femur neck (FN). Subcutaneous adipose tissue samples were analyzed by immunocytochemical analysis. Results: Adipose tissue expression of leptin (LepR) was low and adipose tissue expression of adiponectin (AdipoR1) was higher in COPD than in control. Patients with osteoporosis had lower leptin, OPG and LepR (p<0.01, p<0.05, p<0.01 respectively) in association with increased CTx, RANKL, adiponectin and AdipoR1(p<0.05 for all relationships) than those without. LepR was inversely related to CTx (p=0.014), and directly to serum leptin (p=0.002), to fat free mass (FFM) (p=0.003) and to BMD FN, LS (p=0.02). Serum leptin was correlated positively with OPG (p<0.05) and negatively with RANKL (p<0.05); serum adiponectin was negative association with serum OPG (p<0.05) and positive with RANKL in COPD (p<0.05). AdipoR1 was negatively related to FFM (p=0.003) and directly to serum adiponectin and CTx (p=0.004). OPG expression was related to BMD FN only (p<0.05). Immunofluorescence analysis showed the disappearance of adipokines receptors in the cross-striated muscle. Conclusion: our results suggest that adipose tissue leptin, adiponectin and OPG expressions are related to development of osteoporosis in severe COPD.