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Title: Plasma osteoprotegerin is related to femoral osteoporosis in patients with COPD

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Body: Background: Patients with COPD are at increased risk of osteoporosis, and osteoporotic hip fractures result in more serious adverse outcomes in such patients than in otherwise healthy subjects. Previously, plasma levels of osteoprotegerin (OPG) have been related to the severity of COPD. OPG inhibits osteoclastogenesis and bone loss, however, its relationship to bone mineral density (BMD) in COPD is unexplored. Aim: We hypothesized that femur BMD would be related to plasma OPG levels. Methods: In 56 subjects with COPD (4 female; age, 61.7±6.7 years; FEV_1, 53.6±19.2% pred.), femur BMD was assessed by dual energy X-ray absorptiometry, plasma OPG was measured by ELISA, and β-crosslaps by chemiluminiscence immunoassay. Patients were divided into 3 groups: 32 with normal BMD (T-score≥-1); 14 with osteopenia (-1>T-score>-2.5); and 10 with osteoporosis (T-score≤-2.5); (femur BMD, 1.04±0.11, 0.84±0.05, and 0.61±0.09 $g.cm^{-2}$; respectively). Results: Plasma OPG levels increased from the lowest in patients with normal BMD to the highest in those with osteoporosis (6.6±1.8 vs 7.2±2.9 and vs 8.6±1.5 $pmol.L^{-1}$, p for trend 0.036). In addition, femur T-scores were directly related to FEV_1, and inversely to β-crosslaps (R=0.402, p=0.002; R=-0.347, p=0.01, respectively). In multivariate analysis, OPG independently predicted femur T-scores after adjustments for age, gender, FEV_1 and β-crosslaps (p=0.011, R^2=0.374). Conclusion: In patients with COPD, osteoporosis is associated with increased plasma OPG levels, independently of the severity of airflow obstruction. Our results suggest a possible role for OPG-mediated regulation of osteoclastogenesis in COPD-related osteoporosis. Support: VEGA 1/0227/11 and APVV-0134/11, Slovakia.