# Acute exacerbations of COPD are associated with significant activation of matrix metalloproteinase 9 irrespectively of airway obstruction, emphysema and infection

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BACKGROUND: Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) are associated with accelerated aggravation of clinical symptoms and deterioration of pulmonary function. The mechanisms by which exacerbations may contribute to airway remodeling and declined lung function are poorly understood. In this study, we investigated if AE-COPD are associated with differential expression of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) in bronchoalveolar lavage (BAL). METHODS: COPD patients undergoing diagnostic bronchoscopy, with either stable disease (n = 53) or AE-COPD (n = 44), matched for their demographics and lung function parameters were included in this study. Protein levels of MMP-2,-9,-12 and of TIMP-1 and -2 in BAL were measured by ELISA. Enzymatic activity of MMP-2 and -9 was assessed by gelatin zymography. RESULTS: We observed that MMP-9, TIMP-1 and TIMP-2 were significantly increased in BAL during AE-COPD. Furthermore, there was a significant negative correlation of MMP-9, TIMP-1 and TIMP-2 with FEV1% predicted and a significant positive correlation of TIMP-1 and TIMP-2 with RV% predicted in AE-COPD. None of MMPs and TIMPs correlated with DLCO% predicted, indicating that they are associated with airway remodeling leading to obstruction rather than emphysema. In AE-COPD the gelatinolytic activity of MMP-2 was increased and furthermore, MMP-9 activation was significantly up-regulated irrespective of lung function, bacterial or viral infections and smoking. CONCLUSIONS: The results of this study indicate that during AE-COPD increased expression of TIMP-1, TIMP-2, and MMP-9 and activation of MMP-9 may be persistent aggravating factors associated with airway remodeling and obstruction, suggesting a pathway connecting frequent exacerbations to lung function decline.
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