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| **Epithelial-mesenchymal-transition (EMT) changes in the airways of asthma-COPD overlap (ACO) patients** |
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| **Introduction/Aim:** ACO is a term used to characterise patients exhibiting clinical features of both asthma and COPD. Our previous research has indicated that EMT is active in the airways of COPD patients. However, the role of EMT in ACO remains unexplored. The aim of this study is to evaluate EMT activity in airway tissue from patients with ACO.  **Methods:** In this cross-sectional study, we used large airway endobronchial biopsy samples from patients with asthma (14), COPD (22), ACO (12), normal lung function smokers (NLFS; 12) and healthy non-smoking subjects (HC; 10). Immunohistochemical staining was performed for EMT markers (E- and N-cadherin, Vimentin, S100A4, and Collagen IV). Staining was assessed for the percentage expression of E- and N-Cadherin in the epithelium, Vimentin and S100A4 positive cells in the epithelium and reticular basement membrane (Rbm), and Collagen IV positive vessels in the epithelium, Rbm, and lamina propria (LP). Additionally, we evaluated the degree of Rbm fragmentation.  **Results:** In the epithelium, ACO showed a significantly reduced percentage of E-cadherin expression compared to HC (*p* <0.01), with no change for N-cadherin expression. We observed the most substantial Rbm fragmentation in ACO, which is a key tissue structural marker of EMT and was significantly higher compared to HC (*p* <0.01). Both Vimentin and S100A4 positive basal cells tended to be higher in ACO than in HC. In the Rbm, S100A4 positive cells were markedly elevated in ACO (*p* <0.05) compared to HC. Although Vimentin-positive cells were increased in the Rbm of ACO compared to HC, the difference was not statistically significant. The number of vessels in the Rbm was higher in ACO (*p* <0.05) compared to HC but lower in the LP (*p* <0.01).  **Conclusion:** These findings suggest the presence of an active EMT process in ACO, potentially contributing to severe airway remodelling seen in this cohort.  **Grant Support:** Clifford Craig Foundation |