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Title: Exaggerated airway narrowing is related to increased airway smooth muscle mass in bronchial segments from subjects with a history of asthma

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Body: Background: The mechanism of exaggerated airway narrowing in asthma is unclear and there is little to no biological data on whether increased airway smooth muscle (ASM) increases narrowing capacity. Objective: Determine whether increased airway narrowing in asthma is related to increased ASM mass. Methods: Bronchial segments were acquired from subjects undergoing surgery, mostly to remove pulmonary neoplasms. Subjects reported doctor-diagnosed asthma (n=5) or had no history of asthma (n=8). In vitro airway narrowing in response to acetylcholine (3x10-6M to 3x10-3M) was assessed to determine maximal bronchoconstriction and sensitivity. Fixed airway segments were sectioned for measurement of airway wall dimensions, particularly the ASM layer. Results: Airways from the asthma group had increased ASM (P=0.014), greater maximal airway narrowing (P=0.003) but no change in sensitivity. Maximal airway narrowing was positively correlated with the area of the ASM layer (r=0.58, P=0.039) but was not related to any other morphological parameter including inner and outer wall dimensions. Conclusions: Results suggest that greater ASM mass in asthma contributes to increased maximal airway narrowing in vivo. In contrast, properties of the ASM may not determine increased airway sensitivity.