Biomarkers Of Metabolic Syndrome Predict Accelerated Decline Of Lung Function In Nyc Firefighters That Were Exposed To Wtc Particulates

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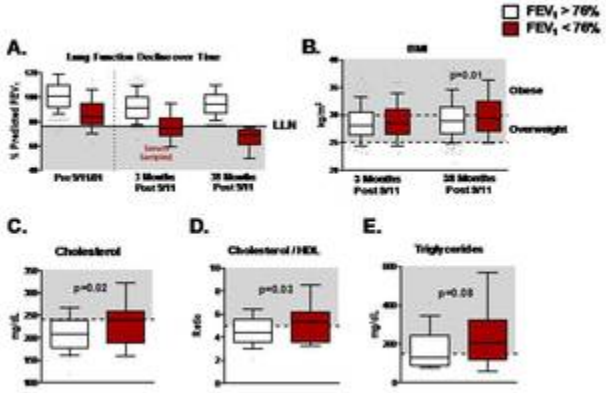
RATIONALE: In the first year post 9/11/2001, there was a decline of 439 mL in FEV_1 in FDNY rescue workers, stabilizing to a 25 ml/year decline in the subsequent seven years. Airflow obstruction predominated in 1720 individuals who sought a subspecialty pulmonary evaluation for treatment. We noted that the most severely obstructed patients had significant weight gain. This well phenotyped cohort had serum drawn within the five months post 9/11/2001, allowing us to investigate relationships of metabolic syndrome biomarkers and decline in lung function.

METHODS: The treatment cohort (N=1720) was stratified by FEV_1 into either obstructed, FEV_1<76% predicted (Lower limit of normal for this cohort), or normal airflow, FEV_1>76% (Figure 1A). A pilot analysis assayed 41 patients' serum drawn 2.88±0.99 months following 9/11 for 15 biomarkers of metabolic syndrome by Luminex; 10 cases were obstructed and 31 were normal. All patients had normal pre-9/11 lung function. Serum cholesterol and triglycerides were available on 157 patients, 20/157 were obstructed. The subspecialty PFT was used to stratify patients, months post-9/11. Data represented as means ±SD and significance was assessed based on p≤0.05 by t-test.

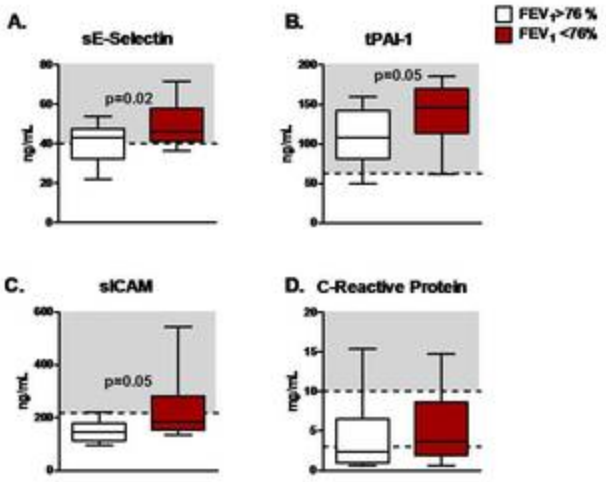
RESULTS: BMIs at the time of serum sampling were no different between individuals with obstruction and normal FEV_1. However, at subspecialty PFT, the obstructed patients had higher BMIs, (Figure 1B). The cohort with the greatest lung function decline had significantly greater cholesterol and Cholesterol/HDL ratios, with a trend towards elevated triglyceride levels, (Figure 1C-E). The subgroup with available Luminex data showed higher levels of sE-Selectin, tPAI-1, and s-ICAM in the obstructed patients, (Figure 2A-C). The same cohort had a trend towards elevated levels of C-peptide (Figure 2D). Individuals with obstruction at treatment entry had accelerated decline in lung function post 9/11, increased airway reactivity, and evidence of air trapping based on elevated RV when compared to those who maintained a normal FEV_1%.

Figure 1:



(A): Evaluation PFT for treatment cohort stratified based on LLN; FEV1% Predicted of 76% (FEV1<76%, N= 298; FEV1>76%, N= 1418). (B): BMI at the time of serum sampling insignificantly different between the two groups (29.0 ±3.99 v. 28.7 ±3.65). After an average of 38 ± 22 months, obstructed individuals had significantly greater BMIs (30.1 ± 4.81 v 29.4± 4.12 p=0.01) (C): Cholesterol and (D): Cholesterol/HDL Ratio was significantly elevated in individuals with decreased lung function. (E): Triglycerides showed a trend towards elevated levels in obstructed individuals. Upper limit of normal shown by dotted lines, and shaded areas denote high risk levels.

Figure 2:



Analytes Associated with Metabolic Syndrome (A): sE-Selectin, (B): Tissue Plasminogen Activator Inhibitor-1 (tPAI-1), and (C): soluble Inter-Cellular Adhesion Molecules (sICAM): are significantly elevated in subjects with accelerated decline in lung function, (N=6) compared with those with less affected lung function (N=7). D: C-Reactive Protein (CRP) in obstructed patients was on average greater than 3, representing moderate risk. In normal individuals, CRP levels less than 3 mg/mL were seen. Upper limit of normal represented by dotted lines. Shaded areas represent high risk levels.

CONCLUSIONS: Blood drawn within 5 months of WTC exposure identified a subgroup of patients with markers of metabolic syndrome. This subgroup had more weight gain and greater decline in lung function during the next 7 years. The finding of metabolic syndrome biomarkers prior to decline in lung function raises the possibility that the combination of irritant exposure and mediators of metabolic syndrome interact and promote lung injury.

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