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# Associations between ambient wood smoke and other particulate pollutants and biomarkers of systemic inflammation, coagulation and thrombosis in cardiac patients

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## ABSTRACT

*Background:* Increased particulate air pollution has been associated with both an increased risk of myocardial infarction (MI) and adverse changes in cardiac biomarkers. Up to 30% of ambient wintertime fine particles ($PM_{2.5}$) in Rochester, NY are from wood burning. Our study examined associations between ambient levels of a marker of wood smoke (Delta-C) and other particulate air pollutants and biomarkers of inflammation, coagulation and thrombosis.

*Methods:* We measured blood concentrations of C-reactive protein (CRP), D-dimer, fibrinogen, P-selectin, platelet factor 4 (PF-4), von Willebrand factor (vWF), and myeloperoxidase (MPO) of 135 patients undergoing cardiac catheterization during the winters of 2011–2013. We coupled these data with hourly ambient concentrations of Delta-C, black carbon (BC; marker of traffic pollution), and ultrafine (10–100 nm; UFP), accumulation mode (100–500 nm; AMP), and fine particles ( < 2.5 μm; $PM_{2.5}$). Using linear regression models, we estimated the change in each biomarker associated with increased pollutant concentrations at intervals between 1 and 96 h preceding blood collection.

*Results:* Each 0.13 $\mu g/m^3$ increase in Delta-C concentration in the prior 12 h was associated with a 0.91% increase in fibrinogen levels (95% CI=0.23%, 1.59%), but unexpectedly in the prior 48 h, each 0.17 $\mu g/m^3$ increase in Delta-C concentration was associated with a 2.75% decrease in MPO levels (95% CI=−5.13%,−0.37%). We did not see associations between Delta-C concentrations and any other biomarkers. Interquartile range (IQR) increases in $PM_{2.5}$, BC, UFP, and AMP concentrations were generally associated with increased CRP and fibrinogen, but not PF4, D-dimer, vWF, or P-selectin.

*Conclusions:* In a population of cardiac patients, we noted adverse changes in fibrinogen associated with increased concentrations of a marker of wood smoke. Increases in $PM_{2.5}$, BC, AMP, and UFP concentrations in the previous 96 h were also associated with adverse changes in markers of systemic inflammation and coagulation, but not with markers of endothelial cell dysfunction or platelet activation.

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## 1. Introduction

Increased ambient concentrations of $PM_{2.5}$ (particulate matter air pollution < 2.5 μm in diameter) and other air pollutants have previously been associated with adverse changes in biomarkers of inflammation and coagulation, as well as the triggering of myocardial infarction (MI) (Brook et al., 2010; Evans et al., 2016; Gardner et al., 2014; Rich et al., 2012a). However, assessments of acute cardiovascular responses to source specific particles (e.g. those from traffic or wood burning) are needed.

We previously found that up to 30% of ambient wintertime fine particles ($PM_{2.5}$) in Rochester, NY are from wood burning (Wang et al., 2012), while global estimates reach higher than 70% in Sweden and New Zealand (Stockfelt et al., 2012). Particulate matter (PM) pollution from wood smoke and biomass fuels has historically been estimated through measurements of black carbon (BC), though BC is also produced by motor vehicle exhaust, including diesel exhaust (Naeher et al., 2007). A more specific estimate of wood smoke pollution is Delta-C, obtained by calculating the difference between ultraviolet BC (UVBC), measured at 370 nm and BC measured at 880 nm with a 2-wavelength aethalometer (Wang et al., 2012). The concept of Delta-C as a marker of wood smoke was originally described by Allen et al. (2004). Our prior study on Delta-C elevations in the context of a forest fire exposure (Wang et al., 2010) studied its independence from vehicle emissions, its ability to detect residential wood combustion (Wang et al., 2011a) and its overall measurement characteristics in two cities (Wang et al., 2011b). Delta-C has proven useful in providing improved resolution of wood smoke and traffic in source apportionment studies (Wang et al., 2012).

Wood smoke has been linked to significant respiratory morbidity and mortality (Boman et al., 2003; Naeher et al., 2007) and recent studies have suggested a link to cardiovascular morbidity through systemic inflammation (Hejl et al., 2013; Swiston et al., 2008) and other physiologic changes (Unosson et al., 2013). However, a recent review concluded that the evidence base for the cardiovascular effects of wood smoke is weak and that wood smoke exposures are highly variable due to the multifactorial nature of wood smoke creation (Adetona et al., 2016). Furthermore, the association between a specific marker of wood smoke (Delta-C) and serum biomarkers of systemic inflammation, coagulation or platelet activity has not been studied.

The relationship between air pollution exposure and cardiovascular disease involves multiple pathophysiologic pathways including systemic inflammation and coagulation (Brook et al., 2010). In response to vessel injury or inflammation, the human body relies on the coagulation factors to strengthen and complete thrombus formation initiated by platelet activity, with fibrinogen being central to this process. C-reactive protein (CRP) and myeloperoxidase (MPO) are markers of systemic inflammation, while D-Dimer is both a marker of inflammation and coagulation. P-selectin is involved in platelet adhesion to endothelial cells, and platelet factor 4 (PF-4) is a marker of platelet activation. Von Willebrand factor (vWF) is stored in endothelial cell and platelet granules and is a nonspecific marker of inflammation, coagulation and thrombosis. Based on our prior studies showing an association between ST elevation myocardial infarction (STEMI) and increased ambient $PM_{2.5}$ concentrations in the previous 1–24 h (Evans et al., 2016; Gardner et al., 2014), we used blood samples obtained from patients undergoing cardiac catheterization due to underlying stable ischemic heart disease (SIHD) or a myocardial infarction, and studied whether increased $PM_{2.5}$, Delta-C, and other particulate air pollutant concentrations were associated with adverse changes in these biomarkers within a similar time frame. We hypothesized that adverse changes in biomarkers of inflammation, coagulation and thrombosis would be associated with increased ambient levels of Delta-C, BC, $PM_{2.5}$, ultrafine particles (UFP), and accumulation mode particles (AMP) in the previous 96 h.

## 2. Methods

### 2.1. Study population

We included participants who were patients over 18 years of age treated at the Cardiac Catheterization Laboratory (Cath Lab) at the University of Rochester Medical Center (URMC) in Rochester, New York in the winter months (November 1 to April 30th) from November 1, 2011 to December 31, 2013. These patients (N=135) presented with either acute coronary syndrome (ACS), including STEMI (n=25) and non-ST elevation myocardial infarction (NSTEMI; n=32), or a non-emergent cardiac catheterization for stable SIHD (n=78). Patients with unstable angina were not included in this study due to variability in their timing to seek medical care. All patients in this database consented to the use of their blood samples and all study activities were approved by the University of Rochester Research Subjects Review Board (RSRB #00034098).

Blood samples were generally drawn at the time of the cardiac catheterization for consented patients. Patients with SIHD were scheduled for intervention in the Cath Lab from the outpatient setting on a non-emergent basis. However, patients with NSTEMI and STEMI presented to the hospital acutely with those presenting with STEMI requiring emergent cardiac catheterization. In the case of NSTEMI, medical management is typically employed prior to cardiac catheterization, which generally occurs in the subsequent 72 h. Given the lead time prior to cardiac catheterization in both the SIHD and NSTEMI groups, consent could typically be obtained prior to the procedure. Therefore, the biomarkers in the SIHD and NSTEMI group were drawn close to the time of entry into the cardiac catheterization lab (time 0). However, patients with STEMI were sometimes unable to provide consent to enroll in the study prior to their emergent procedure due to their severe illness. This resulted in variability in the time of the blood draws for the STEMI group with blood being drawn up to 72 h following the procedure.

Multiple biomarkers were used in this study that represented inflammation, coagulation and thrombosis. Plasma concentrations of D-dimer (ng/ml), fibrinogen (μg/ml), and high sensitivity C-reactive protein (ng/ml) were measured using ELISA by AssayGate, Inc (Ijamsville, MD). Serum von Willebrand factor (ng/ml) concentrations were measured using an ELISA by Sekisui Diagnostics, and plasma concentration of soluble P-selectin (ng/ml), myeloperoxidase (pg/ml), and platelet factor 4 (pg/ml) were assessed by sandwich ELISA, all at Strong Memorial Hospital Clinical Laboratories at the URMC.

### 2.2. Air pollution and weather data

Pollution measurements were collected at the New York State Department of Environmental Conservation (DEC) site in Rochester, NY, at the intersection of two major highways (I-490 and I-590) and state route 96 on the east side of Rochester, NY. Black carbon was measured using a two-wavelength (370 and 880 nm) aethalometer (Magee Scientific, Inc, Berkeley, CA). Delta-C was reported as the difference between BC measured at 370 and 880 nm (Wang et al., 2012). $PM_{2.5}$ mass was measured on a semi-continuous basis with a tapered element oscillating microbalance (TEOM, model 1400ab; Thermo Fisher Scientific, Inc., Waltham, MA). AMP (100–500 nm diameter) and UFP (10–100 nm diameter) were both measured using a 3071 Electrostatic Classifier with a 3010 Condensation Particle Counter (TSI Inc., St. Paul, MN). Ambient temperature and relative humidity were continuously measured at the same DEC site. All of the measured variables were averaged to 1 h values. Since this study used a central site monitor for all patients, we calculated the farthest patient was located 88 miles from the monitor, with an average distance of 24 miles.