



## **Interaction of Genetic Variation in the *ABO* Locus and Short-Term Exposure to Elevations in Fine Particulate Matter Air Pollution Differentially Affects Associations with Acute Coronary Events**

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### **BACKGROUND:**

Fine particulate matter (PM<sub>2.5</sub>) air pollution has been associated with the risk of acute coronary syndrome (ACS) events primarily among patients with coronary artery disease (CAD). *ABO* gene sequence variants rs687289 and rs514659 ( $r^2=1.0$  with rs687289) were previously validated by GWAS to predict myocardial infarction (MI) in CAD patients.

### **HYPOTHESIS:**

Short-term exposure to elevated PM<sub>2.5</sub> is differentially associated with ACS event risk among carriers of the *ABO* rs687289 A allele vs. GG genotype.

### **METHODS:**

Patients who had  $\geq 1$  coronary vessel with flow-limiting CAD ( $\geq 70\%$  stenosis) and residing on Utah's Wasatch Front were studied if they were hospitalized at Intermountain Healthcare for an ACS event (acute MI or unstable angina) between October, 1993 and May, 2007. *ABO* variants rs687289 (primary hypothesis), rs657152 ( $r^2=0.86$  with rs687289), and rs579459 ( $r^2=0.40$  with rs687289) were genotyped. A time-stratified case-crossover design was used in which a patient's PM<sub>2.5</sub> exposure at the time of an ACS event was matched to exposures at non-event times on the same day of the week and in the same month. Odds ratios (OR) for PM<sub>2.5</sub> with adjustment for daily temperature, dew point, and barometric pressure were determined for linear models using a 25  $\mu\text{g}/\text{m}^3$  threshold and in non-threshold models.

### **RESULTS:**

Patient age averaged  $53 \pm 7$  years and 27% were female, and characteristics were similar across genotypes. Short-term PM<sub>2.5</sub> exposure was associated with ACS events in carriers of the A allele, but not in GG genotype (Table). Results also differed by rs657152 A allele carriers (OR=1.23,  $p=0.008$ ) vs. CC genotype (OR=1.12,  $p=0.21$ ), but not by rs579459 C allele carriers (OR=1.19,  $p=0.07$ ) vs. TT genotype (OR=1.15,  $p=0.06$ ).

### **CONCLUSION:**

Short-term exposure to elevations in PM<sub>2.5</sub> was associated more strongly with risk of ACS events in *ABO* risk allele carriers. Additional studies should evaluate interactions of genetic factors with PM<sub>2.5</sub> air pollution.

See Table next page.

**Table.** Association of exposure to short-term elevations in PM<sub>2.5</sub> overall and with stratification by *ABO* rs687289 genetic variation.

	<b>Events (n)</b>	<b>OR (per +10 μg/m<sup>3</sup>)</b>	<b>95% Confidence Interval</b>	<b>P-value</b>
<b><i>Threshold Model</i></b>				
<b>All ACS Events</b>	1285	1.16	1.04, 1.30	0.009
<b>Events by <i>ABO</i></b>				
<b>rs687289 A Carrier</b>	669	1.25	1.07, 1.45	0.004
<b>GG Genotype</b>	515	1.10	0.92, 1.32	0.29
<b><i>No Threshold</i></b>				
<b>All ACS Events</b>	1285	1.07	0.99, 1.15	0.11
<b>Events by <i>ABO</i></b>				
<b>rs687289 A Carrier</b>	669	1.12	1.00, 1.24	0.044
<b>GG Genotype</b>	515	1.05	0.93, 1.19	0.44