

## **Endothelium-dependent Vasodilation is Impaired in Coronary Arterioles after Nanoparticle Inhalation**

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Epidemiological studies have shown that exposure to particle pollution is associated with an increased risk for myocardial infarction (MI). This laboratory has shown in skeletal muscle that nanoparticle exposure produces significantly greater reactive oxygen species (ROS) and microvascular dysfunction than larger particles of the same composition. However, it remains unclear if coronary microvascular endothelial function is affected to a similar degree. Rats were exposed to filtered air (control) or TiO<sub>2</sub> nanoparticles (primary particle diameter, ~21 nm) via inhalation at concentrations relevant to ambient air pollution (9.5 micrograms measured pulmonary deposition). Coronary arterioles (~150 micrometers in diameter) were isolated from the left anterior descending artery distribution and responses to flow (FID) (5-25 microliters/min), acetylcholine (ACh, 10<sup>-9</sup> – 10<sup>-4</sup> M), and the Ca<sup>2+</sup> ionophore, A23187 (10<sup>-9</sup> – 10<sup>-6</sup> M), were assessed. Microvascular ROS was assessed by intraluminal infusion of dihydroethidium (DHE) fluorescence. Endothelium-dependent FID was impaired in coronary arterioles from rats exposed to nano-TiO<sub>2</sub> compared to control rats, even though both groups were exposed to similar rates of shear stress. Similarly, nanoparticle exposure impaired arteriolar dilation to A23187 and ACh as compared to control rats. DHE fluorescence was increased in coronary arterioles from nanoparticle-exposed rats. Co-incubation with tempo (10<sup>-4</sup> M) and catalase (50 units/mL), both ROS scavengers, ameliorated impairments in ACh-induced vasodilation from exposed rats compared to control. Sodium nitroprusside (10<sup>-9</sup> – 10<sup>-3</sup> M) produced comparable arteriolar dilation in both groups, indicating that vascular smooth muscle NO responsiveness remains intact after nanoparticle exposure. These results suggest that nanoparticle exposure significantly impairs endothelium-dependent vasodilation in coronary arterioles and this could be due to increases in microvascular ROS. It is probable that such disturbances in coronary microvascular function contribute to the cardiac events associated with particle pollution exposure. Support: NIH RO1-ES015022 and HEI #4730 (TRN)