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Carbon monoxide levels experienced by heavy smokers impair aerobic capacity and cardiac contractility and induce pathological hypertrophy.

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Cigarette smoke contains hundreds of potentially toxic compounds and is an important risk factor for cardiovascular disease. However, the key components responsible for endothelial and myocardial dysfunction have not been fully identified. The objective of the present study was to determine the cardiovascular effects of long-term inhalation of carbon monoxide (CO) administered to give concentrations in the blood similar to those observed in heavy smokers. Female rats were exposed to either CO or air (control group) (n = 12). The CO group was exposed to 200 ppm CO (100 h/wk) for 18 mo. Rats exposed to CO had 24% lower maximal oxygen uptake, longer (145 vs. 123 microm) and wider (47 vs. 25 microm) cardiomyocytes, reduced cardiomyocyte fractional shortening (12 vs. 7%), and 26% longer time to 50% re-lengthening than controls. In addition, cardiomyocytes from CO-exposed rats had 48% lower intracellular calcium (Ca²⁺) amplitude, 22% longer time to Ca²⁺ decay, 34% lower capacity of sarcoplasmic reticulum Ca²⁺-ATPase (SERCA2a), and 37% less t-tubule area compared to controls. Phosphorylation levels of phospholamban at Ser16 and Thr17 were significantly reduced in the CO group, whereas total concentration of phospholamban and SERCA2a were unchanged. Cardiac atrial natriuretic peptide, vascular endothelial growth factor, cyclic guanosine monophosphate, calcineurin, calmodulin, pERK, and pS6 increased, whereas pAkt and pCaMKII delta remained unchanged by CO. Endothelial function and systemic blood pressure were not affected by CO exposure. Long-term CO exposure reduces aerobic capacity and contractile function and leads to pathological hypertrophy. Impaired Ca²⁺ handling and increased growth factor signaling seem to be responsible for these pathological changes.